BATTICALOA MEDICAL JOURNAL

Established 2005

Volume 9, September 2018

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BATTICALOA MEDICAL ASSOCIATION ANNUALLY ISSN 1800 - 4903

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The official publication of the
Batticaloa Medical Association
Volume 9, September 2018
Annually ISSN 1800 - 4903

All Communication Should be addressed to,
The Editors, Batticaloa Medical Journal

Published by
The Batticaloa Medical Association
2nd Floor, New OPD Complex
Teaching Hospital
Batticaloa

Phone +94 652227312
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Website
http://www. Bmasl.org
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Batticaloamed@gmail.com

Printed by:
Wanasinghe Printers,
496A, Trinco Road,Batticaloa
+94 652227170

BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

EDITORIAL

Teaching in the clinical environment

'To study the phenomena of disease without books is to sail an uncharted sea whilst to study books without patients is not to go to sea at all' ***- William Osler***

Editor : Clinicians do not become teachers by virtue of their medical expertise, but a reflective approach to teaching and professional development can foster excellence in clinical teaching.Teaching in the clinical environment is a challenging, complex and often frustrating task.There are number of roles have been described for medical teachers, grouped into six major tasks, the information provider, the role model, the facilitator, the assessor, the curriculum and course planner; and the resource material creator(1). In a pure educational setting, teachers may have limited roles, but the clinical teacher frequently plays many roles at the same time, switching from one role to another during the same encounter. Most clinical teachers around the world have received rigorous training in medical knowledge and skills but little to none in teaching. As physician become ever busier in their own clinical practice, being effective teachers become more challenging in the context of expanding clinical responsibilities and shrinking time for teaching(2).It is understandable that, clinical teachers have a dual role in medicine, to provide patient care and to teach. However, all doctors are usually well prepared for their clinical roles, few are trained for their teaching roles. Clinical teachers take their role as teachers of future generations of doctors seriously and with enthusiasm. Yet, most lack knowledge of educational principles and teaching strategies thus may be inadequately prepared for this additional professional role(2).

It is obvious that professionals who have graduated from medical faculty and undergone postgraduate training can automatically start teaching the day after they graduate. However, advances in education such as new methods of teaching and learning, a more student-centred teaching, competency-based assessment and emphasis on professionalism; educators today are required to have an expanded tool kit of teaching skills and clinical expertise. The learning may take place in a range of settings. Learning in the clinical environment has many strengths. It is focused on real problems in the context of professional practice. Learners are motivated by its relevance and through active participation. Professional thinking, behavior, and attitudes are "modelled" by teachers. It is the only setting in which the skills of history taking, physical examination, clinical reasoning, decision making, empathy, and professionalism can be taught and learnt as an integrated whole(3). Patients usually regard bedside teaching as enjoyable and not as a burden. Students, interns, residents and clinical teachers all generally appear to favour bedside teaching for the integration and learning of certain important clinical skills(4). Despite these potential strengths, clinical teaching has been much criticized

for its variability, lack of intellectual challenge, and haphazard nature. In other words, clinical teaching is an educationally sound approach, all too frequently undermined by problems of implementation. Bedside teaching seems to be gradually disappearing from medical curricula. As sophisticated diagnostic methods have reduced the need for physical diagnosis at the bedside and increased patient turnover in hospitals, the assumed violation of patients' privacy. Bed side teaching (BST) accounted for 75% of all teaching in the 1960s and 16% in 1978. However more recent estimates quote prevalence between 8% and 19% . The relevance of BST may be declining due to an increased reliance on medical imaging, biochemical testing and subspecialists, leading to as shift in favour of classroom-based learning(5).

Furthermore, bedside teaching mean patient-based and patient-orientated teaching and learning; taking place in real health related environments. Actual bedside teaching can sometimes be a difficult falsifying act to perform. The clinical teacher needs to be aware of not just the learner but also of the welfare of the patient. Many of the environments and opportunities available for bedsidé teaching and learning have changed dramatically in the last 20 years or so making it more difficult. Changes in curricula for health care professionals place an increasing importance of systematic learning of core skills and demonstration of skills acquisition and competency. Changes in the politics of health care with increased accountability and patient autonomy have also affected all clinical learning environments(6). Asking feedback on teaching and reflective practice are key to advancing to the highest level of teaching and moving from being a technically sound teacher to a professional and scholarly teacher. Staff development can provide a conceptual framework for teaching and help clinical teachers adopt and adapt specific teaching behaviors to real clinical settings and introduce clinicians to a community of medical educators interested in furthering clinical teaching and learning.

There are number challenges for teachers in the clinical environment has been noted despite the numerous challenges noted, many clinicians find practical solutions to overcome them and excel in their dual role as clinician and teacher(3). These challenges are include time constraints, work demands such as teachers maintain other clinical, research or administrative responsibilities while being called upon to teach, often unpredictable , difficult to prepare for engaging multiple levels of learners (students, house officers and nursing students), patient related challenges: patients too sick or unwilling to participate in a teaching encounter, lack of incentives and rewards for teaching, and physical clinical environment not comfortable for teaching. In spite of its decreasing prevalence, bed side teaching is highly valued by students for the unique benefits it provides(7). In the face of the belief that bedside teaching is the most effective method to teach clinical and communication skills, the frequency of bedside rounds is decreasing. It is believed that this is a major factor causing a sharp decline in trainees' clinical skills. Now a days, clinical skills are increasingly taught in preclinical courses by integrating clinical scenarios.

Bedside teaching cannot be replaced. We cannot abandon a teaching custom that has a long-valued history of teaching the humanistic aspect of medicine just due to time constraint and some other insufficient reasons. Learning at the bedside also improves professional manners, communication skills, and questioning approaches during history taking. We must give appropriate importance to bedside teaching. There are newer models and strategies for effective bedside teaching. The core message of such models is the educational process. A bedside teacher must learn how to involve patients and learners in the educational process.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

REVIEW ARTICLE

SGLT2 inhibitors in Diabetes mellitus

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Abstract :

Type 2 diabetes mellitus (T2DM) is associated with considerable increases in cardiovascular morbidity and mortality. Although mortality rates in patients with T2DM seem to decrease, rates are still significantly elevated compared with the normal population. Glucose transporters sodium-glucose co-transporter-2 (SGLT2) inhibitors block these receptors which means less glucose gets reabsorbed back into the blood and gets passed out of the body via the urine. SGLT-2 inhibitors (SGLT2) decrease the reabsorption of glucose and increase the excretion of glucose via a selective inhibition of SGLT-2. The glucosuria results in decreased plasma glucose levels and improved glycemic control measured by HbA1c in patients with T2DM.

Keywords: SGLT-2 inhibitors, Glucose transporters sodium-glucose co-transporter-2, Canagliflozin and Empagliflozin

Introduction

The pathogenesis of type 2 diabetes is tangled with multiple different mechanisms, which encompasses decreased insulin secretion, decreased insulin sensitivity, increased hepatic glucose production, decreased responses to incretin hormones, and increased renal reabsorption of glucose. Therefore, multiple strategies are often required to effectively control hyperglycemia in patients with type 2 diabetes(1).Sodium-glucose cotransporter 2 (SGLT2) inhibitors are the latest therapeutic strategy in the treatment of type 2 diabetes mellitus (T2DM). Using an insulin-independent mechanism (glycosuria), they reduce glucose toxicity and improve insulin sensitivity and β-cell function(2). It is understandable that people with type 2 diabetes mellitus have increased risk for coronary heart disease compared to those without diabetes(3). Furthermore, increased risk for cardiac dysrhythmia, sudden death, hypertensive disease, pulmonary embolism, and aortic aneurysm. Oral-hyperglycemic therapy is effective in reducing the microvascular complications of diabetes as nephropathy, retinopathy and neuropathy(4).

The United Kingdom Prospective Diabetes Study (UKPDS) provided evidence that intensive glycemic control can inhibit the incidence or progression of microvascular complications, including diabetes nephropathy, in patients with type 2 diabetes(5). It is obvious that glucose-lowering therapy in diabetes was to reduce microvascular complications and interventional studies focused on intensive glucose reduction in T2D

have only had a minor or no effect in reducing cardiovascular (CV) risk(6). Sodium-glucose transporter (SGLT)-2 inhibitors, which are at present in clinical use in most of the countries, are exceptional as their hypoglycemic effects are completely independent of insulin action. Possible benefits and indications for the treatment of other diseases like circulatory and renal disorders are fascinating attention. SGLT2 inhibitors not only reduce blood glucose levels but also alter the whole-body energy balance to lower body weight, which should result in the amelioration of multiple metabolic disorders like metabolic syndrome.

The cardiovascular outcome results of empagliflozin cardiovascular outcomes and mortality in type 2 diabetes trial (EMPA-REG) and canagliflozin cardiovascular assessment study (CAN- VAS) with empagliflozin and canagliflozin(7), respectively, have demonstrated touchable benefits beyond the thoughts of the diabetes treating community(8)(9).

There is strong epidemiologic evidence linking poor glycaemic control in patients with diabetes and the risk of hospitalization for heart failure. A linear relationship between glycaemic control and heart failure has also been reported across a number of prospective observational studies in type 2 diabetes, such that, on average, the risk of heart failure was increased by 15% for each percentage point higher haemoglobin A1c (HbA1c). Similarly, in the UK Prospective Diabetes Study (UKPDS) study, for every 1% rise in HbA1c, there was a 16% rise in incident heart failure(10).

Mechanism of action

The kidneys normally filter roughly about 180 liters of plasma per day corresponding to 160–180 grams of glucose filtered from the circulation in healthy subjects. At normoglycemia virtually all filtered glucose is reabsorbed (together with sodium) in the proximal convoluted tubule of the nephron to the circulation by the two glucose transporters sodium-glucose co-transporter-2 (SGLT-2) and -1 (SGLT-1)(11).SGLT-2 is located in the first part of the proximal convoluted tubule and is responsible for 80–90% of the total glucose reabsorption to the circulation. SGLT-1 is located more distant in the straight segment of the proximal convoluted tubule and is only responsible for the remaining 10–20% of the glucose reabsorption. SGLT-2 is known primary to be expressed in the kidney, whereas SGLT-1 is also expressed in the small intestine, heart and lung tissue(12). In the small intestine SGLT-1 is responsible for the main part of the absorption of glucose and galactose

The proteins that reabsorb glucose are called sodium-glucose transport proteins. SGLT2 inhibitors block the SGLT2 protein involved in most of the (90%) glucose reabsorption in the proximal renal tubule, consequential in increased renal glucose excretion and lower blood glucose levels. These agents probably also increase insulin sensitivity, decrease gluconeogenesis, and improve insulin release from pancreatic beta cells. This allows the kidneys to lower blood glucose levels and the excess glucose in the blood is removed from the body via urine(13).

Advantages of SGLT2 inhibitors

SGLT2 inhibitors help to remove glucose from the blood and therefore help to lower blood glucose levels. It improved glycemia, and also causing reduction of HbA1C: ranging from 0.6% to nearly 1% in some studies. Secondly, by removing glucose from the body, SGLT2 inhibitors can also have benefits for loss. Thirdly, it was reported that mild reduction in blood pressure, possibly related to sodium loss. Overall, treatment with SGLT2 inhibitors reduces blood pressure in T2DM patients without a compensatory increase in the heart rate (HR). Based on this observation, it has been postulated that the moderate diuretic effect of SGLT2 inhibitors does not activate neurohumoral factors and thus is beneficial for HF. However, even the mechanism of diuresis related to SGLT2 inhibitors is not well understood(14). In contract with this hypothesis, SGLT2 inhibitors have been shown to improve the circadian rhythm of sympathetic activity in rats with metabolic syndrome and to reduce high fat diet-induced elevation of tyrosine hydroxylase and noradrenaline in the kidneys and hearts of mice. Renoprotection by SGLT2 inhibitors has been demonstrated in T2D patients with a high cardiovascular risk in randomized controlled trials (RCTs)(15).

Disadvantages of SGLT2 inhibitors

The main adverse effect is increased risk of renal impairment secondary to dehydration. Furthermore, it encourages to excrete more glucose from the urine which in turn causing genital infections(16). Excess volume depletion causing hypotension, dizziness, and fainting. The co-transport of sodium results in decreased sodium excretion by the kidneys and increased total body sodium content, which potentially can contribute to development and deterioration of hypertension in patients with T2DM(17). Furthermore, possible increased risk of ischemic stroke within the first 30 days of treatment, according to interim results from the Canagliflozin Cardiovascular Assessment Study (CANVAS). Finally, it causes risk of developing urinary ketones or hematuria(18). However, two recent study stated that 4-week treatment with empagliflozin, increased insulin sensitivity, significantly increased glucagon response, and an increase in endogenous glucose production of approximately 25% after 3 hours of fast(19). Researchers highlighted that the rise in endogenous glucose production balanced the amount of glucose lost through renal excretion. Without the rise in endogenous glucose production, they estimated, postprandial glucose levels would have decreased by about 50% instead of 12%, as observed in the study.

Need for SGLT-2 inhibitors in a SriLanka Perspective

One in five adults has either diabetes or pre-diabetes and one-third of those with diabetes are undiagnosed, discloses one of the first nation-wide studies to be conducted in Sri Lanka. This has startling implications for the spread of the disease here. At a predictable incidence of 11.5%, (higher than the incidence of diabetes itself) it seems inevitable that without immediate and effective intervention, pre-diabetes cases will mature into diabetics and that an overwhelmed healthcare system would be left scrambling to cope. SriLanka with type 2 diabetes are more insulin resistant with increased abdominal obesity, unfavorable lipid profiles with high small dense LDH cholesterol, increased CRP level and low adiponectin leads to increased cardiovascular risk. The current therapies used in the treatment of Type-2 DM has several limitations and flaws like weight gain, increased risk of hypoglycemia, failure to control the post-prandial hyperglycemia and associated with gastrointestinal side effects. The new class of SGLT-2 inhibitors will help to address these unmet needs with the currently available drugs for treatment of type-2 DM.

Placing the SGLT-2 inhibitors in the management of DM

It is obvious that first and best drug to initiate therapy in type-2 DM is invariably metformin unless it is contraindicated. After the discovery of SGLT-2 inhibitors, the competition has widened and undoubtedly SGLT-2 inhibitors appear to be a strong competitor for the second-place succeeding metformin as well as the first drug to be initiated among individuals not tolerating metformin. Most of the guidelines accepted that SGLT-2 inhibitors as the drug of choice after metformin. It is understandable that if HbA1c is beyond 8.5%, it is better to start combination of metformin and SGLT-2 inhibitors. Furthermore, SGLT-2 inhibitors are proven to effective along with most of the available anti-diabetes medications such as DPP-IV inhibitors, pioglitazone, sulphonylureas, and insulin. Among all these the combination of DPP-IV inhibitors with SGLT-2 inhibitors appears to be promising. The combination of a GLP-1 agonist and an SGLT2-inhibitor has additive effects on lowering HbA1c and systolic blood pressure, body weight and cardiac risk and has the potential to synergistically reduce cardiovascular events and decelerate renal decompensation(20).

Conclusion

This effect is dependent of the plasma glucose level, but independent of β-cell function and insulin sensitivity. The risk of hypoglycemia and decreased effect due to secondary failure of β-cell function seems there- fore very limited. The promising results obtained in clinical trials show that SGLT2 significantly improves glycemic control and provides greater cardiovascular protection, combined with a reduction in body weight and blood pressure. It has become clear that SGLT2 inhibitors not only improve the blood glucose level, but also show

cardiovascular and renal protective effects irrespective of the reduction of blood glucose in patients with type 2 diabetes mellitus.

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Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

REVIEW ARTICLE

Intermediate syndrome following Organophosphate poisoning

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Abstract :

Organophosphates (OPs) are commonly used as pesticides throughout the world. Exposures to OPs cause a significant number of poisonings and deaths every year. Organophosphates intoxication produce a spectrum of muscarinic, nicotinic, and cholinergic symptoms involving both central and peripheral nervous systems. OP compound's easy availability is accountable for increasing incidences of pesticide poisoning and it being a major reason of morbidity/mortality that poses public health problem in a developing territory. In acute organophosphate poisoning, severe and prolonged acetylcholinesterase inhibition is associated with oxidative stress, detected in erythrocyte membranes, that occurs early during poisoning and may contribute to the development and severity of intermediate syndrome (IMS). However, IMS has been considered as a major causative factor of organophosphate-related morbidity and mortality because of its frequent occurrence and possible consequence of respiratory failure. I performed a review of the published literature. The databases Medline, Embase, Scopus and Google scholar were searched using the terms "Intermediate syndrome", "Organophosphate induce Intermediate syndrome", and "organophosphate poisoning". Data bases were merged, and duplicates were removed. The aim of the article is to bring out the clear idea about the IMS.

Keywords: Organophosphate poisoning, and intermediate syndrome

Introduction

Organophosphate poisoning is the most common pesticide poisoning in developing countries(1).

Prevalence of OP was reported as 10-36.2% in developed countries, 40-60% in African countries and 65-79.2% in developing countries(2). However, in the eastern part of the SriLanka prevalence was 27.3%(3). The intermediate syndrome (IMS) following organophosphorus (OP) insecticide poisoning was first described in the mid-1980s.The OP poisonings are associated with several syndromes, including acute cholinergic crisis, the intermediate syndrome (IMS), and organophosphate-induced delayed neuropathy (OPIPN). The syndrome defined as characteristic symptoms and signs occurring after apparent recovery from the acute cholinergic syndrome(4,5,6). However, IMS has been considered as a major causative factor of organophosphate-related morbidity and mortality

because of its frequent occurrence and possible consequence of respiratory failure(7). Despite a high incidence, the pathophysiology that underlies IMS remains unclear. Previously proposed mechanisms of IMS include different susceptibility of various cholinergic receptors, muscle necrosis, prolonged acetylchol inesterase inhibition, inadequate oxime therapy, down-regulation or desensitization of postsynaptic acetylcholine receptors, failure of postsynaptic acetylcholine release, and oxidative stress-related myopathy(8).

The IMS occurs in approximately 20% of patients following oral exposure to OP pesticides, with no clear association between the particular OP pesticide involved and the development of the syndrome. It usually becomes established 2-4 days after exposure when the symptoms and signs of the acute cholinergic syndrome (e.g. muscle fasciculations, muscarinic signs) are no longer obvious. The characteristic features of the IMS are weakness of the muscles of respiration such as diaphragm, intercostal muscles and accessory muscles including neck muscles and of proximal limb muscles. Thus, some patients may only have weakness of neck muscles whilst others may have weakness of neck muscles and proximal limb muscles. These patients may not require ventilatory care, but close observation and monitoring of respiratory function is mandatory. Management is essentially that of rapidly developing respiratory distress and respiratory failure. Delay in instituting ventilatory care will result in death.

Pharmacology

Organophosphorus compounds are irreversible inhibitors of the enzyme acetylcholinesterase (AchE). They inhibit both cholinesterase and pseudo-cholinesterase activity. The inhibition of acetylchol inesterase causes buildup of acetylcholine at synapses with resultant overstimulation of neurotransmission. The clinical features are due to excess acetylcholine at the muscarinic and nicotinic receptors which leads to initial stimulation and eventual exhaustion of cholinergic synapses. Pralidoxime (PAM) regenerates functional AChE after it has been inactivated by OP, whereas atropine blocks the build-up of excess acetylcholine. However, the added benefit of using PAM in addition to atropine remains unclear. These findings thus challenge previous studies that question the value of PAM in the treatment of OP poisoning [9]. Moreover, they suggest WHO guidelines for the use of PAM should be updated to take into account a flexible dosing strategy based on severity of poisoning, although any such changes to recommendations must first be validated in a larger sample size(9).

Pathogenesis of IMS

The pathogenic mechanisms that lead to IMS have not been clearly elucidated. A study suggested that the slow release of organophosphates from deep tissues and the persistent inhibition of acetylchol inesterase may underlie the development of IMS(10). Electrophysiological studies demonstrated that both pre and post-synaptic defects has been observed in OP poisoning(11). However, Avasthi et al, suggested that desensitization of acetylcholine receptors being responsible for the IMS(12).Furthermore, a study has been conducted by Yang et al, demonstrated that a disruption of energy metabolism and calcium homeostasis played in the occurrence of IMS(13). However, Mathew et al, stated that severe muscle damage in OP Poisoning patients with the magnitude of muscle damage that occurs during the cholinergic crisis determining the occurrence and severity of IMS(14).It has been understood that some amount of muscle necrosis in animals and humans occur after acute organophosphate exposure. However, magnitude of muscle damage is not sufficient to explain the muscle weakness in IMS(10)(15). In acute OP poisoning, severe and prolonged acetylcholinesterase inhibition is associated with oxidative stress, detected in erythrocyte membranes, that occurs early in the course of poisoning and may contribute to the development and severity of intermediate syndrome(16).

The inhibition of cholinesterase activity leads to the buildup of acetylcholine at synapses, causing over stimulation of both central and peripheral nervous systems. Furthermore, OP will interfere with synaptic transmission peripherally at muscarinic receptors and

nicotinic receptors. Nicotinic manifestations include increased or decreased muscle power and skeletal muscle fasciculations. Muscarinic manifestations include excessive salivation, meiosis and diarrhoea. The most frequent signs are reported to be meiosis, vomiting, hypersalivation, respiratory distress, abdominal pain, and depressed level of consciousness and muscle fasciculation(17).The rate and degree of AChE inhibition is dependent on the structure of the OP. Oxon type of OPs, such as dichlorovos are biologically active and capable of inhibiting AChE shortly after administration. On the other hand, thion type of OPs, such as diazinon and parathion, are biologically inactive and require hepatic activation to the corresponding oxon form to produce an AChE inhibitory effect. As a result, the inhibitory effects of a thion OP can be delayed when compared to an oxon OP. OPs initially form a non-covalent electrostatic bond at the AChE active site. When the first alkyl chain is cleaved from OP, a relatively weak covalent bond forms. Therefore, both the electrostatic and initial covalent bond are reversible in nature and the rate of spontaneous reactivation is dependent on the OP's chemical properties(18). The disease entity is believed to be due to the inhibition of a poorly characterized esterase called the neuropathy target esterase(19).

Cholinergic phase

The cholinergic phase usually passes off within 48-72 hours but complete clinical recovery from all the effects may take up to a week. Typically, these effects are grouped based on the affected receptors and include muscarinic, nicotinic and central nervous system (CNS) effects(18). The symptoms are due to stimulation of the muscarinic and nicotinic receptors. The nicotinic features of acute OP poisoning occur due to accumulation of acetylcholine at nicotinic acetylcholine receptors, include increased or decreased muscle power and skeletal muscle fasciculations. Excessive muscarinic receptor stimulation produces the classical manifestations of OP poisoning, include excessive salivation, miosis, diarrhea, bronchorrhoea, bronchospasm, bradycardia, urination. Other signs include vomiting, respiratory distress, abdominal pain, depressed level of consciousness, muscle fasciculations and muscle paralysis. After severe poisoning, generalized weakness can include the respiratory muscles and assisted ventilation may be required. It is worth noting that number of the muscarinic and nicotinic features tend to overlap due to action at the ganglia. As a result, patients may present with a mixed picture. Progression of paralysis may affect the muscles of respiration necessitating ventilatory support. Treatment is supportive with oximes, atropine and mechanical ventilation, in addition to gastric lavage and decontamination

Intermediate Syndrome

Approximately 10 to 40% of acute OP poisonings develop delayed weakness in the proximal limbs, neck flexors and muscles of respiration(17)(20). This constellation of symptoms is known as the intermediate syndrome (IMS), and its etiology is poorly understood. Some researchers have cited insufficient pralidoxime therapy and tissue redistribution as potential causes, though these opinions are not universally shared(9). After the acute cholinergic phase, a second stage of weakness occurs 1 - 4 days later with or without a symptom free interval, and, if left unrecognized, can lead to fatal respiratory depression(21).OP poison-induced IMS was first described in 1987(4). IMS occurred after recovery from the acute cholinergic crisis but before OPIPN. It is usually observed 12–72 hours after OP poisoning and may last up to 5-6 days. This syndrome is characterized by sudden-onset muscle weakness, including the respiratory muscles (particularly the diaphragm), as well as paralysis of the neck muscles (inability to raise the head from the pillow) and weakness of proximal limb muscles. Infrequently, certain cranial nerve palsies, such as the external ocular, jaw, facial and palatal muscles, may be detected(22).Intubation and mechanical ventilation is needed if respiratory failure occurs. One of the devastating cholinergic features of organophosphate poisoning is respiratory failure. The duration of ventilatory care varies between 7 and 21 days. There are quite a few explanations for respiratory failure; central, as well as peripheral mechanisms,

underlie this phenomenon. However, studies have suggested that the major mechanisms regulating respiratory failure associated with OP ingestion are central in origin(23).

Delayed Organophosphate Induced Polyneuropathy

Organophosphate induced delayed neuropathy (OPIDN) is an uncommon clinical condition. It occurs in association with the ingestion of large amounts of organophosphate and manifests as limb weakness persisting long after the acute cholinergic symptoms have subsided. Although acute effects of organophosphate intoxication appear to be directly related to cholinergic overactivity, the pathophysiology of the following neuropathy is less clear and is not related to cholinesterase inhibition(24).The clinical picture is characterized by a distal paresis in lower limbs. Repeated or pro- longed exposure of OPs, even at relatively low levels and without causing acute symptoms, may also result in the neuropathy(25). Ataxia and paralysis are the typical symptoms of OPIDN.

Diagnosis of organophosphate-induced neuropathy rests on recognition of an appropriate exposure in a patient with progressive motor deficit greater than sensory neuropathy. Electrodiagnostic studies demonstrate an axonal neuropathy(26). Nerve conduction studies play an important role in the diagnosis of this rare clinical condition, which may reveal distal- dominant sensory motor axonal polyneuropathy(27).

There are no specific features and nerve biopsy reveals axonal degeneration with secondary demyelination. Features of the toxic neuropathy may be characterized by a distal paresis in the lower limbs associated with sensitive symptoms. Connection of the central nervous system may occur. Pyramidal tract dysfunction may be observed later in the upper limbs(28). Repeated or prolonged exposure of OPs, even at relatively low levels and without causing acute symptoms, may also result in the neuropathy .

These complaints rapidly evolve into an ascending paralysis that seems to occur more frequently in the lower limbs. Eventually the flaccid paralysis resolves, and hypertonicity is seen. Historically, these symptoms are known as "Ginger Jake Paralysis", since thousands of Americans during prohibition became weak or paralyzed after drinking an alcohol-containing ginger extract (Ginger Jake) that had been contaminated with the OP triorthocresyl phosphate (TOPC)(29). These cases typically developed permanent spasticity and an abnormal gait known as "Jake leg" or "Jake walk"(30). The current study suggests TRPA1 is the major mediator of OPIDN and targeting Transient receptor potential cation channel, member A1 (TRPA1) is an effective way for the treatment of OPIDN(31).

Clinical features of IMS

First termed by Wadia et al in 1974 as type II paralysis, IMS is a syndrome characterized by muscle paralysis following the acute cholinergic phase. The terminology was later changed by Senanayake and Karalliedde in 1987 to intermediate syndrome due to the fact that it arises between the period of early cholinergic syndrome and the late onset peripheral neuropathy. IMS develops 12-96 hours after exposure and reflects a prolonged action of acetylcholine on the nicotinic receptors. The clinical features are muscular weakness in the ocular(32), neck, bulbar, proximal limb and respiratory muscles with occasional dystonic posturing, requiring mechanical ventilation in an intensive care unit for several days. Cranial-nerve palsies are common. The risk of mortality is due to the associated respiratory depression. The sensory functions characteristically remain normal and full recovery is evident in 4-18 days.

Types of organophosphate poisoning

Hundreds of organophosphate compounds are currently available to use as insecticides. Statistically, parathion was the causative agent of IMS in up to 75% of cases in previous studies(33). Fenthion, dimethoate, monocrotophos, methamidophos and malathion were also reported to cause IMS but no reported case developed IMS after phenthoate ingestion(34).In the World Health Organization (WHO) classification of OP

pesticides, phenthoate and parathion are classified as class II-moderately hazardous and class-Ia, extremely hazardous, respectively. LD50 (LD: lethal dosage) in rats for phenthoate and parathion mentioned on the online material safety data sheet (MSDS) is > 600 mg/kg and 20–30 mg/kg, respectively. This information shows that the fewer phenthoate IMS cases might be due to its lower toxicity.

Diagnosis of organophosphate poisoning

Many physicians use serum or RBC AChE activity to monitor OP poisoning. Serum AChE, also called pseudocholinesterase or butyryl-cholinesterase (BuChE), is found in the serum, liver, pancreas, heart and brain. It is subject to a high degree of variation influenced by many conditions, such as liver dysfunction, decompensated heart disease, malnutrition, allergic disease and malignant neoplasm. Further, no discernible difference in the serum AChE between day 1 and day 3 after OP poisoning has been observed in IMS patients(35).Hence, there is no predictive value of serum AChE for IMS. In contrast, RBC AChE is more reliable, with better correlation in terms of clinical presentations(36). Increased RBC AChE was noted when the patient recovered from IMS and was successfully weaned off mechanical ventilation(37).

Electrophysiological studies may offer some hints regarding the development of IMS. Three phenomena of electrophysiological studies were observed in IMS: (a) repetitive firing following a single stimulus; (b) gradual reduction in twitch height or compound muscle action potential followed by an increase, with repetitive stimulation of ≥ 20 Hz (decrement-increment response); and (c) continued reduction in twitch height or compound muscle action potential with repetitive simulation (decrementing response)(38).The decrementing response is the most frequent finding during IMS resulting from a marked downregulation of acetylcholine receptors (AChRs) at the post-junctional membrane, along with a failure of the pre-junctional ACh mobilization receptor. Downregulation of AChRs is due to a compensatory response after prolonged exposure to ACh followed by decrease of AChRs resulting from endocytosis(39).

Treatment

Treatment of OP poisoning is a critical and aggressive process which includes decontamination, antidote administration (atropin and oximes), mechanical ventilation support and extracorporeal elimination procedures if needed. Decontamination is essential in the initial management of an acutely poisoned OP patient. All clothing should be removed, and aggressive irrigation should be performed if topical exposure is suspected. Leather-containing materials should be discarded, as OPs cannot be removed from these products. The same measures of aggressive decontamination should also be considered after an oral ingestion, as many OPs tend to be excreted in bodily fluid. Gut decontamination via gastric lavage may be considered if the exposure occurred within 30 minutes of presentation and the patient is not already vomiting. Activated charcoal may limit further absorption and may be considered if the patient has a protected airway.

Moderate-to-severe poisoning may require supplemental oxygen and, in extreme circumstances, endotracheal intubation. Copious secretions can be managed by antagonizing the OP's muscarinic effects with an anticholinergic agent, such as atropine. A doubling dose strategy (atropine 1–3 mg IV, doubling the dose every 5 minutes until effect) is shown to reduce mortality more effectively when compared to a fixed-dosing strategy (atropine 2–5 mg every 10 – 15 minutes). Atropine does not reverse the nicotinic symptoms associated with OP poisoning. Pralidoxime reactivates OP-inhibited AChE by removing the OP from the enzyme, reactivating the AChE enzyme and improving and/or preventing nicotinic symptoms. The World Health Organization (WHO) recommends that pralidoxime be dosed as a 30 mg/kg bolus followed by an 8 mg/kg/hr infusion in adults(40). A recent Cochrane Review concluded that there is insufficient evidence to indicate whether pralidoxime is beneficial or harmful. Pralidoxime is used to treat nicotinic symptoms and to lower the

atropine requirement. It was obvious that the WHO's recommended PAM blood level is not ideal for the management of organophosphate poisoning(41)(42). As proposed by Eyer and other authors, the guideline for the administration of 4 mg/L PAM should be further revised and discussed(43). Pawar et al. suggested that a high-dose regimen of PAM that consists of a constant infusion of 1 g/h for 48 h following a 2 g loading dose reduces the morbidity and mortality of moderately severe cases of acute organophosphorus pesticide poisoning(44). Evidence suggests, however, that the concentration of pralidoxime in the blood might need to be higher to antagonize the toxic effects of many insecticides. Thus, a bolus-loading infusion followed by a maintenance infusion may be the best regimen(45).

Hong-Xiang Liu et al, suggested that Continuous micropump of atropine and pralidoxime chloride combined is more effective than the use of repeated-bolus injection in the treatment of severe acute organophosphorus insecticide poison(46). It has been reported that continuous micropump injection of atropine can significantly reduce the case fatality rate of severe acute OP poisoning(47).Relapsing symptoms can be seen after exposure to highly lipophilic organophosphates(48).Some time, a decline in clinical status was noted after the patient appeared to be improving. All the noted symptoms could potentially be explained by OP redistribution from fat stores, as they were either cholinergic or nicotinic in nature. In these cases, pralidoxime should be restarted, along with additional doses of atropine, as indicated by clinical signs and symptoms. The addition of intranasally administered oximes to the current treatment regimen for organophosphate poisoning would improve efficacy, reducing both brain damage and mortality. Oximes are used to counteract the effects of organophosphate poisoning, but they do not readily cross the blood brain barrier (BBB) when we give intravenously(49).However, morbidity and mortality due to OP poisoning is directly proportional to the age, severity of poisoning and duration of mechanical ventilation and inversely proportional to serum cholinesterase level(50).

Both hemodialysis and hemoperfusion can be used to eliminate OP compounds from blood. There are many cases reporting the effectiveness of these methods. Plasmapheresis is another elimination process has been used to remove immune complexes. Plasmapheresis is effective in elimination of substances with high plasma protein binding capacity (>80%) and low distribution volume (<0.2 L/kg bw)(51). Plasmapheresis is the procedure in which less than 15% of total plasma is removed and is not replaced. Therapeutic plasma exchange (TPE) is another procedure in which separated plasma is replaced with albumin and/or fresh frozen plasma and crystalloids. It may not be only the elimination of OP but replacement of cholinesterase by fresh frozen plasma by plasma exchange which helps in clinical improvement in patients poisoned with OP(51). There are several reports supporting effectiveness of plasmapheresis in OP poisoning and intermediate syndrome(52).

Conclusion

Organophosphate poisoning is the most common pesticide poisoning in developing countries. The mortality rate of OP poisoning is high: fatal issue is often related to a delay in diagnosis or an improper management. Neuromuscular weakness resulting from OP poisoning is divided into three types; firstly, type I paralysis in which, muscle weakness occurring within the first admission day associated with cholinergic signs; secondly, type II paralysis or IMS, delayed muscle weakness occurring after the acute cholinergic phase of OP poisoning; thirdly, type III paralysis, polyneuropathy occurring 2–3 weeks after OP poisoning. Early diagnosis and appropriate treatment, conversely, are often lifesaving, although the clinical course of OP poisonings might be quite severe and necessitate intensive care management. Furthermore, the WHO guidelines for the use of PAM should be updated to take into account a flexible dosing strategy based on severity of poisoning, though any such changes to recommendations must first be validated in a larger sample size.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

ORIGINAL ARTICLE

Clinical profile of End stage Chronic kidney disease undergoing haemodialysis-Study conducted at Teaching Hospital Jaffna, SriLanka

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Abstract :

Chronic kidney disease (CKD) is major public health problems in SriLanka. Furthermore, it is often shared with poor health outcomes and high economical cost to patient, family and national health system. However, we don't have exact incidental or prevalence report in a regional or national level. We conducted descriptive prospective study on end stage renal disease (ESRD) patients who regularly have been undergoing haemodialysis (HD), to see clinical profile including dialysis related expenses at dialysis unit in Jaffna teaching hospital, SriLanka over a period of one month. Out of 84 participants males were 59(70.2%) and females were 24(29.8%). Interestingly, nearly one-third of the population 28(33.3%) not had any risk factors, which labelled as chronic kidney disease of unknown etiology (CKDu), 22(26.2%) of the population had both diabetes and hypertension. However, 12(14.3%) population only had diabetes, while 11(13.1%) participants had hypertension only. Most of the population 54(64.3%) needed once a week dialysis. Unfortunately, 70(83.3%) of the participants did not have kidney transplantation plan. We have suggested following suggestions, firstly Public awareness on CKD is very important that increasing prevalence of CKD and its consequences should be made aware to the public periodically. Secondly, high risk people for CKD should be screened early and periodic review and follow up to be continued per local and international guidelines

Keywords: Chronic Kidney Disease, and end-stage kidney disease

Introduction

CKD has become a major public health problem worldwide. It is often combined with poor health outcomes and high economical cost on patient, family and community health system. The high cost involved in the management of end stage renal failure has led to a substantial burden on global health care resources (1). The management of CKD is even more difficult in developing countries due to lack of resources and restrictions in health care expenditure. In Sri Lanka, recent years, a significant increase in CKD related morbidity and mortality has been observed in some parts of the country initially more pronounced in North Central and then subsequently in North West, Uva, Eastern and Northern Provinces (2).

CKD is defined as kidney damage evidence by structural or functional abnormalities of the kidney with or without decreased Glomerular Filtration Rate (GFR) over a three months period. It has been classified as grades 1 – 5 , based on the National Kidney Disease Outcomes Quality Initiative (KDOQI) criteria (3).There are number causes has been identified as a risk factors such as diabetes mellitus, hypertension, glomerulonephritis, obstructive uropathy and congenital diseases such as polycystic kidney disease(2). However, prevalence of CKD in Sri Lanka largely unknown, it is mainly due to the unavailability of proper CKD registries and insufficiency of studies in the particular field. In last couple of decades, there were increasing prevalence of CKD in North Central province (NCP) of Sri Lanka has been reported. Majority of those patients showed no association with known risk factors for CKD, therefore it was labeled as chronic kidney disease of unknown etiology (CKDu), as the exact aetiology has not been identified despite several theories proposed (4). The disease mainly affects male paddy farmers from poor socio – economic background (5). They showed normal urinary sediment except mild proteinuria and their renal biopsies were reported as interstitial nephritis indicating possible exposure to toxin(6) .

Teaching Hospital, Jaffna, is the largest tertiary care institution for Northern Province, it accommodates patients from all five districts of the province. The haemodialysis unit of the institution was started in 2002 with the support of well-wishers and continues its services throughout the day. Patients do come for haemodialysis following acute kidney injury (AKI) and end stage renal disease (ESRD) which needs renal replacement therapy. Moreover, even in the absence of plan for Kidney transplantation (KT) for patients with ESRD, they are offered regular haemodialysis. It was observed that majority of these patients were from poor socio-economic class and which could be one the major reason for not seeking medical attention in the view of KT.

There were few studies conducted in the past on epidemiology of CKD in the local population of Jaffna which included all the stages of CKD (8) particularly to identify the pattern of aetiology. With the emerging trend of CKDu, it seems to be necessary to evaluate frequently the pattern of aetiologies to identify the spread of CKDu to the surrounding regions from its most prevalent part of the island. To our knowledge there are no published studies on dialysis related expenses in ESRD patients attending Teaching hospital, Jaffna.

Methods and Methodology:

This is a descriptive cross-sectional study on characteristics, aetiologies and dialysis related expenses of End Stage Renal Disease (ESRD) patients who regularly have been undergoing haemodialysis (HD), conducted at the Haemodialysis unit of Teaching Hospital, Jaffna SriLanka, over a period of one month from 01.05.2015 to 31.05.2015. All the ESRD patients who are attending to the dialysis unit for their regular haemodialysis more than one month are considered for the study. Patients who underwent for emergency dialyses which were requested from in-wards and patients who had haemodialysis following acute kidney injury were excluded from this study. All the patients undergoing for regular haemodialysis at Teaching hospital, Jaffna were recruited for this study. The Patient's demographic data, CKD related details, economic status and personal expenses towards dialysis were collected through the interviewer administered questionnaire. Approval for this study was granted by the Ethics Committee of Faculty of Medicine, University of Jaffna, Sri Lanka. Written informed consent was obtained from all participants. Gender, age in completed years and residency district were included in the demographic data. Aetiology for CKD, the year of diagnosis of CKD, the year of initiation of regular dialysis, dialysis frequency, route of dialysis and whether having a kidney transplantation (KT) plan were taken from them. In addition to that we also collected details of social issue comprised of average monthly income, distance to dialysis centre from home and consumable cost i. The harvested data were analyzed, student's T-test for numerical variable and chi-square test were used for categorical variables. All statistical tests were two-tailed and performed with the statistical package for social science (SPSS-21)

Results:

Total 84 ESKD patients were enrolled in this study. Out of 84 patients ,59 (70.2%) were males and 25(29.8%) were females. The Male to Female ratio was approximately 2:1. ESKD affects wide range of age group between 17 to 73-year -old. Nearly half of the patients were in the category of middle age group (45-65 years). One-third of them seemed to be young (less than 45 years). When we consider the district wise, two-third of the population55(65.5%) were from the Jaffna district, rest of the population from Vavuniya 12(14.3%), Mullaitivu 10(11.9%), Kilinochchi 6(7.1%), and Mannar1. Aetiology of ESKD vary, 28(33.3%) ESKD was not due to any obvious causes, it is labelled as chronic kidney disease of unknown aetiology (CKDu). Both Diabetes and hypertension were found in 22 people with ESKD (26.2%). Diabetes alone was the sole cause of ESRD in 12 patients (14.3%) , hypertension in 11 participants (13.1%) and both adult polycystic Kidney disease(APCKD) and glomerulonephritis each in 3 (3.6%) participants(Table 1) .Out of 84 ESKD, 23(27.4%) needed regular dialysis in every 3-4 days , while 54(64.3%) needed in 5-7 days dialysis and 7 people needed (8.3%) it once in 10 – 14 days. All participants were created arterio-venous fistula (AVF)for dialysis.

Time window between the diagnosis of CKD and initiation of regular Dialysis

The time duration between commencement of regular hemodialysis and the time of labeling having CKD showed a wide range from one month to 85 months with the mean of 17.21 months. From the cohort, 49 people (58.3%) had started their regular dialysis within one year of labeling as having CKD. 62 participants (73.8%) had initiated their regular dialysis by the end of 2 years. Only for seven people (8.3%) it took more than 5 years

Kidney transplantation (KT)Plan

Out of 84 ESKD patients 70(83.3%) participants including 52 males and 18 females did not have KT plan. People who were willing for KT were less than 41 years. The reasons for not having a KT plan were; financial difficulties for 64 (91.5%) patients, severe co morbidity 4(4.8%), advanced age 1(1.2%) and difficult to find donor 1(1.2%).

Travelling Distance for Dialysis

The travelling distance for dialysis from residency to hospital ranges from 2 to 215 kilometers with a mean of 56.98 km. 51(60.7%) participants from Jaffna District only needed to travel to reach the hospital less than 30 km including 26(30.9%) of them just travelled less than 10 km and only four patients had to travel 30 – 50 km. Rest of the cohort, 29(34.5%) participants who were from other district travel for this purpose more than 50 km including, 25(29.8%) people who had travelled more than 100 km.

Average monthly Income

Income of 62 (73.8%) people was less than 20,000 Sri Lankan rupees (LKR) per month including 18 patients (21.4%) with the monthly income of less than 10,000 LKR. Only nine people (10.7%) had an income of more than 30,000 LKR per month.

Causes	N	%
CKDu	28	33.3
DM & HTN both	23	26.2
DM only	12	14.3
HTN only	11	13.1
Adult Polycystic Kidney disease	3	3.6
Glomerulonephritis	3	3.6
Alport Syndrome	1	1.2
Obstructive Uropathy (BPH)	1	1.2
Nephrotic Syndrome	1	1.2
Neurological Bladder	1	1.2
Total	84	100

DISCUSSION

Total 84 ESKD patients were participated in this study. This study clearly highlights the demographic and socio-economic characteristics, and aetiologies of ESKD patients at Teaching Hospital, Jaffna SriLanka. Out of 84 ESKD patients ,59 (70.2%) were males and 25(29.8%) were females and also ESKD more predominant among middle age groups. Nearly half of the patients were in the category of middle age group (45-65 years). One-third of them seemed to be young (less than 45 years). A similar study was conducted in East part of the SriLanka, where males were 59.5% and females were 29.8%. In both studies, clearly shown that ESKD more prevalence among middle age group. In this study, leading causes for ESKD was CKDu (33.3%), followed by diabetes nephropathy (14.3%), hypertensive nephropathy (13.1%), APCKD (3.6%), Glomerulonephritis (3.6%) and rest of the causes were (1.2%) for each. But, irrespective of the causes, majority of them have become dialysis dependent within two years from the labeling of having CKD. Aetiology of ESKD vary in eastern part of the SriLanka, where most common etiology in the present study was diabetic nephropathy (54.8%) followed by hypertensive nephropathy (30.4%) and ADPKD (2%)(4), (15).

A hospital base study conducted at NHSL in 2006 reported that Diabetes was the leading cause for CKD, 30.6%, in western province, Sri Lanka (15). In 2012, a cross sectional demographic study was conducted in Jaffna with a study sample of 89 revealed that Hypertension was the leading cause for CKD (79.8%) followed by Diabetes, and CKDu was the reason for 6.7%9 . However, in recent years there have been alarming and increasing reports on CKDu in Sri Lanka, particularly from North-central province and surrounding regions19. Although our study too reveals that Diabetes and Hypertension seem to play the leading role for the development of CKD, one third of study patients have been labeled as having CKDu, which is highly significant compared to previous study conducted in Jaffna (33.3% vs. 6.7%) (9).

Similar studies were conducted in other part of the SriLanka, where it was clearly indicating that males are affected more than the female(5)(6)(9). There are several reasons behind it, males are more addicted with alcohol and smoking than females. Furthermore, SriLanka is the agricultural country, where males are predominantly involved in handling the herbicide and weedicide than female. When the age group is considered, 80% of the study population was under 65, this is the age group deemed as economically productive group. Again, another important factor to influence on family earnings and maintenance. Therefore, this factor would definitely have a significant impact on the family income of affected families. From the analysis, it could be seen that 75% of the affected claimed their family monthly income was less than 20 000 LKR, other poor socio-economic indicator of the affected individuals and families.

Chronic kidney disease with unknown aetiology (CKDu) has been a burning issue as a health burden within Sri Lankan health system due to increased prevalence and incidence in the recent past years particularly in North central province and surrounding regions. Several environmental risk factors have been recognized as aetiologies for CKD such as heavy metals (arsenic, cadmium, lead, mercury and chromium) agrochemicals, water hardness and exposure to nephrotoxic substances (20). Medical examination of the renal biopsies of CKDu revealed that the pathophysiology has been chronic tubular interstitial diseases and has very slow progression to end stage renal failure (21). The following factors are recognized causes for renal tubular interstitial diseases; heavy metals, chronic hypokalemia, chronic hypercalcemia, drugs such as allopurinol and sulfa containing drugs, infections (viral, bacterial, parasitic), radiation nephritis, polycystic kidney disease, cystinosis, Sjogren syndrome, sarcoidosis, multiple myeloma cast nephropathy(20).

At the time of data collection at Jaffna Teaching hospital SriLanka, which was the one and only hospital providing long term regular dialysis for patients with ESRD in Northern Province. Therefore, patients from other districts of Northern Province such as Kilinochchi, Mullaitivu, Vavuniya and Mannar attended to this institution for dialysis purpose. Relatively, people from these districts need to travel more than 100 km to reach

the dialysis centre. Usually travelling in public transport to this distance takes about 2.5 to 3 hours. A usual chronic dialysis session for a patient is 3 hours and, including the waiting time at the hospital, a person has to spend 9 to 10 hours per session when they come from these places. This cohort shows that one-third of them were from outside of the Jaffna peninsula. It was noted almost all of them had come with another accompanying family member. From the above-mentioned factors, it is prudent to assume that how severely these patients and their families would be affected financially

As already mentioned, travelling cost is another issue particularly patients coming from neighboring districts. Nearly 1/3 of study population has to travel more than 100 km to reach the institution. Most of them needed to travel 4 - 10 times a month for this purpose. Each time every patient has to be accompanied by another family member. Therefore, the total travelling cost per month becomes a significant impact on their financial status when compared to their monthly income.

The time duration from labeling of having CKD to commencement of regular dialysis for nearly 75% of the study population was less than 2 years. In fact, more than half of the cohort has ended up dialysis dependant within a year from the labeling. Usually for diabetes and hypertension this time duration could be 7-10 and 10-15 years respectively18. Other aetiologies have variable presentations. In this study group, this could be multifactorial. One of them would be delay in labeling CKD which in turn probably delay in seeking medical advice promptly as early stages of CKD are asymptomatic and failure to screen the high-risk group early. Another factor could be the rapidity of disease progression that could be due to follow up failure, failure to adhere on medical advice of exposure to multiple nephrotoxic environments19. For an example, when having hypertension only, 53% had developed ESRD within a year whereas when it was combined with diabetes 73% had become dialysis dependent within a year. Therefore, it is prudent that early detection and prompt appropriate intervention should be implemented on time to slow down the progression of disease.

It was obvious that at some period, patients had to spend themselves on consumable for dialysis, more than half of them have experienced buying dialysis related consumables at some points with an expense ranging from 2000 - 5100 per session purely due to non-availability of such consumables at the dialysis centre at those particular times. The hospital renders not only the chronic dialysis but acute dialysis service also for the entire Province, therefore it does experience shortage of dialysis consumables at some points until getting the next supply from the ministry of health, Sri Lanka. When the dialysis is due in these periods, patients had to spend money to buy consumables. Fortunately, these days unlimited supply of dialysis related fluids or equipment to the Hospital.

The best long-term treatment for ESRD is RRT in the form of Kidney Transplantation. But number of factors influence on this issue. ABO compatibility and HLA mismatching is the far most important factor for the selection of transplantation. Physical fitness of recipient also plays a major role on deciding the transplantation; presence of multiple co-morbidity, advanced age, and abnormal anatomical structures relevant to particular surgical procedure would make them less suitable for KT. In developing countries, like Srilanka, the financial support for initial assessment is an unavoidable factor because some of the investigations of initial assessment cannot be done at government sectors in Sri Lanka and not available island wide either. A common factor everywhere in the world is waiting list for surgery; currently the state sectors offer this surgery are National Hospital of Srilanka and Kandy Teaching Hospital. After the surgery, post-surgical management expenditure is an important part particularly for immunosuppressive medications, these are costlier (government tries its best to supply on free of charge but not widely available in all hospitals).

Analysis of this study clearly shows that the main factor preventing seeking KT plan is financial restriction, 92% of patient have not considered for a surgery due to financial reason, which is sensible when compared to their income status. Because, for the initial assessment for KT, patients should travel to those state

hospitals which are approximately 300 kilometers away from their residencies. Therefore, the cost will include for travel, accommodation, meals, and other medical investigation expenses. They may need to visit frequently before finalizing for the surgery. This will have a big impact on the essential expenditure for their family chores.

Conclusion

CKD and its consequent ESRD are burning issue in Sri Lanka due to their increasing prevalence and subsequent high impact on health sector. This study clearly identified some important issues from the patients who attend teaching hospital, Jaffna for their regular dialysis. Subsequently which lead to the following likely recommendations to counteract those problems. Firstly, Public awareness on CKD is very important that increasing prevalence of CKD and its consequences should be made aware to the public periodically. Health institutions, health personnel and media should be used in this purpose. High risk people for CKD should be screened early and periodic review and follow up to be continued per local and international guidelines. This would pick up the disease at early stage and appropriate intervention in time would delay the progression of disease. Prompt specialist referral should be made when appropriate. The study clearly identified 1/3 of the population had been labeled as CKDu. This also should be considered seriously because previous study, noted 3-years back that only 6.7% having CKDu. Therefore, further extended studies on this issue should be carried out on a larger sample. Every CKD patient including ESRD patients should be encouraged to adhere to medical advice at each visit. Multidisciplinary approach including renal specialist input would help the patient more and which might delay the commencement of RRT in some patients.

Ethics approval and consent to participate: was taken

Consent for publication: Consent was obtained from the director, Teaching Hospital Jaffna for publication of this article.

Availability of data and material: All data gathered during this study are included in this published article.

Conflict of interest: None declared

Funding: This research received no funding support

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

ORIGINAL ARTICLE

Clinical profile of Intermediate Syndrome following Organophosphate Poisoning

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Abstract :

Background: Organophosphate (OP) poisoning is a worldwide problem, associated with more than 200,000 deaths every year. In the developing countries, such as Sri Lanka and India, these events are more prevalent and connected with higher mortality rates. Typical OP poisoning, followed by three well-defined clinical phases, are commonly seen in the clinical practice. The initial phase is an acute cholinergic crisis, then Intermediate Syndrome (IMS) develops after 24-96 hours (of acute cholinergic crisis) and lastly Organophosphate Induced Delayed Polyneuropathy (OPIDPN) presents 2-3 weeks after OP exposure. The characteristic features of the IMS are weakness of the respiratory muscles such as diaphragm, intercostal muscles, accessory muscles, neck muscles and proximal limb muscles. Methods: This descriptive, prospective, cross-sectional study was conducted at the Teaching Hospital, Batticaloa, Sri Lanka, over a period of 6 months from 1st March 2017 to 1st August 2017. Results: Of the total 65 patients recruited, 39 (60%) were male and 26 (40%) were female. All the patients were poisoned through the gastrointestinal route. The prevalence of IMS among deliberate self-harm (DSH) with OP poisoning was 5 (5.88%). Conclusion: All five IMS patients have developed neck, facial and proximal muscle weakness, while 2 (40%) of IMS patients showed extra-ocular muscle weakness. Intermediate syndrome develops 24-96 hours after phase I resolution.

Keywords: Organophosphate poisoning, intermediate syndrome

Introduction

Organophosphate (OP) poisoning is a worldwide problem, associated with more than 200,000 deaths every year(1). In the developing world, these events are more prevalent and connected with higher mortality rates. Acetylcholine is a neurotransmitter present at the neuromuscular junctions in peripheral and central nervous systems. Acetylcholinesterase (AChE) is an enzyme that usually hydrolyses and breaks down acetylcholine. OP compounds cause phosphorylation and inactivation of this enzyme leading to the accumulation of acetylcholine which is responsible for the features of cholinergic syndrome(2). Typical OP

poisoning is followed by three well-defined clinical phases. The first phase manifests as a cholinergic syndrome; the symptoms include miosis, nausea, vomiting, diarrhea, dyspnea, and bradycardia. Seizure, coma, and respiratory failure may also occur(3). Secondly, the Intermediate Syndrome (IMS), comprised of characteristic signs and symptoms occurring after apparent recovery from the acute cholinergic syndrome. As the syndrome occurred after the acute cholinergic syndrome, it was called 'Intermediate Syndrome'. Thirdly, OP induced Delayed Polyneuropathy (OPIDPN) develops at several weeks after exposure(4). OPIDPN is an occasional neurotoxicity effect, happening 1 to 6 weeks following acute cholinergic crisis resulting in muscle weakness, pain, and paresthesia. Reason for this delayed effect is the phosphorylation of nervous tissue proteins resulting in Wallerian axonal degeneration(5,6). However, OP induced Delayed Neuropathy is reported to persist after two years of follow-up(7).

The IMS occurs in approximately 20% of patients following an oral exposure to OP pesticides but, there is no clear association between the particular OP pesticide involvement and the development of the syndrome. It usually becomes established 2-4 days after exposure when the symptoms and signs of the acute cholinergic syndrome are no longer obvious(8). The characteristic feature of the IMS is weakness of the muscles of respiration such as diaphragm, intercostal muscles and accessory muscles, neck muscles and proximal limb muscles. The underlying pathology behind the Intermediate Syndrome (Nicotinic Syndrome) is that nicotinic transmission requires inhibition of at least 80% of the synaptic acetylcholinesterase (AChE) enzyme unlike the muscarinic synapses and nerve endings where AChE can be easily inhibited, and the nicotinic syndrome occurs only in severe poisoning. The result is hyperstimulation of the Neuromuscular Junction by excessive acetylcholine, primarily resulting in fasciculation, which later is followed by neuromuscular paralysis; the effect of IMS may last for 2-18 days. The aim of this study is to highlight the clinical profile of the IMS following organophosphate poisoning (9).

Methodology

This descriptive, prospective, cross-sectional study was conducted at Batticaloa, Teaching Hospital, Sri Lanka, over the period of 6 months from 1st March, 2017 to 1st August, 2017. Patients, with less than 12 years of age and pregnant patients were excluded from this study. Informed written consent was obtained from all patients, who were involved in the study. Though it was initially not possible to get consent from the patients, therefore it was obtained from the accompanying relatives, however, later we managed to get consent from the patients once they regained consciousness. The consent was taken from the head of the institution for conducting this study as well.

OP poisoning was confirmed by the history from the patient and/or relatives, containers brought to hospital, records in patient-transfer forms, characteristic smell in the breath, and clinical features typical of OP poisoning. A possible diagnosis for IMS was developed on the base of Senanayake and Karalliedde's original description , namely significant muscle weakness in at least three of the following muscle groups (extraocular, neck flexor, proximal limb, and facial) observed at least 24 hrs. after ingestion of OP. The weakness of proximal muscles and neck flexion was considered significant when the muscle power was grade 3 or less according to the Medical Research Council [MRC] grading . Weakness of respiratory muscles was not considered a requirement for the diagnosis. Patient's demographic data were collected from medical records. We included all adults and adolescents, aged 12 years or more with deliberate self-harm (DSH) with definite organophosphate poisoning. We excluded any patients with uncertainty regarding type of poisoning. A total of 65 patients were included in this study. The clinical symptoms and signs of IMS were collected from the medical records. Once the recovered amount of poison was taken from the patient, however this is not an accurate method, it may give any relation with the IMS. The data were analysed by descriptive statistical method using SPSS 19 software. Results are presented as frequency and percentage with charts and tables.

Results:

Of the total 65 patients recruited, 39 (60%) were male and 26 (40%) were female. All patients were poisoned through the gastrointestinal route. The prevalence of IMS among DSH with OP poisoning was 5 (5. 88%). It was obvious that IMS was more prevalent in males 4 (80%) than females 1 (20%). All five IMS patients developed neck, facial and proximal muscle weakness, while 2 (40%) of IMS patients showed extra-ocular muscle weakness. The estimated average time for admission to the emergency department after the exposure of OP poisoning was 7.6 hours. In our study, almost all IMS patients required ventilatory support. The most frequent initial clinical signs were meiosis (100%), change in mental status (100%), hypersalivation (100%), agitation (60%) and fasciculations (60%) (Table 1). Out of five IMS patients, only one patient developed acute kidney injury.

Clinical Profile	Case-1	Case-2	Case-3	Case-4	Case-5
Sex	male	male	female	male	male
Age (in years)	53	27	23	45	20
Acute renal failure	no	yes	no	no	no
Neck muscle weakness	+	+	+	+	+
Extraocular muscle weakness	-	-	+	-	+
Proximal muscle weakness	+	+	+	+	+
Facial muscle weakness	+	+	+	+	+
Average time interval between time of poisoning and hospital admission (hours)	8	12	5	7	6
Myocarditis	Absent	Absent	Absent	Absent	Absent
ARDS	Absent	Absent	Present	Present	Absent
Epileptic movements	Present	Absent	Absent	Absent	Absent
Meiosis	Present	Present	Present	Present	Present
Ventilatory support	Needed	Needed	Needed	Needed	Needed
Change in mental status	+	+	+	+	+
Hypersalivation	+	+	+	+	+
Agitation	+	+	+	-	-
Fasciculations	+	-	+	-	+
Duration of mechanical ventilation (days)	4	7	5	8	4
Acute renal failure	no	yes	no	no	no

Discussion:

In the Neuromuscular Junction (NMJ) acetylcholine is released when a nerve impulse reaches terminal axonal end and it disperses across the synaptic cleft and binds to cholinergic nicotinic receptors on the muscle fibers(10). In the resulting classical OP poisoning, three well-defined clinical phases are seen, initial acute cholinergic crisis, the Intermediate Syndrome and Organophosphate Induced Delayed Polyneuropathy. In 1987, IMS was described in Sri Lanka by Senanayake and Karalliedde(11). According to the study conducted by Umakanth M, the prevalence of OP poisoning among DSH in the east part of the Sri Lanka was 19%(12)(13). Intermediate Syndrome develops 24-96 hours after exposure and imitates a prolonged action of acetylcholine on the nicotine receptors. The clinical features are muscular weakness in the ocular, neck, bulbar, proximal limb and respiratory muscles(9). It is now emerging that the degree and extent of muscle weakness may vary following the onset of the IMS (9). In our study, prevalence of IMS among DSH among OP poisoning was 5.88%. This percentage is less than the study conducted by Pradeepa Jayawardane, where prevalence was 8.8%(8). However, reported frequency of

intermediate syndrome varies from 8% to 49%(14,15,16). Consequently, some patients may only have weakness of neck muscles whilst others may have weakness of neck muscles and proximal limb muscles(17). However, in this study all patients had weakness of proximal muscles, neck muscles and facial muscles. Most patients with IMS develop respiratory failure, which requires mechanical ventilation. In this study, mechanical ventilatory support was needed for all 5 IMS patients. The average duration of mechanical ventilation was 5.6 days. Most of the death from acute OP poisoning could be attributed substantially to respiratory failure through the following effects: depression of the respiratory center in the brainstem, neuromuscular paralysis, excessive respiratory secretions, and bronchoconstriction(18). Our patient developed respiratory failure on 4th to 7th day of poisoning which is the typical duration for Intermediate Syndrome. However, out of five IMS patients, no patient died in this study.

OP can influence other organ systems which, although rare, can worsen the presentation and prognosis of the patient. One of the organs affected are the kidneys. Although the exact mechanism of acute kidney injury (AKI) is unclear, numerous hypotheses have been proposed. In our study, only one IMS patient developed acute kidney injury. One cohort study found that patients with OP poisoning had a 6.17 fold higher risk of AKI compared with the comparison cohort(19).

Conclusion

The three phases of neurological illness following OP intoxication are well-reported. Phase I (acute cholinergic crisis) occurs secondary to continued depolarization at the neuromuscular junction. Phase II (intermediate syndrome) develops 24-96 hours after phase I resolution. In Intermediate Syndrome characteristically muscles of the neck, proximal limb, and the eyes, bulbar and respiratory groups are affected. Patients with severe organophosphate poisoning can have delayed cholinergic manifestations which would need large dose of atropine administration. Thorough evaluation of clinical features is needed to titrate the dose down and discontinue it. Moreover, careful follow-up is needed for the rare complications of organophosphate poisoning like IMS and OPIDPN.

Consent to participate

Consent was taken from the patient and/or relatives.

Consent for publication

Written informed consent was obtained from the patients for publication of this case report.

Availability of data and material

All data gathered during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

Funding

This research received no funding support

Acknowledgements

We thank the patients for accepting the publication of this article.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

ORIGINAL ARTICLE

Evaluation of the Efficacy and Safety of Foley Catheter for Cervical Priming of Pre-Induction of Labour

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Abstract :

Induction of labour (IOL) refers artificial initiation of uterine contractions by medical or surgical means before the onset of spontaneous labour. The Favourable uterine cervix increases the chance for a successful vaginal birth. Modified Bishop Score of less than 6 usually require cervical ripening. The trans-cervical extra-amniotic Foley catheter (FC) insertion is used for IOL in women with an unfavourable cervix for pre-induction cervical priming. This study was aimed to assess the efficacy and safety of pre-induction using a Foley catheter. It is a retrospective study done over a period of three months at University Teaching Unit, Teaching Hospital, Batticaloa, Sri Lanka. Seventy-five pregnant mothers underwent cervical primed with Foleys catheter. The balloon reservoir is inflated with 80 ml of normal saline. The balloon was retracted so that it rested on the internal os of cervix. The catheter was left in situ for maximum 48 hours. It was removed before it when mothers developed labour sign. Majority of the mothers (64%) were nulliparous. The commonest cause for induction was past date i.e.> 40 weeks of gestation. Majority of the studied population (49.3%) was within the age of 25 and 35 years. 45 had Foley catheter was left in situ for 24 hours. Remaining 30 mothers had Foley catheter inside for 48 hours. During catheter induction 74.67% tolerated the procedure of catheter insertion and20% had only mild discomfort. Foley Catheter was deflated in four women in 24 hour of insertion due to discomfort and they had Bishop Score of more than 8 at the time of deflation and they have been included in the analysis. Among 75 mothers, 45.3% had bishop score of 3 or less and 54.7% had score of 4-7 at the time of catheter insertion. After catheter removal only 4.0% of them had score of 3 or less, 20.0% had score of 4-7 and 76.0% had score more than 8. 64.0% had NVD, 20.0% had emergency LSCS, 13.3% had elective LSCS and 2.7% had instrumental delivery. Mean birth weight of the new-borns was 3214 +/- 433.12 g, mean Apgar score was 9.6 +/- 0.78. No perinatal or maternal deaths occurred during the study period to the studied population. This study shows that none of them had any complication such as hyper-stimulation, PPH, chorio amnionitis or neonatal complications related to Foley catheter. Foley's catheter (FC) can be recommended for low resource settings insertion as it is an effective, cheaper method with a high vaginal delivery rate with minimal complications.

Keywords: Organophosphate poisoning, intermediate syndrome

Introduction

The foetus travels from the intrauterine to the extra-uterine environment during the labour process. It can be defined as the initiation and perpetuation of uterine contractions with the aim to produce progressive cervical effacement and dilation. The exact mechanism of labour process remains enigma [1].

Induction of labour (IOL) refers to the process whereby uterine contractions are initiated artificially by medical or surgical means before the onset of spontaneous labour. About 15-30% of pregnancies are induced. The most common indications include prolong pregnancy, preeclampsia, intrauterine foetal growth retardation (IUGR) and Medical disorders such as diabetes mellitus.

It is learnt that in the case of IOL, the chance for a successful vaginal birth is low with unfavourable cervix. Therefore, the modified Bishop Score; a scoring system has been introduced for cervical assessment in an objective way. This helps to triage pregnant mothers who would most likely to achieve a successful vaginal birth. The duration of labour is inversely correlated with the Bishop score; a score that exceeds 8 describes the patient most likely to achieve a successful vaginal birth. Bishop scores of less than 7 usually require that a cervical ripening method be used before other methods [2-5].

IOL is common obstetric procedure with rising rates worldwide. Sri Lanka has a rate of IOL of 37.5%, which is one of the highest rates in the world [6].

Different methods are used for IOL in women with an unfavourable cervix. Mechanical methods such as transcervical extra-amniotic Foley catheter (FC) insertion and pharmacological methods such as vaginal prostaglandin E2 and misoprostol are used for IOL in women with an unfavourable cervix for pre-induction cervical priming [7,8,9].

Both mechanical and pharmacological methods are used for IOL in women with an unfavourable cervix, and vaginal delivery rates are similar [10]. The WHO recommends the use of a balloon catheter for IOL. However, both IOL methods are associated with induction failure and caesarean delivery [11,12]. The risk of caesarean section in such cases is high, up to 50 %, especially among nulliparous women [13,14,15]. Foley catheter gives fewer maternal and neonatal side-effects in comparison with vaginal prostaglandins [10]. When compared with oxytocin, mechanical methods reduce the risk of caesarean section [16].

Recent Cochrane review has concluded that IOL using mechanical methods such as Foley catheter result in similar caesarean section rates to prostaglandins and yield a lower risk of hyper-stimulation with or without foetal heart rate changes compared to prostaglandins [16]. Mechanical methods are as effective in achieving delivery within 24 h of intervention as with any prostaglandins [16].

Foley catheter for cervical ripening is a far cheaper option to prostaglandin or oxytocin in terms of medication/device cost. The latter methods also incur significant additional cost in monitoring the maternal and foetal wellbeing during the process. Therefore, Foley catheter is a logical option to consider in limited-resource settings with relative lack of monitoring facilities. Other potential advantages of mechanical methods over pharmacological ones may include wide availability and reduction of some of the side effects [16].

To improve the efficacy of induction, different balloon inflation sizes and ripening time have been compared. Balloon inflation sizes of 30–80ml have been reported and two randomized controlled trials showed that larger balloon volume was associated with shorter induction to delivery interval without affecting caesarean section rate [17,18]

AIM OF THE STUDY:

To assess the efficacy and safety of labour pre-induction using a Foley catheter

MATERIALS AND METHOD

It is a retrospective study done over a period of three

months at the University Teaching Unit, Teaching Hospital, Batticaloa, Sri Lanky. During the study period unit had a total of 910 deliveries and seventy-five pregnant mothers underwent cervical priming with Foleys catheter. All were recruited for this study over 3 months. The mothers with singleton pregnancy, cephalic presentation, completed 36 weeks of gestation, Bishop Score less than 8 points and normal CTG were included. The exclusion criteria were: placenta previa, uterine infection, unexplained bleeding, abnormal foetal heart rate, and other reasons preventing vaginal delivery.

First Sims speculum was inserted to visualise the cervix. The cervix cleaned with Betadine solution. The catheter is introduced through the endo cervix into the potential space between the amniotic membrane and the lower uterine segment. The balloon reservoir is inflated with 80 ml of normal saline. The balloon is retracted so that it rests on the cervical internal os. The catheter was left in situ for the maximum duration of 48 hours. Catheter was removed on mothers developed features of labour early.

The study group was divided into subgroups according to parity. Indications for induction and its complications were evaluated. The condition of the new-borns was evaluated using the Apgar score, and infant birth weight. Bishop Score was compared before the insertion and after the removal of the catheter on mothers not developed labour features. The results were compared between the subgroups. Data were processed using SPSS version 21. Descriptive statistics methods were used to analyze the results as whole numbers, percentages, tables, and charts

RESULTS

A total of 910 deliveries occurred during the study period. Seventy-five consecutive cases which were primed with Foley Catheter, recruited for the study over 3 months.

Out of 75 mothers, 45 had Foley catheter was left in situ for 24 hours. Remaining 30 mothers had Foley catheter in situ for 48 hours. Among 75 mothers, 34 (45.3%) had Bishop score of 3 or less and 41 (54.7%) had score of 4-7 at the time of catheter insertion. After catheter removal only 3 (4.0%) of them had score of 3 or less, 15 (20.0%) had score of 4-7 and 57 (76.0%) had score more than 8. No significant difference was noted between Bishop Scores at Foley's insertion and removal (p- 0.111). (Table 2)

During the procedure, 56 (74.67%) mothers tolerated the discomfort of catheter insertion and 15 (20%) had only mild discomfort. (Table 3) [Foley Catheter was deflated in four women in 24 hours of insertion due to discomfort and they had Bishop Score of more than 8 at the time of deflation and they have been included in the analysis].

Majority of the mothers (64%) were primiparous. Major cause for induction was past dates i.e. over 40 weeks of gestation (53.3%). About half of the studied population (49.3%) was within the age group of 25 and 35 years. (Table 1)

Among the 75 mothers, 8 (10.7%) had Gestational diabetes mellitus (GDM) and 11 (14.7%) had pregnancy induced hypertension (PIH) others didn't have any comorbid conditions. Among the 8 mothers who had GDM 4 (50%) had NVD, 2 (25.0%) had Instrumental delivery, [(12.5%) had EM/LSCS, 1 (12.5%) had EL/LSCS] others (2) had delivered by Lower segment Caesarean Section (LSCS). Among the 11 cases with PIH, 5 (45.4%) had NVD, [3 (27.3%) had EM/LSCS and 3 (27.3%) had EL/LSCS] and others (6) had LSCS.

Among the 45 mothers who had Foley catheter was left in situ for 24 hours, 34 (75.6%) had normal vaginal delivery (NVD), 2 (4.4%) had instrumental delivery, 6 (13.3%) had emergency LSCS (EM/LSCS), 3 (6.7%) had elective LSCS (EL/LSCS). Remaining 30 mothers who had Foley catheter inside for 48 hours, 14 (46.7%) had normal vaginal delivery, 9 (30.0%) had emergency LSCS and 7 (23.3%) had elective LSCS..None of them had FC left more than 48 hours. Therefore, overall among 75 mothers who had FC induction, 48 (64.0%) had NVD, 15 (20.0%) had emergency LSCS, 10 (13.3%) had elective LSCS and 2 (2.7%) had instrumental delivery. (Table 2) This study shows that none of them had any complication such as hyperstimulation, PPH, chorioamnionitis or neonatal complications related to Foley catheter.

This study shows that none of the patients showed any clinical signs of infection during postpartum period. Mean birth weight of the new-borns was 3214 +/- 433.12 g, mean Apgar score was 9.6 +/- 0.78. No perinatal or maternal deaths occurred among the studied population.

Table 1; Demographic details of the study group

DEMOGRAPHIC DETAILS	FREQUENCY
1. Age in years	
• <25	33 (44.0%)
• 25-35	37 (49.3%)
• >35	05 (6.7%)
2. Period of gestation	
• <37 weeks	01 (1.4%)
• 37-40 weeks	34 (45.3%)
• >40 weeks	40 (53.3%)
3. Parity	
• P1	48 (64.0%)
• P2	14 (18.6%)
• P3	08 (10.7%)
• P4	03 (4.0%)
• P5 and above	02 (2.7%)

Table 2; Mode of deliveries after catheter induction.

	Mode of Delivery	Frequency
1) Catheter inserted		
24 hours (45 Mothers)	NVD	34 (75.6%)
	EM/LSCS	06 (13.3%)
	EL/LSCS	03 (6.7%)
	Instrumental delivery	02 (4.4%)
48 hours (30 Mothers)	NVD	14 (46.7%)
	EM/LSCS	09 (30.0%)
	EL/LSCS	07 (23.3%)

Table 3; Changes of Bishop score before and after catheter insertion

Bishop score at insertion of Foley catheter	Frequency
<=3	34 (45.3%)
4-7	41 (54.7%)
Bishop score after insertion of Foley catheter	Frequency
<=3	03 (4.0%)
4-7	15 (20.0%)
>7	57 (76.0%)
P=0.111	

DISCUSSION:

Seventy five pregnant mothers underwent cervical priming with FC were recruited for this study. As shown in the above results, subjects who were primed with FC followed mostly delivered vaginally (64%).Maturity of 39 week Asian fetuses may be equal to that of a 41 week Caucasian fetus, implying that Asian fetuses mature sooner than Caucasians [19].

The length of gestation of South Asian and black women is shorter than Caucasian indicating the likelihood of high early perinatal complications in south Asian and black women [19]. Therefore, in Sri Lanka, it is the common practice to induce labour at 41 weeks of gestation for women with otherwise uncomplicated pregnancies. Latest guideline by SLCOG also supports this practice [20]. Falling with the same line; it is the common practice to induce by 41 weeks of gestation in our unit too. Further the FC is cheaper when compared to vaginal prostaglandin tablets. A FC costs 90 LKR (0.7 USD), while 3 mg of prostaglandin costs about 1500 LKR (11.5 USD). Therefore, it is obvious that FC is a cost effective method in low resource countries like Sri Lanka. It has also shown to be a safe method in cervical priming and found to have same efficacy when compared with prostaglandins [21,10]. Many studies have reported that both FC and prostaglandin E2 gel are equally effective in pre-induction cervical ripening [16,22].

FC is a safe method of labor induction for the

mother, fetus and newborn [23]. Some studies from developing countries on IOL have attempted to find out an economically feasible method as a cervical priming agent. A report from an Australian trial explains that FC as a better cost-effective method. In that study the only difference in cost between the three groups (Foley, double balloon catheter and prostaglandin E2) relate to the cost of the cervical ripening device as there were no differences between groups in length of time in labour ward, mode of delivery, postnatal complications, and duration of hospital admission or re-presentation to hospital after discharge [9]. The cost of ripening devices used in the trial were substantially lower for the Foley catheter (AUS$2.00) compared with the double balloon catheter (AUS$81) and prostaglandin E2 gel (AUS$124 for two doses) [9]

On the other hand, The PROBAAT trial in Netherlands has evaluated cost-effectiveness of IOL at term with a FC compared to vaginal prostaglandin E2 gel [10]. The FC group showed higher costs due to longer labour ward occupation and less cost related to induction material and neonatal admissions [10]. However, FC usage has showed a comparable caesarean section rate compared with prostaglandin induction and therefore the incremental cost-effectiveness ratio has not been informative [10]. It was observed that FC use resulted in fewer neonatal admissions and asphyxia/ postpartum haemorrhage compared with prostaglandin use [10]. Therefore, FC and prostaglandin E2 gel labour induction generate comparable costs [10].

In a setting, like in Sri lanka where cost of labour ward stay is relatively less due to cheaper labour cost, FC seems to be a cost-effective solution for cervical priming. A study from India concluded that vaginal misoprostol is a cheap, highly effective, stable at room temperature and easy to administer agent for labor induction [24].

They have shown that misoprostol is superior to FC/oxytocin [11]. However, this result is debatable. A meta-analysis reported that vaginally administered misoprostol was more effective than dinoprostone vaginal insert for cervical priming and IOL and the safety profile of both drugs were similar [25].

This indicates that both FC and misoprostol has some economic advantages over prostaglandin. But misoprostol is not licensed for induction of labour in Sri Lanka [20]. Therefore, FC becomes more important in IOL cost reduction in our setting.

This study shows that normal vaginal delivery rate was 64.0%. a study by Ekele and Isah reported that a 91% vaginal delivery rate within 72 h of insertion [26]. But in a study by M. Patabendige total vaginal delivery rate of 79% [27].

According to M. Patabendige[27] 78% nulliparous women vaginal delivery rate. Study done in Australia, 41%nulliparous women had spontaneous vaginal delivery rate [7]. In a study by M. Patabendige subjects who have completed 41 weeks of gestation with otherwise uncomplicated pregnancies and who were primed with FC alone (21/32) had reported 83% rate of vaginal delivery. Amongst who have completed 41 weeks, there were 15 nulliparous women reporting 13/15, 87% of vaginal delivery rate. This indicates that FC is a good option for the subjects with completed 41 weeks and especially nulliparous women. However, a study comparing nulliparous women with uncomplicated post term pregnancies with FC induction versus spontaneous labour has shown that Foley induction resulted in a six-fold increase in risk of caesarean section rate (odds ratio 6.2) [28]. But among parous women it was low and not significant [28]. In our study, single arm study and did not have a control group to compare. Goonewardene M et al has shown that intracervical FC for 24 h was better than two oral doses of 25 µg misoprostol administered 4 h apart, for pre-induction cervical ripening in prolonged pregnancies [29]. There FC has shown to be effective for both nulliparous and multiparous giving higher modified Bishop Score and lower caesarean section rate.

The following complications were observed in this study group after insertion of the catheter: Nine (12%) cases developed prelabour rupture of the membranes, but none of them occurred when inserting the catheter. Four (5%) patients requested catheter removal before the scheduled time due to pain and discomfort.

This study shows that none of the patients showed any clinical signs of infection during postpartum period. Mean birth weight of the new-borns was 3214 +/- 433.12 g, mean Apgar score was 9.6 +/- 0.78. In one previous study, Foley catheter IOL was associated with increased infectious morbidity [28]. On the other hand, in several other studies, as well as in a recent Cochrane review, Foley catheter IOL has not been linked to increased maternal or neonatal infection rates [30,31,32]. This agrees with the result of this study.

In a study by Kruit et al [33] the rate of neonatal clinical sepsis was similar to that in previous studies but the rate of suspected neonatal infections was higher

Conclusions

Foley's catheter (FC) insertion is an effective method in cervical priming for IOL. This method is not only a cheaper method and gives acceptable levels of patient comfort but also a high vaginal delivery rate with minimal complications. As there is no risk of uterine hyperstimulation which occurs with synthetic prostaglandins preparation, it does not require close observation following insertion of the FC. Therefore, it can be recommended for low resource settings. The FC alone could be an effective method of IOL for uncomplicated, prolonged (41 weeks of gestation). Cost-effectiveness in low resource settings and pregnant women satisfaction with FC has to be better evaluated by further studies. This study was with a relatively small sample size and being a single arm study might have an impact on results. There is no comparison with another method.

CONFLICT OF INTEREST

None

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to Dr.Ibralebbe, Director, Teaching Hospital, Batticaloa for providing me opportunity to do this research in Teaching Hospital, Batticaloa.

I sincerely thank to my research assistant Dr Hemika for tiredless work.

I also wish to express my gratitude to the officials and other staff members of Teaching Hospital, Batticaloa who rendered their help during this research period.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

A Rare Case of a Spontaneous Resolution of a Ruptured Middle Cerebral Artery Infectious (Mycotic) Aneurysm, in a patient with Sub acute Bacterial Endocarditis

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Introduction

Sir William Osler first described a patient with sub – acute bacterial endocarditis (SABE), who at autopsy had a ruptured aortic aneurysm. (1) At the turn of the 19th century the term 'Mycotic' was used to describe any aneurysm resulting from infection, however recently the more accurate term 'Infectious aneurysm' has supplanted Mycotic aneurysm in the neurosurgical literature. (2) Mycotic aneurysms are rare accounting for 0.7 – 5.2% of all intracranial aneurysms. (3) The spontaneous rupture results in subarachnoid and Intracerebral hemorrhage, they are associated with significant morbidity and mortality, 60 – 70% in earlier case studies and 12 – 32% in recent reviews. (4) We report a rare case of a complete spontaneous recovery following rupture of a middle cerebral artery infectious aneurysm in a patient with SABE.

Keywords: Intracranial Infectious Aneurysm (IIA) / Mycotic Aneurysm, Spontaneous Resolution, Sub acute Bacterial Endocarditis (SABE), Intracerebral Hemorrhage (ICH)

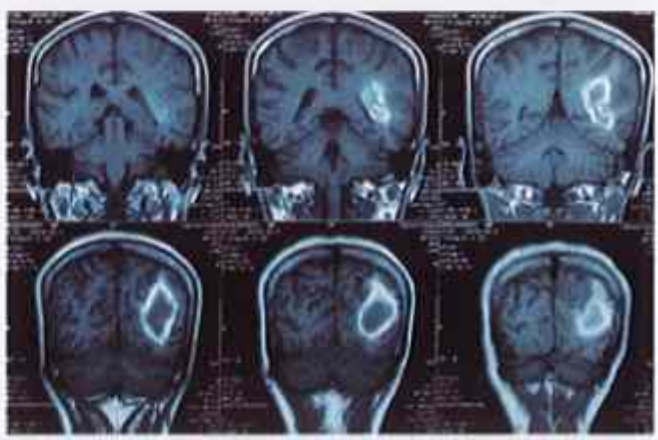
Case Report

Mr. R a 22 year old male, a known patient with Grade III Aortic Regurgitation (AR) and Grade II Mitral Regurgitation (MR) presented to our ward with fever with chills and rigors for 1 week duration. He did not have any other symptoms attributable to specific organ system.

On admission he had high fever, but was not pale or icteric. There were no signs of heart failure or features of embolic or immunological phenomena of SABE. He was tachycardic, and blood pressure was 100/50 mmHg. Cardiac examination revealed collapsing pulse, Cardiomegaly, Grade II AR and Grade II MR. The rest of the system examination was normal.

The inflammatory markers were elevated, with three repeated sets of blood cultures growing Viridans group of Streptococci. The trans thoracic echo cardiogram (TTE) as well as the trans – esophageal echocardiogram (TOE) were revealed features highly suggestive of SABE, and the patient was started on standard antibiotic therapy as per the national antibiotic guidelines (benzylpenicillin 2.4g, 4 hourly and gentamicin 80mg 12 hourly) for 28 days. The fever subsided and he went onto make a seemingly uneventful recovery.

On the morning of the last day of antibiotics (D 28) Mr. R complained of severe Left sided occipital headache, which was not relieved by analgesics. Later that morning he developed sudden unresponsiveness and Right sided tonic clonic seizures. Ruptured Intracerebral infectious aneurysm (IIA) was suspected and he was sent for urgent non – contrast CT scan of the brain which reveled large



BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

A rare presentation of overlap between Miller fisher and pharyngeal-cervical-brachial weakness variants of Guillan Barre syndrome.

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Abstract :

Miller fisher (MF) is an atypical variant of Guillain-Barre syndrome(GBS) which consists triad of symptoms: ataxia, areflexia and ophthalmoplegia. It is a monophasic paralyzing illness which some symptoms and course of the disease is similar to GBS. Though it is a clinical diagnosis, can be confirmed with presence of anti GQ1 b-anti bodies in serum. Pharyngeal Cervical Brachial variant (PCB) is often presents with acute oropharyngeal neck, shoulder muscle weakness with difficult swallowing. Very rarely these two variants can have overlap symptoms with anti GQ1b-antibodies positivity. We reported a rare case of a 29-year- old female presented with dysphagia, dysphonia, unilateral partial ptosis followed by bilateral lower limb, shoulder muscle and neck muscle weakness who responded to plasmaparesis.

Keywords: Guillain-Barre syndrome, Pharyngeal Cervical Brachial variant and Miller fisher syndrome

Case presentation

A 24-year-old female presented with nasal speech, difficult with swallowing and difficult to stand from squatting position for four days duration. Her symptoms started with dysphagia for solid food and then for liquids. Third day of admission, her condition got worsened with nasal speech, facial and neck muscle weakness. Forth day of her admission, she developed ataxia and unable to stand from squatting position which revealed that she had evidence of proximal muscle weakness. she also complained that she had flu like symptoms 2 week before current symptoms which improved spontaneously. Fifth day of her admission, she further deteriorated since she developed shortness of breath and drooling down upper eye lid of left eye and she was electively intubated due to impending respiratory arrest.

On examination she had partial left sided ptosis. Both pupils were normal. Direct and consensual reflexes were normal. Optic discs didn't reveal any papilledema or optic atrophy. There was no ophthalmoplegia. Visual acuity was 6/6 in both eyes and no colour blindness. Bilateral partial lower motor type facial nerve palsy was noted. Lower cranial nerves; IX, X, XI, and XII lower motor type paralysis were noted. Upper and lower

limb examination revealed, reduced power and tone both bilateral upper (2/5) and lower limbs (3/5). Upper limb weakness more than lower limb weakness. Deep tendon reflexes, all over the upper and lower limbs were diminished. All sensory modalities were preserved, and plantar reflex was down going in both lower limbs. Blood pressure was 110/70 with regular pulse rate 78 bpm, and no murmurs. Her lungs were clear with vesicular breathing. Abdomen found to be non-tender without any organomegalies and free fluid.

Her complete blood count revealed WBC 3000 N- 78% L- 14%, HB 12.1, PCV 36.8, PLT 273, MCV 84. ESR -102mm/hr, CRP <5, Na+ 136, K+ -4.1, CSF sample revealed plymorphs-00, lymphocytes -06, RBC-00, protein- 104mg/dl, sugar 64mg/dl (RBS-96mg/dl). cytology revealed no abnormal cells. Organisms - nil. Non-contrast CT, CXR, USS abdomen, UFR, ECG, Liver profile revealed normal, blood culture and urine culture were negative for organisms. Her CPK levels 145 (95-170). nerve conduction studies revealed latencies for median and ulnar nerve were prolonged with no definite evidence of demyelination. Ice pack test was positive. Acetyl choline receptor antibodies- negative. Anti GQ1 b antibodies not available.

Third day of her admission, we started Intravenous immunoglobulin (0.4 g/kg daily), and continued for three days, however symptoms did not improve following immunoglobulin treatment. The we started plasmaparesis. She had a complete recovery after five cycles of plasmaparesis.

Discussion

Initially this patient's presentation misleads us towards myasthenia gravis and acute demyelinating encephalomyelitis, because she had mixture of weakness with brain stem signs. Furthermore, icepack test was positive, we strongly believed that it could be myasthenia gravis. As we don't have Tensilon test, we straight away started neostigmine to this patient, following day patient conditions were deteriorated. We stopped neostigmine and stated intravenous immunoglobulin.

Atypical variants of Guillain-Barre syndrome is not uncommon but overlap between them can be uncommon. PCB variant of Guillain-Barre presents with acute oropharyngeal muscle, facial and upper limb weakness. Involvement of lower limbs is not a common presentation. In our patient, ataxic gait with diminished reflexes, ptosis and progressive oropharyngeal and facial muscle weakness resembled a picture of overlap between PCB and MF variants.

Both PCB and MF variants are being identified with evidence of axonal neuropathy rather than demyelinating neuropathy. Specific auto antibodies for MF variant considered as Anti GQ1B where Anti GT1a is more common in PCB variants. Many studies have shown that cross reaction between these two antibodies are well known feature.so in absence of either of these antibodies would not have excluded the particular variant.

No randomizes controlled studies have studied the effect of Plasmaparesis(PE) or intravenous immunoglobulin(IVIg) in patients with miller fisher syndrome (MFS). Observational studies have suggested that the final outcome in patients with MFS is generally good. Some clinicians believe that IVIg and PE did not influence the outcome of patients with MFS, presumably because of good natural recovery. For PCB variant the general principles of GBS management and timely immunotherapy, including the use of intravenous immunoglobulin or plasma exchange, have been recommended since its rapid progression and negative consequences.

Although in treating GBS and its variants, PE and IVIg considered as equally effective. patients who deteriorating despite of either treatment, best option still unknown. Time window to start second treatment option when patient is continuously deteriorating is still unclear. Our patient started to improve with PE which commenced on day three after completing the full course of IVIg.

Conclusion

Atypical GB variants may cross react certain autoantibodies.so absence of antibodies may not exclude the particular disease. Time interval between first and second treatment modalities should be

determined with a progressively deteriorating patient. A patient with worsening overlap symptoms of pharyngeal cervical brachial weakness and Miller fisher variant, one may suggest plasma exchange over immunoglobulin as it has rapid response.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Rare Presentation of a Rare Disease: Parsonage-Turner Syndrome

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Abstract :

Parsonage turner syndrome (also known as neuralgic amyotrophy) (PTS) is an acute brachial neuritis of an unknown origin,first reported by Dreshfeld in 1887 . Patients with Parsonage-Turner Syndrome initially presents with an acute onset of excruciating pain over the shoulder. Lower motor neuron type paralysis with or without sensory impairment develops several days to weeks after initiation of pain. The disease sometimes is self-limiting. Pain management is essential in the beginning of the course of the disease. Treatment with immunosuppressive therapy such as steroids and/or IV immunoglobulin (IV IG) remains controversial.

Keywords: Parsonage turner syndrom and neuralgic amyotrophy

Introduction

Parsonage turner syndrome (also known as neuralgic amyotrophy) (PTS) is an acute brachial neuritis of an unknown origin,first reported by Dreshfeld in 1887 (1). Thisrare disease affects mainly the lower motor neurons of the brachial plexus and/or individual nerves or nerve branches .The incidence was found to be 1.64 per 100,000 (in the population of Minnesota, United States)(2). It commonly affects men between the third and seventh decades of life (1). This usually presents as an acute onset of unilateral shoulder pain, followed by flaccid paralysis of shoulder muscles and para-scapular muscles several days later. PTS could be inherited or acquired, and the acquired form is idiopathic. However there is evidence to support that the acquired brachial neuritis could be due to an immune mediated reaction (3). Pathogenesis may be due to axonopathy or due to conduction block (4). The Hereditary form of neuralgic amyotrophy is autosomal dominant and it could be triggered by environmental factors (5).

Patients with Parsonage-Turner Syndrome initially presents with an acute onset of excruciating pain over the shoulder. Lower motor neuron type paralysis with or without sensory impairment develops several days to weeks after initiation of pain. The disease process is preceded by a viral or bacterial infection, vaccination or surgery. When the pain starts to subside,

the weakness develops. PTS also could present with involvement of the brachial plexus or involvement of isolated or multiple nerves rather than the plexus per se. As a result multiple muscles can be involved. Rarer forms of PTS could involve isolated or multiple cranial nerves too (6). Furthermore PTS patients can present with shortness of breath due to the involvement of the phrenic nerve and bilateral phrenic nerve palsy also has been reported (7).

PTS patients are diagnosed with nerve conduction test and electro-myelogram. Lumbar Puncture and nerve biopsies are not indicated.

The disease sometimes is self-limiting. Pain management is essential in the beginning of the course of the disease. Treatment with immunosuppressive therapy such as steroids and/or IV immunoglobulin (IV IG) remains controversial. A retrospective study using 47 patients (who have been followed up for 12 years) suggested that there is a place for IV IG (8). However, there are not enough randomized control study data to suggest the benefit of steroids or IV IG in treating patients with PTS due to the rarity of the condition.

Case Presentation

A 59 year old farmer presented with bilateral shoulder pain (R>L) for one week and weakness of both shoulders (R>L) over one day duration. The pain has been sudden onset and progressive. The pain score on the right was 8/10 and the left was 6/10. He was unable to abduct the right arm against gravity and he could abduct the left arm against gravity with much effort. Lower limbs were not weak. There was no history of trauma or any vigorous movements of the upper limbs and had no cervical spine pain.

He was treated for a bacterial infection two weeks ago. On examination tenderness over bilateral deltoid muscles were noted with fasciculation over the right deltoid and no tenderness over the cervical spine. On his neurological examination, the findings were confined to the upper limbs. Power on abduction and adduction of the right shoulder were 3/5 and the power of flexion and extension at elbow was 3/5. Power of the same functions of the left upper limb was 4/5. The motor functions of both upper limbs below the elbow was normal. There was a sensory impairment over the C-5 dermatome bilaterally. The Cranial nerve and the lower limb examination was unremarkable.

Complete blood count was normal and the ESR was 26. UFR and Creatinine Kinase was found to be normal. X-ray cervical spine showed intervertebral space narrowing at C6-C7. Nerve conduction studies and the electromyogram revealed bilateral asymmetrical sequential predominantly proximal brachial neuritis with demyelinating pathology. Cerebrospinal fluid analysis was normal.

Parsonage-Turner Syndrome was diagnosed as the patient had features of brachial neuritis with demyelination without a history of trauma and following a recent history of bacterial infection. The patient was treated with IV Dexamethasone and then with IV Immunoglobulin for 5 days after which the patient showed dramatic response. Meanwhile patient was referred for physiotherapy as well.

Discussion

Parsonage-Turner Syndrome is a rare syndrome affecting mainly the lower motor neurons of the brachial plexus and/or individual nerves or nerve branches. This usually presents as a unilateral brachial neuritis. The course of the disease is as such that it usually follows an infection. Patient develops a pain over the shoulder few days to weeks after the infection as this case. Several days later the pain declines and the weakness starts to develop (9). Therefore when a patient presents with a weakness followed by pain, the clinician should be vigilant to suspect PTS as one of the differential diagnosis.

Bilateral brachial neuritis as in this patient is a rare presentation of PTS. Furthermore the patient developed the weakness while the pain was persisting where the usual presentation is weakness preceded by the pain. Therefore this is a rare presentation of this rare disease.

Initially the patient was started on IV dexamethasone. As this patient developed bilateral PTS and the response to steroids was poor he was

started on IV immunoglobulin to which the patient responded dramatically. Therefore we would like to suggest that IVIg is a more appropriate treatment option in severe cases of PTS.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Hemi facial microsomia

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Abstract :

Hemi facial microsomia (HFM) is a congenital deformity that involves an absence or an underdevelopment of structures that arise from the first and second branchial arches on one side of the face. It is primarily a syndrome which manifests as hyperplasia of the face, the external ear, the middle ear and the mandible due to tissue deficiencies.Hypoplasia of the temporomandibular joints, masticatory muscles and facial nerve (second branchial arch) may coexist with HFM.The surgical management with distraction osteogenesis of a case presenting with HFM is reported.

Keywords: Hemi facial microsomia, hypoplasia,facial nerve, distraction osteogensis

Introduction

This rare developmental syndrome is the most common craniofacial anomaly following cleft lip and palate, with a prevalence of one in 5600 live births1,2. It affects males more than females in the ratio of 3: 2 with right side more affected than left side. 5

Goldernhar syndrome, also known as oculo-auriculo-vertebral (OAV) syndrome,which is characterized by incomplete development of the ear, nose, soft palate, lip, mandible, vertebral anomalies and epibulbar dermoids is associated with anomalous development of the first and second branchial arches. OAV is considered to be a variant of HFM3.

Treacher- Collins syndrome is an inherited condition in which there is lack of development of some bones in the face including mandible, zygoma with bilateral ear abnormalities. These patients present with micrognathia, hypoplastic zygoma and slanting of palpebral fissures9.

According to Converse et al when cranial defects are associated with HFM, the condition is called craniofacial Microsomia17.

The term hemifacial microsomia was coined by a German physician Carl Ferdinand von Arlt when he came across a case with an asymmetrical face, eye, and ear in 1881.

The etiology of HFM remains unresolved, but both genetics and environmental factors are implicated in the pathogenesis of the syndrome. There are other theories described in the literature based on embryologic, clinical and laboratory studies. laboratory studies

suggest that an early loss of neural crest cell may be the specific reason for this condition4 and vascular abnormalities appear to involve a disruption in the development of the first and second branchial arches during the first 6 weeks of gestation4.Hypoxia attributed to living at high altitude, maternal diabetes and teratogen including thalidomide and retinoic acid acting individually or collectively have been considered as possible causative factors for HFM. Poswillo postulated that the maternal intake of 10 mg/kg thalidomide as causing the rupture of stapedial artery leading to the development of this condition8.

There are so many classifications of HFM in the literature. The simplest classification is that of Paruzansky who classified HFM into three grades:

- Grade 1 - small but normal shaped mandible
- Grade 11 - abnormal and small shaped ramus
- Grade 111 - absence of ramus including TMJ7.

The characteristic diagnostic features of HFM include asymmetry of the face due to hypoplasia of the mandible, microtia and preauricular skin tags. The shifting of the facial midline to the affected side causes slanting of the mouth due to the corner of mouth higher on the normal side compared to the affected side8.

The disorder varies from mild to severe and occurs mainly on one side.

Conventionally grade 11 and 111 are treated by segment repositioning and costochondral graft reconstruction to increase the ramus volume.8. However, advanced treatment for Grade 1 and 11 is by the utilization of the technique of distraction osteogenesis (DO) for the correction of mandibular asymmetry6. Some cases with milder deformity may be treated with functional orthodontic therapy for induction of jaw growth (grade 1, 11)9.

Advanced imaging tools are useful for diagnostic and treatment purposes of HFM including cone beam computed tomography (CBCT), multi – slice computed tomography (MSCT), magnetic imaging (MRI) and three-dimensional surgical stimulation models.

The goal of treatment is to improve facial symmetry and to achieve a good function and facial profile. Multidisciplinary team approach is needed to manage patients with wide spectrum of disabilities. HFM should be managed in early life with the involvement of a multidisciplinary team of specialists including geneticist, physician, pediatrician , audiologist, speech therapist, plastic surgeon, maxillofacial surgeon, pedodontist, prosthodontist and orthodontist. Surgical management is staged with restoration of hard tissue during pre and post growth phases with procedures utilizing grafts to correct defects in the region and osteotomy procedures to correct the micrognathic mandible . Costo-chondral graft can be utilized to provide new growth sites. Distraction osteogenesis and genioplasty are common current procedures to restore hard and soft tissues deficiencies. The soft tissue deficiency in HFM is currently managed with microvascular free flaps.

Distraction Osteogenesis(DO) is a biological process of new bone formation between the surfaces of bone segments that are gradually separated by incremental traction. The process is initiated when a traction force is applied to bone segments and continues as long as the callus tissue can be stretched.
Distraction forces applied to the bone also create tension in the surrounding soft tissues, initiating a sequences of adaptive changes termed distraction histiogenesis13 .

The concept of bone lengthening by distraction was first described by Dr.A. Codivilla from Italy in 1905 he used external skeletal traction after an oblique osteotomy to lengthen the femur19.It was further developed and refined by Dr.Gavrilllizarov a Russian orthopedic surgeon in 1951 . He used the distraction osteogenesis for correction of post traumatic deformities of lower extremities of Russian war veterans15.

The use of distraction on craniofacial skeleton was reintroduced by McCarthy and colleagues in 199216.

In severe case of HFM (grade 111) distraction osteogenesis alone is not sufficient to correct the deformity without relapse. Combination of conventional orthognathic procedures and unilateral distraction osteogenesis will be required for these cases.

Case Report

A 20-year-old university student reported to the Oral and Maxillofacial unit, teaching hospital, karapitya with the main complaint of deformity of the right side of his face since birth. The patient was born full term to non-sanguineous parents with no significant family or antenatal history, but hearing defect on right side was detected in childhood. There was no history of HFM in the family. His medical history was not significant.

On examination, he was found to be fit and well with average build and normal mental status. Clinical examination revealed pronounced facial asymmetry involving the right side of his face. The right side face was found to be hypoplastic with an under developed mandible involving the ramus, the angle and the body. The mandible was retrognathic with deviation of the chin to the right on mouth opening. The right ear was found to be malformed (microtia). There were two preauricular skin tags on right and left side. Mouth opening was normal and no clicking sound noticed in both temporomandibular joints. Masticatory muscles showed no significant abnormality in size and consistency. Facial expression was normal. The patient was found to have right sided conductive hearing loss.

Intra-orally high arched V- shaped palate was noticed with crowding and inclination of the anterior teeth towards affected side.

Base on the main complaint and the clinical presentation a provisional diagnosis of HFM grade 1 of right side was made.Panoramic radiographs showed hypoplasia of the ramus, condyle, coronoid and body of the mandible on the right side with prominent antigonial notch(Fig. c). Lateral cephalogram revealed under development of mandible and highlighting a steep mandibular plane (Fig. d).

Surgical procedure

A surgical extra-oral incision was placed 2 cm below the inferior border of mandible at the angle. A blunt dissection done to reach the mandibular border and a subperiosteal dissection of the masseter muscle was performed. Osteotomy line was marked on the mandible outer cortex; the mandibular distractor was correctly positioned and fixed with four monocortical screws. The devices were then removed, a deepening of the osteotomy line with reciprocating saw was done on cortical bone and the osteotomy was completed. fracture accomplished and separated by osteotome. Care was applied when opening the ostectomy site to preserve the alveolar nerve. The devices were re-positioned to the mandible using the same screw holes and assessed for stability. Trial activation was done for checking movement of mandibular cut edges then deactivation done. The masseter muscle was repositioned and sutured to the medial pterigoid muscle with resorbable sutures. After one week, distracter was activated by two turns (1mm) per day for 25 days. The devices was removed, following the consolidation period (2 months).

Discussion

In this case distraction osteogenesis technique was used for the correction of mandibular deformity on right side and orthodontic treatment to correct the lower teeth crowding. If needed orthognathic surgery and soft tissue augmentation by microvascular surgery can be performed in future.Our patient wsa satisfied with this appearance denied further surgery on face.

Although bilateral sagittal split osteotomy is another alternative for HFM.

Advantages of distraction osteogenesis over bilateral sagital split osteotomy are relatively inexpensive, less invasive, less surgical time, good vector control , results are more predictable and reliable method of increasing the bone in a deficient mandible.

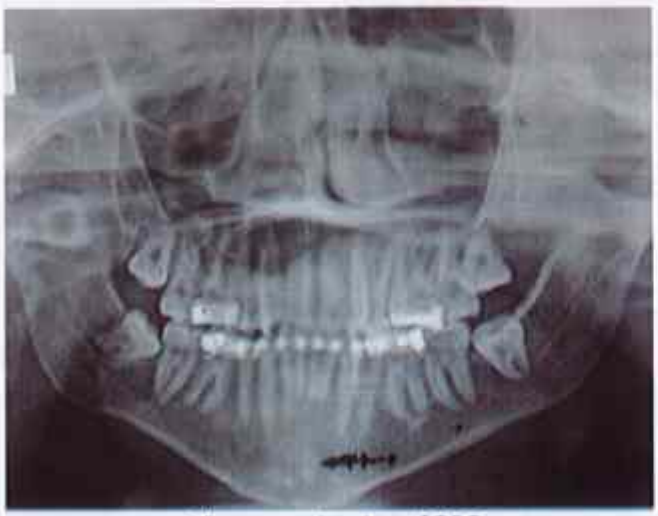
Some disadvantages have been encountered such as there is a chance to damage adjacent roots during osteotomy cut and hardware complications, fibrous nonunion or premature union of bone, infection that may hinder osteogenesis, treatment failure due to poor compliance, scarring of the skin with external devices, and malocclusion due to poor vector control.

Conclusion

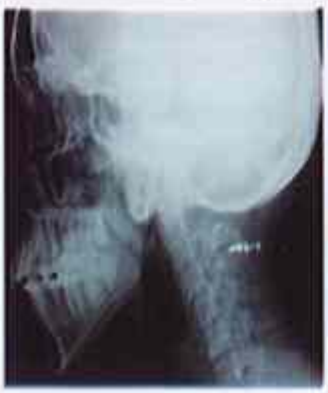
Satisfactory results in terms of dental occlusion and facial aesthetics were achieved in the case reported here of grade 1 hemi-facial microsomia patient where distraction osteogenesis and orthodontic treatment were employed as treatment modalities. We are in the process of referring this patient to a plastic surgeon for reconstruction of ear.

a) Pre-operative photograph front view

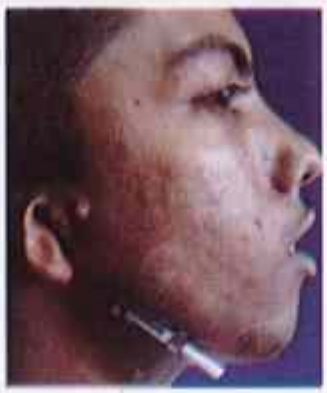
b) Profile view with mandibular osteo-distractor



c) Pre-operative view of OPG



b) Profile view with mandibular osteo-distractor



b) Profile view with mandibular osteo-distractor

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Recurrent Pulmonary Embolism in a Patient with Chronic Deep Venous Thrombosis Complicated with Recurrent Haemoptysis end up with Pulmonary Tuberculosis

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Introduction :

Venous thromboembolism (VTE) that includes deep vein thrombosis and/or pulmonary embolism is a frequent, severe, and potentially lethal disease. After a first episode, VTE has a strong tendency to recur1. Deep-vein thrombosis (DVT) is regarded a chronic disease as it often recurs. DVT affects most frequently the lower limbs2.Furthermore, the incidence of late, clinically important consequences (post-thrombotic syndrome and/or chronic thromboembolic pulmonary hypertension) increases in case of recurrent events1. Chronic thromboembolic pulmonary hypertension (CTPH) is associated with considerable morbidity and mortality3.Thromboembolic complications associated with infection by Mycobacterium tuberculosis have been reported in the literature that occurred in 1.5–3.4% of TB infection, which is a risk factor for deep vein thrombosis (DVT) related to the hypercoagulable state secondary to the inflammatory state(4). We reported a rare case of CTPH complicated with pulmonary tuberculosis4.

Keywords: Recurrent pulmonary embolism, deep venous thrombosis, pulmonary tuberculosis

Case history

A 43 years old salesman, known patient with epilepsy since age of 20, he is on regular medications, presented with progressively worsening exertional shortness of breathing for one year. He was investigated and found to have moderate to severe pulmonary hypertension (TRPG 58mmHg) in the 2D Echocardiogram. Trans Oesophageal Echocardiogram (TOE) revealed no intra cardiac shunts and structurally normal heart. His HRCT Chest showed a small pleural based opacity in the right side upper zone, which could be either a loculated small effusion or pleural thickening.

Two months later he developed left side leg swelling with shortness of breathing and found to have chronic DVT in left side lower limb deep venous system. CT Pulmonary Angiogram (CTPA) revealed major pulmonary embolism seen in right main pulmonary artery at the bifurcation to upper and lower lobes. His thrombophilic screening was normal (INR 1.08 and APTT 32 seconds). Echocardiogram at that time showed severe pulmonary hypertension (TRPG 88 mmHg).He was started on Warfarin and he maintained the therapeutic range of INR(2 -3) with a relatively higher dose of Warfarin (11.5mg) as he is on Sodium Valproate (enzyme inhibitor) and Carbamazepine (enzyme inducer) for his epilepsy treatment. Last month he developed four to five episodes of haemoptysis without any other

bleeding manifestations, fever, chronic cough or calf pain. All the times his INR was within the therapeutic range. Finally his sputum revealed Acid Fast Bacilli (AFB) positive in 3 samples and TB PCR was positive in Gene Expert study. He was started on anti-tuberculosis treatment.

Discussion

Venous thromboembolism (VTE) that includes deep vein thrombosis and/or pulmonary embolism[1]. Newly diagnosed DVT appears to occur in around 5 per 10 000 of the whole population per annum of whom 2 per 10 000 are idiopathic. An additional 1–2 per 10 000 have a new DVT combined with pulmonary embolism. The incidence of DVT is very strongly age related and in the population as a whole is comparable in men and women[6]. After a first episode, VTE has a strong tendency to recur. Though the current standard therapy, based on immediate anticoagulation with heparin or derivatives followed by vitamin K antagonists (VKAs), is very effective, recurrent VTE episodes or extension of the disease occur in a non-negligible portion of patients (≈4%after a DVT), even in the presence of adequate therapy. Furthermore, the benefit of anticoagulation is lost after discontinuation. Symptoms and/or signs that can be attributable to recurrent VTE occur frequently during the natural history of the previous event. This is why diagnosis of recurrent VTE should be based on objective assessments[1].

The risks of major bleeding during extended VKA treatment can be estimated in a range of 0.9–3.0% per year on the basis of the results of trials on duration of anticoagulation[1]. Symptomatic Chronic Thromboembolic Pulmonary Hypertension (CTPH) affects approximately 4 percent of patients within two years after a first episode of symptomatic pulmonary embolism, with no subsequent increase in incidence. These results challenge the current belief that CTPH is rare after an episode of pulmonary embolism and occurs long after the acute episode[3]. In our patient pulmonary hypertension got worsen from moderate to severe pulmonary hypertension within a period of three months. He had recurrent episodes of haemoptysis and initially we thought that it was the consequence of pulmonary hypertension.

Although deep venous thrombosis in association with tuberculosis is considered a rare occurrence, yet it should be considered particularly in the setting of severe pulmonary or disseminated tuberculosis5.The co-occurrence of tuberculosis and deep venous thrombosis is reported to be high during initial phase of the disease. Hypercoagulability in tuberculosis can be attributed to several factors like decreased anti-thrombin III and protein C, elevated plasma fibrinogen levels, and increased platelet aggregation. In addition, systemic inflammatory state prevalent in tuberculosis causes endothelial cell damage which in turn predisposes to local thrombosis5.Couple of weeks later, haemoptysis got settled and we continued his warfarin and anti-epileptic medications.

Conclusion

Even though recurrent pulmonary embolism manifesting as recurrent haemoptysis is an expected finding in a patient with chronic Deep Venous Thrombosis (DVT), clinician should be aware of the rare co-occurrence of DVT and tuberculosis as well.

Competing interests

The author declares that no competing interests.

Funding

This research received no funding support

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Therapeutic dilemma: Acute Hypertensive Cardiac Failure during pregnancy due to Thyrotoxic Crisis

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Introduction

Hyperthyroidism is a common metabolic disorder with cardiovascular manifestations. It often causes classical high output heart failure because of decreased systemic vascular resistance and increased resting heart rate, left ventricular (LV) contractility, blood volume, and cardiac output. However, thyrotoxic cardiomyopathy with severe LV dysfunction (dilated cardiomyopathy) is rare. Heart failure (HF) is most commonly seen as a result of longstanding, often untreated, thyrotoxicosis with coexistent atrial fibrillation (AF). HF is a major cause of morbidity and mortality in pregnancy. Cardiac failure during pregnancy is usually related to preeclampsia/eclampsia. While hyperthyroidism can easily lead to hypertensive cardiac failure and may harm the fetus. Furthermore, it is sometimes difficult to distinguish hyperthyroidism from normal pregnancy. Early diagnosis and treatment are important to rescue both the mother and the fetus. We reported a rare presentation of thyrotoxicosis in pregnancy with left ventricular dysfunction.

Keywords: Hyperthyroidism, cardiac failure and thyrotoxic cardiomyopathy

Case Presentation

A 27-year-old pregnant mother with 3rd pregnancy, admitted to ward because of progressive difficulty in breathing and both hand fine tremors at the period of amenorrhea(POA) 33 week of gestation. she complained of palpitation and chest discomfort without history of syncope or fainting episode. She had bilateral pitting leg edema up to mid calf level. Her antenatal records saw poor weight again in this pregnancy period (only 4kg gain). She was pointed out hypertension without proteinuria during this ward admission. She was alert but showed severe hypertension and tachycardia with anterior neck lump. Her oxygen saturation rapidly deteriorated to 94% with reservoir mask supplying 10 L/min oxygen, she was transferred to our CCU for the non-invasive ventilation. On admission, her blood pressure was 180/100 mmHg, pulse rate 130 beats/min, and body temperature 37.6◦C. Laboratory data showed mild hepatic dysfunction and proteinuria. Chest X-ray exhibited bilateral pulmonary infiltration and cardiac dilatation (cardiothoracic ratio, 62%) (Figure 1). Echocardiography showed decreased wall motion (ejection fraction-20%) and global hypokinasia with evidence of thyrotoxic cardiomyopathy with sever LV impairment. She was initially treated as having acute

cardiac failure due to pre-eclampsia/eclampsia. Nitroglycerin (0.5–1μg/kg/min) and furosemide infusion were administered to decrease preload and after load. Blood pressure not controlled then managed with intravenous hydralazine infusion. Caesarian section was performed on the 2nd day of admission. Her baby was 2.3k g female and APGAR score was normal and admitted to SBCU because of general anesthesia. The baby handed over to mother on 2nd day. On postoperative, pulmonary congestion and oxygenation were improved. Immediate after Caesarian ECHO (EF 45%) and she was successfully extubated. On post-operative day of 3, she was discharged to general ward. On the same day, thyroid function tests taken on admission showed elevated serum free triiodothyronine and thyroxine levels and physical findings and found that she had hoarseness and felt shortness of breath on effort before pregnancy, and her thyroid was diffusely enlarged. Grave's disease was suspected, and carbimazole (60 mg) and propranolol hydrochloride (30 mg) were administered, where upon her pulse rate declined from 130 to 100 beats/min. At the time of discharge, echocardiography showed improved wall motion (ejection fraction 50%), and blood pressure was back to near normal. Thyroid function tests taken after discharge which showed that decreased serum-free triiodothyronine and thyroxine levels and declined thyroid stimulating hormone level (Table 1).

Table 1 Thyroid function test

Table 1	1st report	3rd day	On discharge
TSH	<0.016	<0.015	<0.015
FT4	>90	77.8	59.5

Figure 1 Chest X-ray

Discussion

We encountered a patient who suffered acute hypertensive cardiac failure due to hyperthyroidism. There are several causes of hypertension during pregnancy. Among these causes, pre-eclampsia/eclampsia is most common. Hyperthyroidism is less common cause for hypertension with low-output heart failure during pregnancy. However, approximately 10% of women with untreated thyrotoxicosis develop heart failure, and uncontrolled hyperthyroidism during pregnancy is associated with spontaneous abortion, premature labor, low birth weight, stillbirth, preeclampsia, and heart failure. In this case, we initially assumed her symptoms were attributed to pre-eclampsia/eclampsia, simply because it is causes of secondary hypertension during pregnancy. Eclampsia/pre-eclampsia, Renovascular disease, Pheochromocytoma, Primary aldosteronism, Oral contraceptives, Sleep apnea syndrome, Hypothyroidism, Hyperthyroidism Primary hyperparathyroidism and Cushing's syndrome the most common cause of cardiac failure in pregnancy. It is difficult to distinguish hyperthyroidism during normal pregnancy because some of the symptoms of pregnancy are similar to those of hyperthyroidism. While she had several clues such as shortness of breath after 30weeks of pregnancy with bilateral fine tremors and poor weight gain during this pregnancy period. However, careful examination of thyroid gland might lead to earlier diagnosis. Poor pregnancy weight gain and intrauterine growth retardation also corresponded to hypertension. We used vasodilators and diuretics to alleviate pulmonary congestion, which were also ineffective in thyrotoxicosis. Rapid delivery of the baby might reduce mother's oxygen demand; however, if hyperthyroidism was diagnosed earlier, Caesarian section might not be avoided.

Conclusion

We encountered a case of acute hypertensive cardiac failure secondary to undiagnosed hyperthyroidism during pregnancy. Although diagnosis of endocrine disorders during pregnancy is difficult, we should bear in mind that it may cause cardiac failure during pregnancy

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

A rare case of pulmonary hypertension secondary to Hereditary spherocytosis without splenectomy; is it a rare coexistence or causally related

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Abstract :

Pulmonary hypertension (PH) is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC)1. WHO classifies PH into five classes, chronic hemolytic anemia and splenectomy describes under PH with multifactorial mechanisms 2. Here we present a case of pulmonary hypertension associated with hereditary spherocytosis, without splenectomy.

Keywords: Pulmonary hypertension and hereditary spherocytosis

Introduction

Chronic hemolytic anemia is a known condition to cause pulmonary hypertension. Various mechanisms have been postulated in its pathogenesis. Thalassemia and sickle cell anemia are well known to cause PH mainly due to chronic thromboembolic disease. The pathogenesis of pulmonary hypertension in hemolytic disorders is likely multifactorial, including hemolysis, impaired nitric oxide (NO) bioavailability, chronic hypoxemia, chronic thromboembolic disease, and asplenia3. Though the pathophysiology of sickle cell anaemia causing PH is well understood, there are only limited literature for HS associated with PH. Splenectomy has been identified as a risk factor for the development of PH, particularly in patients with hemolytic disorders. Splenectomy may trigger platelet activation, promoting pulmonary micro thrombosis and red cell adhesion to the endothelium3. Smedema JP et.al described case of hereditary spherocytosis lead to pulmonary hypertension after splenectomy4. In this case occurrence of PH without splenectomy warrants consideration of alternate pathophysiology in causality.

Case report:

31year old housewife presented with gradual onset of exertional dyspnea over last 3months duration. Which was progressive. She also noticed yellowish discoloration of her eyes during last 2 months. She had similar few episodes in the past which did not require blood transfusions and was self-limiting. She denies any family history of similar episodes. She didn't have pale stool or dark urine. She has never been transfused any blood products. And she denied any high risk behaviors. Her past medical history was otherwise unremarkable. She was not on any medications including native medications. She was a product of consanguineous

marriage and she has three siblings, but none of them exhibit similar condition.

She was pale and icteric, mildly dyspneic at rest. Jugular venous pressure was elevated and she had mild pitting ankle edema. Her pulse rate was 80 beats per minute, sinus rhythm. Blood pressure was 120/80 mmHg. there was parasternal heave, loud second heart sound, dual rhythm and no murmurs. Her abdominal examination revealed mild hepatosplenomegaly and no free fluids.

Her 2D echo showed severe pulmonary hypertension as evidenced by TRPG of 100 mmHg and right ventricular dilatation. Both trans thoracic and esophageal echo didn't reveal any shunts. ejection fraction was 50%. Her full blood count (WBC 12.27 x 103 /mm3, Hb 10.8 g/dl, Platelet 273 x 103 /mm3) and blood picture revealed Spherocytic hemolytic anemia. Reticulocyte count was 4.5%. LDH was mildly elevated with negative direct and indirect coombs tests. Her transaminases were normal but she had persistent indirect hyperbilirubinemia, (total bilirubin 255umol/l, indirect bilirubin 241umol/l) ultra-sound abdomen revealed multiple gallstones in gall bladder and mild hepatosplenomegaly. Osmotic fragility test, which is a screening test for HS, was positive.

Her chest x ray and HRCT were normal. Lung function test revealed only mild restriction. ABG was normal other than mild hypoxemia which may be secondary to pulmonary hypertension. CT pulmonary angiogram didn't reveal thromboembolism. Her renal profile, transaminases and hepatitis serology, thyroid functions, retroviral screening, ANA were normal. She was diagnosed as severe pulmonary hypertension and hereditary spherocytosis.

She was started on diuretics, sildenafil and folic acid. Arranged medical and hematology clinic follow up with functional assessment with a 6-minute walk test. Family screening was arranged and her daughter also showed positivity for osmotic fragility test.

Discussion

Hereditary spherocytosis (HS) affects one in 3000 people with dominant inheritance in 75% of cases worldwide5. There are only a few reported cases of hereditary spherocytosis causing pulmonary hypertension, in a patient who had not undergone splenectomy. Prevalence of idiopathic pulmonary hypertension is 10 cases per million. So co-existence of two rare diseases in a one person is a rarity, hence this may be causally related. Impaired NO bioavailability and chronic hypoxemia may play etiological role here, which need further evaluation in future.

Our index case is unique for two reasons. One is PH was diagnosed first and HS was a retrospective diagnosis. Secondly in our patient PH developed without splenectomy.

Conclusion:

Occurrence of pulmonary hypertension in HS without splenectomy may causally related. And pulmonary hypertension is an unusual presentation of the disease.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Rheumatoid arthritis patient on Methotrexate presented with subacute onset shortness of breath: A case of Methotrexate induced hypersensitive pneumonitis

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Abstract :

Abstract : Methotrexate is a disease modifying anti rheumatoid drug commonly used in treatment of rheumatoid arthritis and in many other inflammatory conditions. This is a case of methotrexate(MTX) induced hypersensitive pneumonitis in a patient with rheumatoid arthritis describes, clinical presentation, investigation findings and management principals of the infrequently encountered diagnosis.

Keywords : Methotrexate, hypersensitive pneumonitis, pulmonary toxicity, rheumatoid arthritis

Introduction

Methotrexate, a folic acid analogue, can be used to manage a spectrum of inflammatory and neoplastic disorders. Approximately 1% to 7% of patients receiving MTX treatment will develop pulmonary side effects (1,2). MTX pneumonitis characteristically presents with respiratory symptoms such as, shortness of breath, exertional dyspnea, nonproductive cough with or without fever, usually within one year of treatment (3). It has been documented after four months up to eleven years following treatment initiation (4). It's a diagnosis of exclusion. HRCT chest is the investigation modality of choice, which demonstrate ground glass appearance, reticular nodular appearance, with or without focal consolidation. Lung function test may demonstrate restrictive pattern, while bronchoscopy, bronco alveolar aspirate analysis would be nonspecific. Rheumatoid associated interstitial lung disease (RA-ILD), atypical pneumonias such as pneumocystis cainii and pneumocystis jiroveci, diffuse alveolar hemorrhage would be the close differential diagnosis for MTX pneumonitis. Cessation of MTX may itself be sufficient for symptom resolution and condition reversal (2). However, corticosteroid treatments have anecdotally been shown to be effective in accelerating symptom improvement. Outcomes for patients who experience MTX toxicity are usually good, with a low rate of progression to pulmonary fibrosis.

Case report

54 years old female house wife, previously diagnosed patient with rheumatoid arthritis for ten years, on MTX for similar duration presented with gradual onset progressive moderate shortness of breath and nonproductive cough over four days' duration

without fever. She has had deforming poly articular rheumatoid arthritis involving both hands symmetrically, which was in clinical remission with good functional status. Her past medical history was unremarkable apart from seropositive rheumatoid arthritis. she had no pets at home and she denied any high risk sexual behaviors.

She was dyspneic, tachypneic, afebrile and her SpO2 was 68% on room air. she had deforming poly arthritis involving both hands which was in clinical remission. Her respiratory examination revealed bilateral coarse crepitations over lower and mid lung zones. Her cardiovascular, abdominal and neurological examination was otherwise normal.

Her arterial blood gas analysis demonstrated type 1 respiratory failure with severe hypoxemia of PO2 38mmHg on room air. Her full blood count revealed neutrophil leukocytosis with raised inflammatory markers (ESR-120mm/1sthr). chest radiograph showed reticular-nodular shadowing(fig.1). Her HRCT chest revealed ground glass appearance, air trapping, areas of focal consolidation and mild background lung fibrosis (fig. 2a). Her bronchoscopy revealed normal bronchial anatomy and bronco alveolar lavage showed nonspecific lymphocyte predominate aspirate. Her trans bronchial lung biopsy was normal and negative for malignancy or granuloma. BAL for bacterial culture

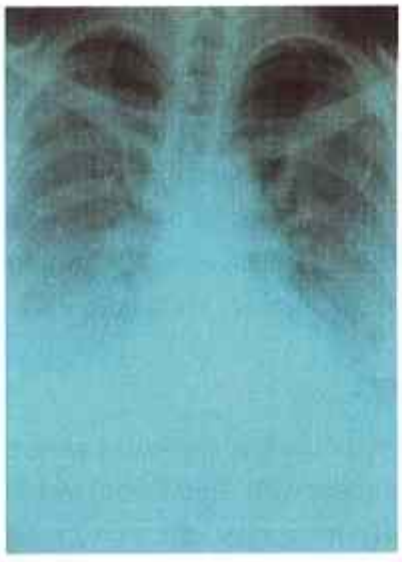

Fig.1

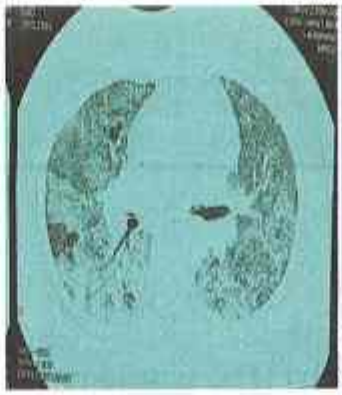

Fig.2a

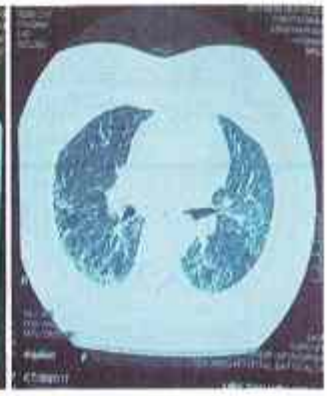

Fig.2b

and pneumocystis cainii PCR was negative. Her STD screening was normal including HIV status. Her rheumatoid factor titer was elevated.

MTX- pneumonitis was suspected and treated with intravenous methyl prednisolone, followed by oral prednisolone. Her clinical respond to therapy was monitored with serial arterial blood gas analysis, which showed marked improvement in saturation and hypoxemia with the therapy. Her repeated HRCT chest following one week of treatment showed marked improvement (fig.2b). Methotrexate was omitted and replaced with azathioprine. She made a good recovery.

Discussion

With the given history of subacute nonspecific respiratory involvement in the background of rheumatoid arthritis and therapeutical use of methotrexate, warrants, to think about RA-ILD, MTX –pneumonitis, atypical pneumonias such as PCP/ PJP as the close differential diagnosis. Cryptogenic organizing pneumonia (COP) may present in similar fashion with good respond to steroids. But radiological findings, clinical course of the disease and quicker treatment respond to steroids were more favors towards hypersensitive pneumonitis than COP. Negative retroviral screening and negative PCP –PCR in bronco alveolar aspirate ruled out pneumocystis carinii pneumonia.

Since HRCT chest showed background mild fibrosis it is advisable to change methotrexate to another immunosuppressant. These patients need long term monitoring of lung functions in order to detect potential progressive lung fibrosis.

Conclusion

MTX – pneumonitis is infrequent, potentially treatable condition with generally good short and long term outcomes. Clinical suspicion, supportive investigations and exclusion of other conditions aid for diagnosis. Treatment is with stopping the culprit drug and administration of steroids.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Thrombotic microangiopathy due to Russell's viper bite in Batticaloa

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Introduction

There are several species of snake present in SriLanka, among that seven species of snakes are medically important poisonous snake such as Russell's viper, Hump nosed vipers, Cobra, Saw scale viper, Indian Krait, Common Krait and Sea Snake. Snake bite can cause different types of clinical manifestation such as neurological manifestation, clotting abnormalities, renal toxicity, local reaction and muscle damage. We reported case of acute kidney injury due to possible thrombotic microangiopathy (TMA) following Russell's viper bite, which is rare entity in snake bite (1). Our case highlights the importance of considering TMA in the differential diagnosis of persistent renal impairment after snake bite. Furthermore, early plasmapheresis hasten the recovery and prevent the permanent renal damage.

Keywords: Russell's viper, thrombotic microangiopathy and acute kidney injury

Case History

A 60-year-old lady was transferred to emergency department at Batticaloa Teaching hospital, six hours after Russell's viper bite on her tip of Right middle finger. Snake was identified by local hospital medical officer and noted in transfer form. There was past history of Bronchial Asthma but not on regular medications. On admission, she was experiencing nausea, abdominal pain, and local pain at the bitten site. On examination there was local swelling of the bitten hand. Her blood pressure was140/80mmHg, and pulse rate was 88/min. She didn't have any neurological signs. Other system examination was unremarkable. Her 20-min whole blood clotting test (20WBCT) on admission was abnormal. She was treated with three cycles of Anti venom in six hourly interval until her 20WBCT become normal. She developed Venom Induced Consumption coagulopathy (VICC) on first day of admission with evidence of thrombocytopenia (76000), increased APTT (39sec) and increased INR (2.08). Clotting abnormalities resolved next 48hours. Thereafter patient developed oliguric acute renal impairment, persistent thrombocytopenia and dropping hemoglobin (Table-1).Her blood picture revealed that evidence of hemolysis and also she had elevated LDH. As patient developed triad of acute renal impairment, thrombocytopenia, intravascular hemolysis with normal clotting profile Thrombotic microangiopathy (TMA) diagnosis was made. After diagnosis of TMA she underwent five cycles of plasmapheresis and three cycles of hemodialysis. Her renal function gradually improved and repeated blood picture revealed no evidence of hemolysis.

Table-1 Summary of investigation

	15/6	16/6	17/6	18/6	20/6	24/6	27/6	29/6	2/7	4/7	10/7
WCC* 10^3	7.02	19.36	20.88	18.94	12.18	10.05	17.50	31.04	8.29	10.16	
N/L	53/40	95/4	82/14	82/12	67/14	76/12	96/2	90/7	68/17	67/16	
Hb(g/dl)	11.0	9.1	7.3	7.9	7.2	7.6	8.6	7.9	9.2	8.9	
Plt* 10^3	76	154	105	106	101	209	256	172	155	118	
BU(mg/dl)	32	110	167		87	61	85	118	111	88	44
S.cr(mg/dl)	1.0	3.1	5.1		3.0	6.9	6.6	8.3	7.9	6.1	1.9
CRP(mg/l)					40		10	166	37		
INR	2.08	1.38	1.23	1.0		1.0		1.15	1.15		
APTT(sec)	39	68	31	39		39		27			
UOP+(ml)	500	170	100	30		650	1100	1050	1300	2475	
RX*			HD	HD	HD	TPE	TPE	TPE			

* RX- Treatment, +UOP- Urine output for 24 hours

Discussion

Russell's viper bit showed a spectrum of clinical manifestations ranges from neurological manifestation, clotting abnormalities, renal toxicity, local reaction and muscle damage.Venom-induced consumptive coagulopathy (VICC), a commoner and well-known hematological manifestation of snakebites due to activation of the coagulation cascade via a snake procoagulant toxin (2). VICC is rapid onset and resolution of coagulopathy within 24–48 hours, and the absence of non-renal end organ damage seen in VICC make it a separate entity from DIC. TMA is a rare complication of snake bite which is characterized by the triad of acute renal failure, thrombocytopenia, and MAHA (2). TMA tends to occur soon after VICC or can co-exist with VICC. But persistent renal impairment with thrombocyto penia in the absence of clotting abnormality should raise the suspicion of TMA and should be undergone blood picture examination to look for evidence of hemolysis. Although exact mechanism of TMA in snakebites remains largely unknown, most of authors accepted mechanism is a toxin in the venom may be precipitating endothelial damage that culminates to TMA (3).

Conclusion

Russell's viper bit showed a spectrum of clinical manifestations ranges from neurological manifestation, clotting abnormalities, renal toxicity, local reaction and muscle damage. Venom-induced consumptive coagulopathy (VICC), a commoner and well-known hematological manifestation of snakebites due to activation of the coagulation cascade via a snake procoagulant toxin. Early blood picture may alert you weather patient go to TMA or not. Early plasmapheresis is the mode of treatment for TMA(4). Further studies needed to find exact mechanism of TMA and survival benefit of plasmapheresis on TMA

Competing interests

The author declares that no competing interests.

Funding

This research received no funding support

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Unusual presentation of a cryptogenic brain abscess

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Abstract :

Brain abscess is a focal intracranial infection characterized as an area of cerebritis that evolves in a collection of pus surrounded by a vascularized capsule. Intracranial cerebral abscess is a potentially fatal neurosurgical emergency. bacterial species represent the most common etiology in immunocompetent individuals. The incidence of brain abscesses ranges from 0.4 to 0.9 per 100,000, with a high predisposition among immunocompromised patients and in those with disruption of the blood-brain barrier. Organisms can reach the central nervous system by spreading from a contiguous source of infection, hematogenous dissemination, or trauma, but there are cryptogenic brain abscesses in 10%-35% of cases. The frontal lobe is the predominant site of cerebral abscess in patients with paranasal sinusitis. We reported a case of a 54-year- old male, presented with headache and sudden loss of vision, affected by left occipital brain abscess compressing ipsilateral occipital horn with midline shift of the lateral ventricles.

Keywords: Cryptogenic brain abscess, and brain abscess

Case report

A 54- year-old school teacher with a past history of hypertension, presented with throbbing type headache for 10days and while in the medical ward developed sudden loss of vision.There was no history of fever, photophobia or association with nausea or vomiting, seizure or altered behavior. However, he developed memory impairment with right side upper and lower limb weakness 48hrs following the admission. On general examination patient was alert, on admission GCS was 15/15, Mini mental state examination (MMSE) 29/30, however 48 hours later his GCS was 11/15 and MMSE 18/30. Blood pressure was 150/100 with pulse rate was 76/min, no murmurs or thrills or added heart sounds were noted. Respiratory and abdominal examination revealed normal. There was no neck stiffness. Visual acuity 4/6 in B/L eye. Right side homonymous hemianopia. Fundus was normal in both eyes. Other cranial nerves were intact. On admission both upper and lower limbs power was normal, but 48 hours after admission., there was an obvious weakness in right upper and lower limbs with reduced power (3/5), increased tone, exaggerated reflexes with up going plantars. All kind of sensory modalities were preserved.

Full blood count was 9.68 X109/l with neutrophil leukocytosis, Hb was 14.1g/dl, Platelets was 215 X109/l, ESR was 17mm/h, CRP was 05, ECG revealed sinus rhythm without any ischaemic events. Liver profile, lipid profile, blood and urine cultures did not reveal any abnormalities. In Echo cardiogram there was concentric left ventricular hypertrophy without vegetations. Fasting blood sugar was 95mg/dl. HBV, HCV, VDRL and Retroviral studies were negative. Non-contrast computed tomography revealed left occipital region hypodense area with clear demarcation (Figure 1).

Patient was transferred to national hospital SriLanka, where contrast T2W MRI brain performed and there was a mass lesion in left occipital region size measuring 4.7cmX4.2cmX2.8m with large amount of perilesional oedema which caused displacement of the left occipital horn and midline shift of the ventricles. According to the MRI, radiological diagnose was made as a left side occipital abscess and immediately intravenous empirical antibiotic treatment was started and neuro navigation guided excision of abscess was performed. Pus culture and gram stain revealed gram positive cocci in clusters-Staphylococcus aureus. Intravenous co-amoxiclav and ciprofloxacin continued for 10days of duration where patient had complete recovery without residual deficits.

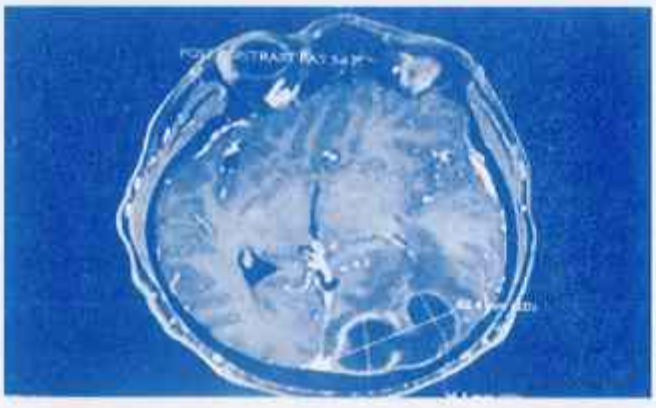

Figure: CT-brain revealed abscess located at left occipital area.

Discussion

Brain abscess is a serious and life-threatening clinical entity. Pyogenic infection of brain parenchyma begins with a localized area of inflammatory change referred to as cerebritis. Brain abscesses are often attributed to hematogenous spread, contiguous spread, recent neurosurgical procedure, or penetrating head trauma. The most common causative organisms found were Streptococcus species, particularly S.viridians and S.pneumonia, Enterococcus, and Staphylococcus species, mainly S.aureus and S.epidermidis(1). The frontal lobe is the predominant site of cerebral abscess in patients with paranasal sinusitis(2)(3). However, causes are remaining unknown about 30% of overall cases. Staphylococcus aureus accounts for 10%- 20% of isolates of brain abscesses in a general population, usually reported in patients with cranial trauma or endocarditis. An important risk factor for the development of a brain abscess is an acute or chronic immunosuppressed state(4), particularly patients who are solid organ transplant recipients, bone marrow transplant recipients, or persons with the acquired immunodeficiency AIDS(5). Brain abscesses tend to progress through a pattern of early cerebritis progressing to encapsulation. The encapsulation process involves neovascularization, fibroblast accumulation, and gliosis, often leading to seizures during the encapsulation phase and as long-term sequelae(6).

It is unusual in our patient to have staphylococcus brain abscess, without having a source, route and relevant clinical symptoms at presentation. Since patient is a school teacher occupational hazardous is less likely. Initially we thought that it could be a stroke, because of the presentation, however subsequent CT brain gave us little bit suspicion about the lesion. Furthermore, MRI diagnosis was made as a left side occipital abscess and immediately intravenous empirical antibiotic treatment was started and neuro navigation guided excision of abscess was performed

Conclusion

Advanced magnetic resonance imaging techniques, such as diffusion, perfusion, susceptibility weighted imaging, and magnetic resonance spectroscopy, enhance the imaging differences between different pathologies, it is crucial to diagnose brain abscesses with atypical presentation. High clinical suspicion and timely investigations will increase the accuracy of diagnosis and positive outcome.

Conflict of interest: None declared

Funding: This research received no funding support

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Prosthetic management of a patient with Acquired Palatal Defect.

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Introduction

The palate is the barrier between oral and naso-maxillary cavities and the violation of this barrier creates an anatomical defect which allows these cavities to become one confluent chamber(1) and it interferes with normal physiological functions of speech, mastication and deglutition. Further, this defect creates serious consequences such as nasal regurgitation, recurrent infections, changing facial appearances and psychological implications. The reconstruction of this defect may restore these functions and improve the quality of life for the patient. Although the surgical reconstruction with a tissue graft was reported to restore these surgical defect, it is not always possible due to the reduced vascularity of this region(2). On the other hand, prosthetic-obturator provides an immediate rehabilitation without a need for further surgery and it also provides an easier access to inspect the surgical wound(3). This case report describes the management of a young patient with a palatal defect following the surgical resection.

Case report:

A 20 year-old male patient had been diagnosed to be suffering from a malignant peripheral nerve sheath tumor in maxilla and referred to the Restorative Unit A, Institute of Oral Health, Maharagama for prosthetic rehabilitation of future surgical defect, since he was awaiting to undergo maxillectomy.

His past medical history was not significant. He had an experience in dental treatment. His oral hygiene practice was ordinary. He was not consuming alcohol and any forms of tobacco.

On examination, there was no facial deformity. He had all teeth except upper right lateral incisor & upper left 3rd molar and the upper left 2nd premolar & lower left 1st molar had composite restorations. There was a lesion in the right side, anterior part of the palate extending through alveolar ridge in between right central incisor & canine with a dimension of about 3cm length and 1.5cm width. Margin of lesion was erythromatous and slightly oedematous (fig 3.1).

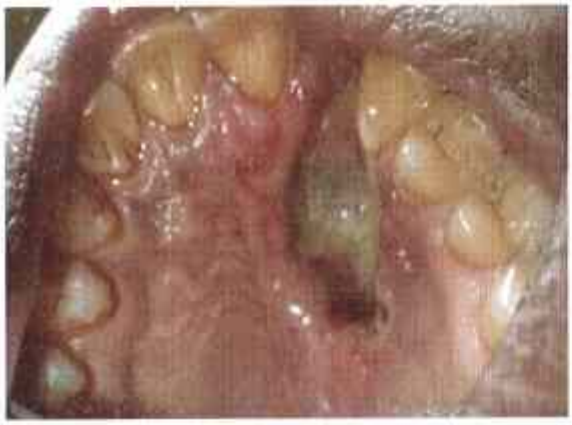

Figure 3.1: Pre surgical lesion (mirror view)

His mouth opening was within a normal range and no signs of xerostomia were detected. The pulp sensibility test showed that upper left 2nd premolar & lower left 1st molar were non-vital. The radiographic examination (Dental Panoramic Tomography -DPT) revealed the endodontic treatment of these non-vital teeth (fig 3.4).

Considering the patient' treatment needs and expectations, the following pre-surgical and post-surgical management plan was formulated.

Pre-surgical management;

Patient was educated on the importance of oral hygiene and the correct brushing and dental flossing techniques were educated. Advice was given on the self use of fluoride such as fluoridated tooth paste. Full mouth scaling was carried out. Upper and lower study casts were made to fabricate the immediate-obturator according to the surgical incision line suggested by Oral Maxillo- Facial surgeon.

Post-surgical management;

On examination, the surgical lesion was packed with a roll of gauze. On the removal of gauze, the lesion was appeared in the anterior part of right maxilla, but it crossed the midline and was passing between left lateral incisor and right 1st molar (Figure 3.2).

Preliminary-impression was taken using the alginate impression material (fig 3.3), from which the preliminary-cast was poured. From this cast acrylic special-tray was fabricated and special-impression made.

Figure 3.2:
The lesion following surgery

Figure 3.3:
Preliminary impression

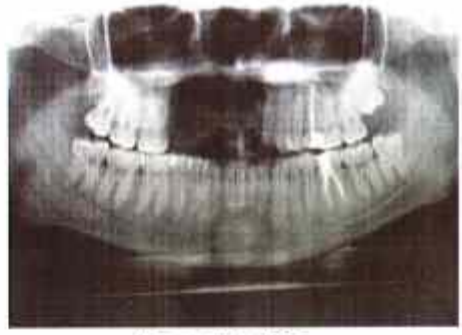

Figure 3.4: DPT

use of fluoride such as fluoridated tooth paste. Full mouth scaling was carried out. Upper and lower study casts were made to fabricate the immediate-obturator according to the surgical incision line suggested by Oral Maxillo- Facial surgeon.

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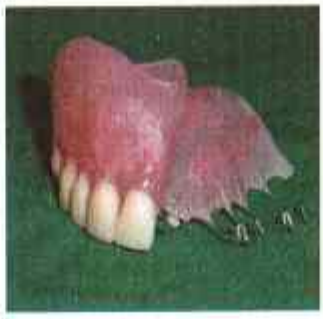

Figure 3.5:
Intermediate-obturator

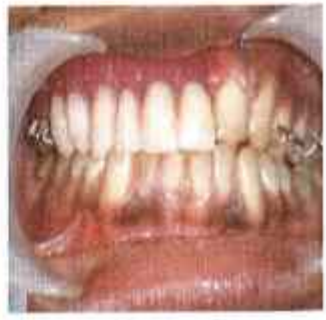

Figure 3.6:
Obturator inside the mouth

During the review period, necessary modifications in the prosthesis were carried out. At the end of fifth month, surgical defect was well established therefore, the definitive-obturator was planned.

The study casts were made and surveyed and the following designs of the framework were adopted based on Aramany guide line.

1. Cingulum rest with minor connector on left lateral incisor.
2. Occlusal rests on left 2nd premolar& 1st, 2nd molars and right 1st,2nd molars.
3. Gingivally approaching I-bar clasp on left lateral incisor, reciprocated by palatal major connector.
4. Occlusally approaching clasps on 1st and 2nd molars in both sides, reciprocated by palatal major connector.
5. Guide planes on mesial proximal surfaces of left lateral incisor and right 1st molar.

According to the design, tooth preparation was carried out to adopt the components of obturator. Two-stage putty wash impression was taken (fig 3.7) to construct the metal framework (fig 3.8).

On the following visit, the cobalt-chromium metal framework was tried-in to confirm its retention and stability. The jaw relationship registrations were performed. These were mounted on a semi-adjustable articulator with the help of inter-occlusal records and setting up of the teeth was carried out.

Denture part of the obturator tried-in and then processed it in heat cure acrylic (fig 3.9 to 3.12). Thereafter, impression of the defect was taken using heavy body silicone. The silicone was cut back around 2mm in the tissue surface, after it set and tissue conditioner was applied. Impression procedure was made again. It was repeated until a satisfactory defect tissue registration was obtained. During this procedure the assessments for speech and nasal regurgitation were performed. Finally this part of the prosthesis was processed in heat cure acrylic resin (fig 3.13).

Figure 3.7:
Two stage silicon wash impression

Figure 3.8:
Metal frame work

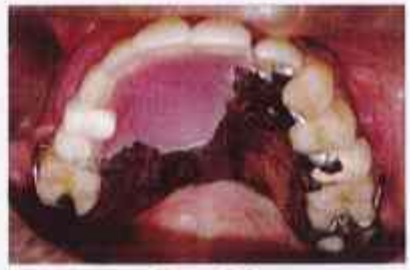

Figure 3.8:
Metal frame work

The final prosthesis was checked. The absence of nasal regurgitation and reduced hyper nasality were tested and verified by asking the patient to swallow and speak respectively. The patient was instructed on its maintenance.

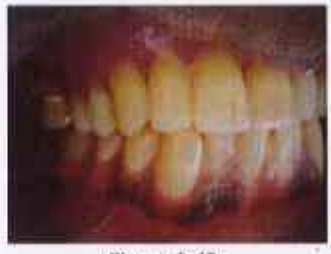

Figure 3.10:
Right occlusal view

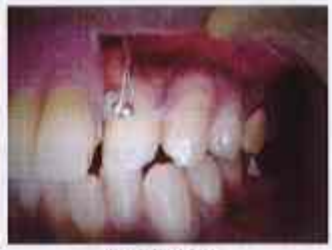

Figure 3.10:
Right occlusal view

Figure 3.13:
Definitive obturator with a hollo bulb

In the review appointment, it was noted that patient was satisfied with the functional and esthetic outcome of the prosthesis. Thereafter patient was reviewed in three months intervals to monitor his plaque control & hygiene of the prosthesis and to identify any complications.

Discussion;

The management of oro-maxillofacial cancer patients is very complex and a multidisciplinary approach is indicated with large contribution from the Prosthodontist.

Since the surgical resection of affected tissues is the treatment of choice in majority of cases, the prosthodontic rehabilitation of this surgical defect

becomes an essential part of the management. The major advantage of this rehabilitation is that in a short period, patient can improve the function and aesthetics and therefore, takes part in normal social life4.

The treatment plan should be designed immediately after diagnosis of the cancer. It initially aimed to preserve the remaining healthy oral and dental tissues to achieve an adequate retention and stability of future prosthesis. Further, the prevention measures should be made to reduce the harmful side-effects of radiotherapy, if the patient undergoes radiotherapy as an adjunct to the surgery which can cause several unwanted side effects including xerostomia, radiation associated caries and trismus and those effects might severely interfere with prosthetic management.

The treatment was started pre-surgically with prevention phase which included physical and chemical plaque control, usage of fluoride tooth paste as well as full mouth scaling.

Following the surgery patient was managed prosthodontically in three phases by fabrication of immediate, interim and definitive-obturators.

Immediate-obturator is constructed on a pre-operative study cast. Before the surgery, an incision line should be drawn in this cast suggested by the oro-maxillofacial surgeon and the immediate-obturator is constructed accordingly5. The obturator is inserted at the time of surgery in the operation room and left in place for about 7 to 14 days6. However in the case described here, the anticipated surgical line had to be changed and fabricated immediate-obturator was not fitted properly. Therefore, defect was packed with gauze instead of obturator.

The interim-obturator was provided to patient within few days of the surgery. The patient should bear interim-obturator for a period of 3 to 6 months. Since the active remodeling of soft tissues around the defect takes place in this period, the prosthesis should be adjusted accordingly to accommodate the continuously changing tissues7.

Definitive-obturator can be provided only after surgical site is adequately healed and dimensionally stable2. Aramany et al (1978) classified the maxillary defects into six classes in relation to remaining abutment teeth and provided a basic principle of designing the prosthesis for each classes8.

In this case, 5 months following the surgery the wound healed adequately and the definitive prosthesis was designed based on Aramany's principle. Retention and stability of the prosthesis were gained from remaining teeth and residual hard palate. The obturator was extended into the defect as a hollo bulb to improve them further.

Conclusion:

Prosthetic rehabilitation of the cancer patients commences from pre-surgical period and is continued throughout the patient's life. Therefore, providing the optimum management is mandatory to improve the quality of life of these patients which helps them to return to their normal social life again.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Rare Presentation of Macrophage Activation Syndrome in Mixed Connective Tissue Disease

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Abstract :

Hemophagocystic lymphohistiocytosis is a clinical condition characterized by the activation of either macrophages or histiocytes with a prominent hemophagocytosis feature in the bone marrow and other reticuloendothelial systems. It can be associated to infections, malignancies, autoimmune diseases, drugs and a variety of other medical conditions. We report a case of a 40-year-old man developed hemophagocytosis at the same time that fulfilled diagnostic criteria for mixed connective tissue disease.

Keywords: Haemophagocysticlymphohistiocytosis (HLH) and macrophage activation syndrome (MAH)

Introduction

First diagnosed in 1939 as histiocytic medullary reticulocytosis, hemophagocystic lymphohistiocytosis (HLH) is a rare autoimmune disorder. It has also been identified as macrophage activation syndrome (MAH) when associated with connective tissue disease. HLH can rapidly progress to multiorgan failure and death, thus early diagnosis and treatment are essential to survival1. Common manifestations include high fever, pancytopenia, hepatosplenomegaly, weight loss, lymphadenopathy, abnormal liver function test, hyperferritinemia and high blood triglyceride level.

Mixed connective tissue disease (MCTD) is an autoimmune disease with it has overlapping features of many connective tissue disorders and presence of anti-U1RNP 2. It is a separate entity other than undifferentiated connective tissue disease and overlap syndromes. We report a case of MAS that occurred as manifestation of MCTD treated with high dose of intravenous methylpredni solone. This case represents an atypical presentation of this rare disorder in adult. We hope this case report will assist in early identification of HLH and serve as a testimonial toward a possible relationship between HLH and MCTD.

Case report

A 40-year-old man with a past history of rheumatoid arthritis since 2012 presented with high grade fever, erythematous rash over face and chest with photosensitivity, facial puffiness, myalgia and loose stools for one-week duration. He had recurrent oral ulcers for last 3 months and discoloration of fingers after exposure to cold for last six months. He had

symmetrical small joint involvement of hands with early morning joint stiffness for one hour. He had fatigue and generalizes malaise for last 5 years. He had been prescribed analgesics and steroids on multiple occasions for the joint pain. He defaulted treatment for last 6 months and got admitted because of worsening symptoms. Duration of hospitalization, the patient developed mucosal bleeding and respiratory distress. Fever was not responded to antibiotics and clinical condition worse with time.

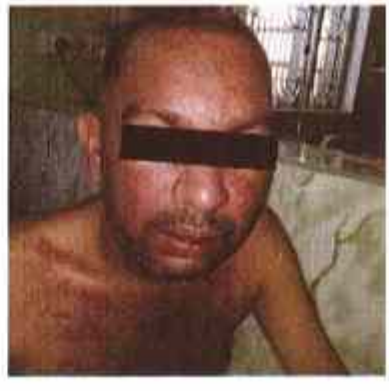
On clinical examination, he looked unwell, was febrile at temperature of 39 C, pallor, periorbital swelling, erythematous rashes in both cheeks including nasal bridge with photosensitivity and erythema over anterior and posterior chest, Raynaud's phenomenon, and multiple ulceration in soft palate (Picture-1). His pulse rate was 100/min, and Blood pressure was 100/ 70 mmHg. Abdominal examination revealed hepatomegaly and splenomegaly. Diffuse tenderness in both thighs with power of 4+/5 in proximal lower limb muscle. Suspected differential diagnosis of MCTD with varied severity of rheumatoid arthritis, systemic lupus erythematosus (SLE), polymyositis and Overlap syndrome was demand further extensive investigations.

Laboratory data revealed pancytopenia with significant leucopenia (1.9 × 103 cells/μL), neutropenia (0.95×103 cells/μl), thrombocytopenia(98×103platelets/μl), Hb, hyponatremia (127millimoles/L) and abnormal liver function studies with aspartate aminotransferase (AST) 147units/L, alanine aminotransferase (ALT) 278units/L, hypoalbuminemia (2.7g/dl) with normal Alkaline phosphatase and INR. Initial inflammatory markers were normal. He was empirically started broad spectrum antibiotics of meropenem and vancomycin. Blood cultures were negative. Viral screen was negative including human immunodeficiency virus, hepatitis A, B and C.

Imaging of the hands showed juxta articular osteopenia suggestive of RA with positive rheumatoid factor. An antinuclear antibody was positive, extractable nuclear antigen panel was positive for smooth muscle ribonuclear protein antigens. However anti-double stranded DNA antibody, anti-smith antibody, anti-neutrophil cytoplasmic antibody, anti-jo-1 antibody and anti-lo antibody were all negative. Creatinine phosphokinase level was elevated at 2797units/L. He had proteinuria with urine albumin 2+ with Urine protein creatinine ratio of 55 with normal serum creatinine levels. Two-dimensional echo was normal.

Blood picture revealed pancytopenia with mild iron deficiency anemia and bone marrow biopsy revealed mildly hyperplastic granulopoiesis with normal maturation and there is no evidence of increase in haemophagocystic activity. Ultrasound of her evidence of mild hepatomegaly and mild splenomegaly. His ferritin level was greater than 20000nmilliliter/ml and lactate dehydrogenase 4434units/L. Fasting triglyceride level was elevated (486mg/dl). Facility was unavailable to asses natural killer cell function and soluble interleukin-2. Initial concern was for neutropenic sepsis and treated with broad-spectrum antibiotic without any clinical benefit. Clinical criteria was sufficient for diagnosis of HLH.

We managed with pulsed methyl prednisolone for three days followed by tapering oral steroid, resulting in significant clinical recovery with complete resolution of his fevers, pancytopenia, elevated liver enzymes and proteinuria. The patient remains hemodynamically stable. The ferritin level was decreased from greater 20800 to 4300n/ml. Later patient acquired nosocomial pneumonia which was successfully treated with piperacillin+ tazobactam and cotrimoxazole. The patient was discharged after three weeks of hospitalization. As outpatient, mycophenolate mofetil was started. He is on current medication includes hydroxychloroquine and prednisolone taper. He is well and disease activity is under control.



Picture 1-malar rash, and photosensitive rash

Discussion

Alarcon-Segovia's criteria are simple and comprises five clinical manifestations in addition to the serological status3. Our patient followed the Alarcon-segovia diagnostic criteria with positive serology on the basis of elevated antinuclear antibody and smooth muscle ribonucleoprotein antigen and three of the five clinical criteria's namely Raynaud's phenomenon, synovitis and myositis depicted by high serum CPK value, allowing for a diagnosis of MCTD.

On the basis of our review of the existing literature, there was only two documented case of HLH secondary to MCTD. Association between HLH and autoimmune disease is formally called as macrophage activation syndrome. It has also been reported including mixed connective tissue disease, systemic juvenile idiopathic arthritis, SLE Sjogren syndrome, progressive systemic sclerosis, rheumatoid arthritis, Crohn disease, vasculitis and sarcoidosis4. The pathogenesis of MAS is not totally known. It is considered as intensive systemic inflammatory reaction, caused by a massive dysregulation of macrophage-lymphocyte interactions, which provokes increase in the level of several cytokines, particularly TNF-α, IL-1, IL-6 and IFNγ5.

Although its clinical presentation is often similar to bacterial sepsis or SIRS, HLH can be life threatening and can rapidly progress to multiorgan failure and death. The extremely high ferritin, with normal CRP could not be explained by any other factor than HLH. Liver dysfunction and excessively high ferritin fit well in HS and are caused by high levels of circulating cytokine. Ferritin is a valuable marker because levels above 10000g/dl were 90% sensitive and 96% specific for the HLH6. Hemophagocytosis may not be obvious on bone marrow biopsy early in the course of disease. BM demonstrate very nonspecific findings such as increased or decreased unilineage or multilineage hematopoiesis7. These infiltrates also have been described in the spleen, lymph nodes and liver. Due to significant therapeutic implications, careful consideration of remainder of the clinicopathologic criteria is essential in diagnosing HLH. Diagnosis can be made in a patient who meets 5 of 8 of the following criteria: fever, splenomegaly, bicytopenia, hypertriglyceri demia or hypofibrogenemia, pathology confirming hemophagocytosis, elevated ferritin count, low NK cell activity and high soluble IL-2 receptor levels.8 In the case of secondary HLH underling trigger may need to treat. The cornerstone is represented by steroid. An intravenous methylprednisolone pulse therapy, some time Management required second line therapy with intermittent cyclophosphamide pulse therapy in corticosteroid resistant HLH in MCTD patients9.

MCTD which was first described by Sharp and colleagues in 197210. The disease was considered unique as it has overlapping features of systemic sclerosis, systemic lupus erythematosus, rheumatoid arthritis, polymyositis and the presence of anti-U1RNP. Many patients complain of easy fatigability, poorly defined myalgias, arthralgias and Raynaud's phenomenon in the early phases of MCTD. The absence of severe renal disease is a hallmark of MCTD. Over a period of time, it may be transition to a classic connective tissue disease.

Very high titers of ANAs are usually present often in a speckled pattern in MCTD. The absence of anti-Sm antibodies and anti-DNA antibodies in a seropositive for anti U1RNP is an important discriminating finding for MCTD from SLE11. The term overlap syndrome has been used to describe patients who have signs of two or more connective tissue disease simultaneously12. Some investigators consider MCTD to be an overlap syndrome.

Conclusion

MCTD has relatively good prognosis and benign course. The major causes of death include progressive pulmonary hypertension and its cardiac complications. When it is complicated with HLH, is diagnostic and therapeutic challenging. Early diagnosis and initiation of immunosuppressant prevent the death.

Competing interests

The authors declare that no competing interests.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Pregnancy with Ventriculoperitioneal(vp) Shunt

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Abstract :

Hydrocephalic women reaching the child-bearing age is increasing due to treatment advances. Pregnancy with VP shunt are reported internationally. This is Mrs.X, 29 years old Primigravid mother with VP shunt, admitted for induction of labour at 38 weeks of gestational age of her first pregnancy. . Otherwise this pregnancy was uncomplicated. She remained normotensive and fetus is appropriately grown for gestational age On Examination, her general condition is satisfactory. Her cardiovascular and respiratory system are clinically normal. Her obstetric examination suggests smaller symphysial-fundal height, longitudinal lie of the fetus in cephalic presentation. Cervical ripening was done with Foley's catheter induction. Then amniotomy oxytocin infusion was commenced, the labour progressed well and achieved vaginal delivery. Neither intrapartum antibiotic or instrumental delivery was used. She was discharged following day.

Keywords: pregnancy with ventriculo-peritioneal (vp) shunt

Introduction

Hydrocephalic women reaching the child-bearing age is increasing due to treatment advances. Pregnancy with VP shunt are reported internationally. In event of late stage of pregnancy and delivery there is a risk of rise of intracranial pressure due to high intra -abdominal pressure [1].

Apart from usual problem there may be inadvertent injury of peritoneal end of vp shunt during caesarian section. Complications of VP shunt includes shunt infection, shunt blockage or disconnection. Intra-abdominal complications include: intestinal obstruction, gut perforation, pseudocyst formation [2].

Other complications are reported in literature include CSF ascitis, inguinal hernia, and intestinal volvulus [3]Nikolov A., et al. [4].

Made a series of twelve pregnant women with VP shunt. They found that shunts do not affect the pregnancy outcome. Only in one case shunt obstructed six weeks after delivery. Then revision was done. They concluded vaginal delivery in women in shunts can be provided successfully with analgesics medicine those don't increase intracranial pressure

The shunt malfunctions can occur commonly during pregnancy. The presence of neurological

symptoms warrants careful evaluation of shunt function. Anesthetic management for labor and delivery varied and was dependent on shunt function. Epidural analgesia appears to be safe in women with functional shunts

Since the first report on maternal shunt dependency in 1979 by Monfared et al. [5] other series addressing various shunt problems during pregnancy and delivery have been published in literature [6-5]. Based on these findings Bradley et al. [6.]

Wisoff et al. [7], Kleinman et al. [8], Soava et al. [9], reported shunt related complications in VP placed shunts during pregnancy and in the postpartum period.

Case History

She is Mrs.X, 29 years old Primigravid mother presented at 38 weeks of gestational age and admitted for induction of labour. she suffered with Tuberculous meningitis at her 19years of age and developed Hydrocephalus for which she is on VP shunt. She has been married for 3 years ago and this is her first pregnancy.

Her Expected date of delivery is on 29/06/208 which was confirmed by early dating scan. She was on preconception folic acid from 3 months before became pregnant. She had one episode of urinary tract infection in this pregnancy. Otherwise this pregnancy was uncomplicated. She remained normotensive and fetus is appropriately grown for gestational age

She also had bladder calculus which was removed surgically several years ago. She has allergic to certain foods. Her mother has diabetic mellitus. Her husband is a manual worker earns 25,000/- per month. Her family support is satisfactory.

On Examination, her general condition is satisfactory. Her cardiovascular and respiratory system were clinically normal. Her obstetric examination suggested smaller symphysial-fundal height for her gestational age, longitudinal lie of the fetus in cephalic presentation.

Cervical ripening was done with Foley's catheter induction. Then amniotomy oxytocin infusion was commenced, the labour progressed well and achieved vaginal delivery. Neither intrapartum antibiotic or instrumental delivery was used. She was discharged following day.

Discussion

Women with VP shunt are just one of the challenges a modern obstetrician is facing.A multidisciplinary approach is necessary in management. Functional occlusion of the shunt most often appears in the third trimester because of the rise in intraabdominal pressure caused by the enlarged uterus. Symptoms include disorders of consciousness, irritability, light sensitivity, hyperesthesia, nausea, vomiting, headache, vertigo, migraines, seizures, weakness in the arms and legs, nystagmus, strabismus, double vision and cranial nerve palsies. In these cases, an emergency evaluation of the condition and consultation with the neurosurgeon is required.

Contrary to what is expected in most of the pregnancies, this woman was not complicated by the shunt itself. Preconceptionally, pregnancy should be planned, and these women need to be fully evaluated by both neurosurgeons and obstetricians. Before conception, it would be necessary to do CT or MRI to check the size of the ventricle and confirm the adequate shunt function.

Pregnancy care is standard consists of usual prenatal diagnosis and regular ultrasound monitoring. In the second trimester shunt revision should be accomplished. Like this pregnancy, full-term delivery could be expected in women with no neurological complications with no shunt malfunctioning (shunt obstruction or very rare abdominal cyst at the distal end of the catheter) and with no concrete obstetric indications vaginal delivery is preferred.

Antibiotic prophylaxis, in both vaginal delivery and caesarean section, is still not defined. Vacuum extraction is preferred, with episiotomy, due to the shortening of the second stage of labor.

Nikolov A., et al. [10] reported that vaginal delivery in women in shunts can be provided successfully with analgesics medicine those don't increase intracranial pressure. Obstetrical indications and in cases of increased intracranial pressure, caesarian section is the method of choice.

Conclusion

Pregnancy with VP shunt is not a common case in Srilanka and there are not enough articles published internationally on this issue. Presence of VP shunt may cause various problems in pregnancy and delivery [11,12]. However, in this case there was no pregnancy or delivery related complications.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Distinguish functional hypothalamic amenorrhea and Isolated FSH and LH deficiency in newly diagnosed diabetes women

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Abstract :

A 38-year-old patient admitted to ward because of polyuria and polydipsia and weight loss with secondary amenorrhea which persists for 6 months. She was suspected as androgen secreting tumors. However, she had functional hypothalamic amenorrhea (FHA). Functional hypothalamic amenorrhea (FHA) is characterized by absence of menstrual cycles for longer than 6 months without any endocrine/systemic causal factors. FHA is a diagnosis of exclusion. Causes of secondary amenorrhea can be confused to evaluate sometimes, so accurate medical history and physical investigation is necessary for true diagnosis.

Keywords: Secondary amenorrhea and functional hypothalamic amenorrhea

Introduction

Functional Hypothalamic Amenorrhea (FHA) is characterized by absence of menstrual cycles for longer than 6 months without any endocrine/systemic causal factors. FHA is mainly associated with stress factors such as psychological, physical or metabolic. Severe stresses such as dieting, heavy training, or intense emotional events with or without body weight loss induces FHA. Consequently, FHA is a diagnosis of exclusion. A good anamnestic investigation including menarche, menstrual cycle pattern, time and duration of amenorrhea is necessary for diagnosis. Other causes of amenorrhea (endocrine, metabolic and systemic diseases) should be excluded.

Case presentation

A 38-year-old mother of three children, for last child 6years, presented with complaints of gradual weight loss for three years , polyuria and polydipsia for 6month with amenorrhea for the past 6month.She was noticed past 6months increase urine frequency ,Increased 1-2times to 10-15times day time and from nil to 5-7 times at night, volume of urine also compare to previous it was high but not measured total volume of urine (polyuria) Polydipsia- increased from about 1-3 liters day to 5-6 liters per day,4-5 times wakes up at night to drink water ,She noticed weight loss gradual in past 3 years from 65kg to 44kg (21kg/3year) ,She had B/L leg swelling, extended up to ankle, not progressive ,No facial or periorbital swelling or abdominal distension. She had an uneventful pregnancy with normal delivery of 3 children, last child 6year. Age of menarche 14year,

Regular monthly menstrual cycles Last menstrual period 6month back, No history of Menorrhagia and Dysmenorrhea. She complains abnormal hair distribution in face, chest and abdomen (Hirsutism). Underwent LRT during 3rd child birth, no Use of hormonal contraceptive method .No history of Vaginal discharge or itching or underwent D&C. No history of hot flashes, vaginal dryness or poor sleep suggestive of postmenopausal symptoms, no history of galactorrhea or breast tenderness. Sexual history libido is normal. No history of dysuria or fever or loin pain or frothy urine or hematuria, no history headache or visual disturbance or recent head trauma, no palpitation or sweating or chronic diarrhea or altered bowel habit or heat in tolerance or neck swelling, No history of chronic cough or hemoptysis, No history of Recent dieting or heavy exercise. There was no history of similar symptoms in the parents, siblings or close relative, but family members all have excessive hair growth(hirsutism), no Family history of infertility, not on long term any medications, house wife, husband working in Colombo, she is non-alcoholic and non-smoker.

On examination on August 2018, her height was 162 cm and weight 44 kg, BMI-17.1kg/m2. She didn't have marked hoarseness of voice, temporal balding she had facial hirsutism. Local examination revealed hair on chest and male pattern pubic hair. She was found normal genitalia. Her speculum and vaginal examination revealed a normal size uterus and normal length of vagina. She was normotensive and her blood pressure was 110/70 (figure 1).thyroid examination normal.

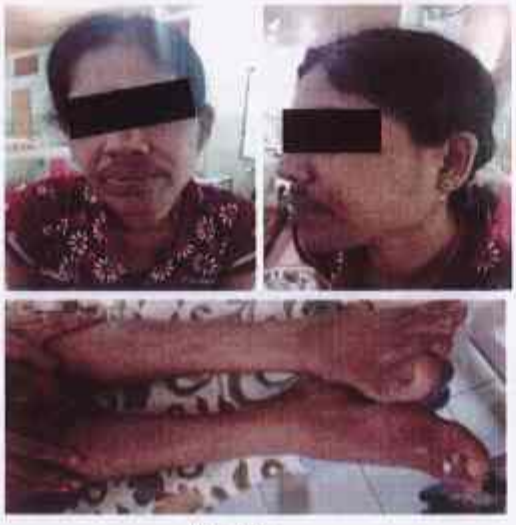


Figure1

Investigation

- Thyroid-stimulating hormone (TSH) 2.29 miu/ml, FT4-18.6pmol/l (both normal)
- Luteinizing hormone/follicle stimulating hormone <0.216/1.09 miu/l (both low).
- S prolactin 183 ng/ml(normal)
- Fasting blood sugar 9.1mmol/l(high) ,HbA1c-12.2%
- Total testosterone 34.96 (range 14.0–76.0 mg/dl)
- Dehydroepiandrosterone sulphate 182 µg/dl (range 35–430 µg/dl)
- 17-A-hydroxy progesterone 1.4 ng/ml (range 0.19–4.69 ng/ml)
- Ultrasonography— uterus was normal-sized; both ovaries were normal-sized and no adrenal mass was noted.
- Serum electrolytes were in the normal range.

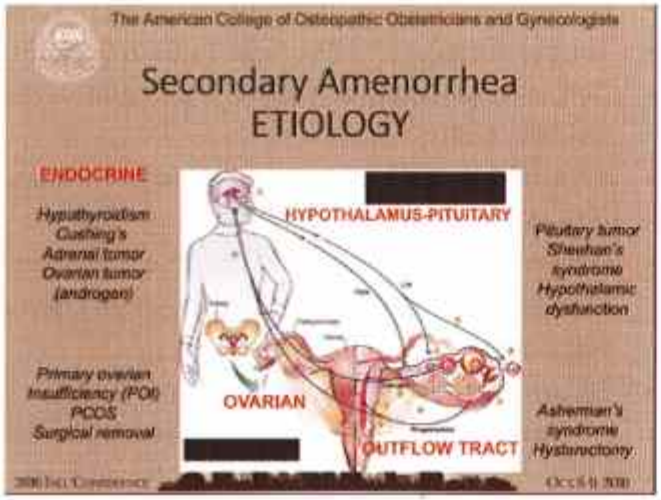
On analysis, she was diagnosed DM with significance weight loss with familial hirsutisum , investigation revel total FSH and LH was markedly low with normal testesterone, there was no androgen-secreting adrenal or ovarian tumour. Dehydroepiand rosterone sulphate levels were on the side of normal and 17-A-hydroxy progesterone was normal. A diagnosis of Diabetes with secondary amenorrhea made due to hypothalamic GnRh suppression due to sever weight reduction was considered.

Discussion

Amenorrhea (absence of menses) can be a transient, intermittent, or permanent condition resulting from dysfunction of the hypothalamus, pituitary, ovaries, uterus, or vagina. It is often classified as either primary (absence of menarche by age 15 years) or secondary (absence of menses for more than three months in girls or women who previously had regular menstrual cycles or six months in girls or women who had irregular menses). Missing a single menstrual period may not be important to assess, but amenorrhea lasting three months or more and oligomenorrhea (fewer than nine menstrual cycles per year or cycle length greater than 35 days) require investigation. An intermenstrual interval greater than 45 days is considered abnormal in adolescent girls who are ≥2 years post-menarche. The etiologic and diagnostic considerations for

oligomenorrhea are the same as for secondary amenorrhea.

This article discussion main consideration secondary amenorrhea causing common endocrine disease or important endocrine problem need to be exclude before becoming the diagnosis. (pig-1)



Hypothalamic dysfunction is a common cause (30%-35%). It is more often seen as a result of stress, intense exercise, weight loss and eating disorders at least need minimum of 18% body fat to bleed. it can cause by infiltrative disease (Craniopharyngioma, sarcoidosis, histiocytosis).

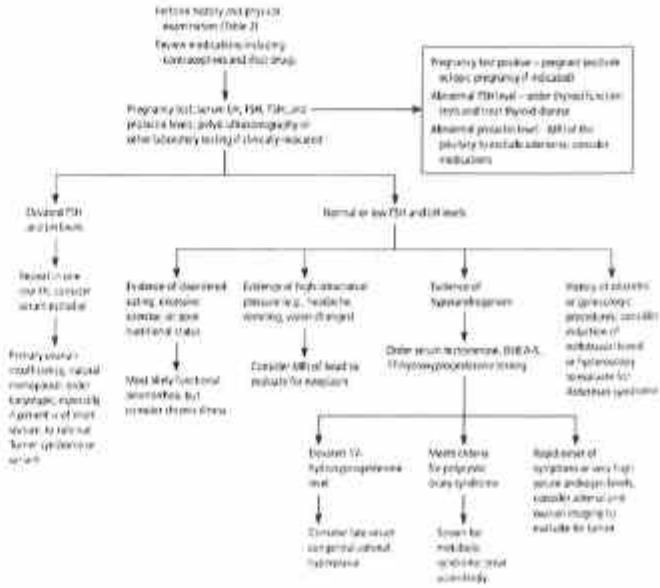
Pituitary failure is usually the acquired type as the result of trauma, treatment of pituitary tumor or infarction after massive blood loss (Sheehan's syndrome) Pituitary tumor and Hyperprolactinemia which cause secondary amenorrhea. Hyperprolactinemia accounts for 20% of cases of amenorrhea. Prolactin inhibits GnRH release from the hypothalamus, drugs that may cause hyperprolactinemia are Phenothiazines, Methyldopa, Cimetidine, Butyrophenones and Antihistamines.

Thyroid disorder and Cushing's disease interfere with the normal functioning of the hypothalamic - pituitary – ovarian axis presents with amenorrhea. High level of thyroxine inhibits FSH release. Androgen – secreting tumors of the ovaries cause secondary amenorrhea.

Late Onset Congenital Adrenal Hyperplasia cause by Mutation 21-hydroxylase, At least half of patients are compound heterozygotes, One of, them coding for several alleles17-OH->200 ng/dL 100% negative predictive value 90% sensitive >1500ng/dL after ACTH stimulation confirms diagnosis.

other than above condition autoimmune polyendocrinopathy syndrome also present with amenorrhea with poly endocrine failure. Its classified in to three types, type-1 is autosomal recessive and is caused by AIRE gene mutation. This condition is also associated with non-endocrine manifestation. The AIRE gene is present in epithelium of the thymus and involved in the presentation of self-antigens to thymocytes. Mutation will allow persistence of thymic lymphocytes, which react against self-antigens and development of autoimmune disorders. Mucocutaneous candidiasis often develops before the onset of endocrine deficiencies, such as hypothyroidism, Addison's disease, type-1diabetes, hypoparathyroidism, primary hypogonadism, nail dystrophy, vitiligo and dental enamel hypoplasia. Type2-is not associated with candidiasis and is also known as Schmidt syndrome, typically when hypothyroidism, Addison's disease, type-1diabetes, myasthenia gravis and primary hypogonadism are present in combination celiac disease is also an association.

type3-is involves autoimmune thyroid disease along with another organ specific autoimmune disease not including adrenal disease.it is further subdivided into three groups: a. involves type 2 diabetes mellitus, b. with pernicious anaemia and, c. with vitiligo or alopecia.The evaluation and approach of secondary amenorrhea based once pregnancy has be ruled out follow up evaluation algorithm show in pig-2



management goals in women with secondary amenorrhea include correcting the underlying pathology, helping the women to achieve fertility and preventing complication of the disease process(osteoporosis and cardiovascular risk).In hypothalamic amenorrhea explaining the need for adequate caloric intake to much energy expenditure sometimes results in increased caloric intake or reduce exercise, followed by resumption of menses. thyroid and cortisol problem need to treat according to which endocrine organ deficient.

Diagnosis of secondary amenorrhea was not challenging for this patient. FHA was the only disgnosis for this patient after excluding other causes. Reversible inhibition of the hypothalamic-pituitary-ovarian axis causes FHA. The overall prevalence of functional hypothalamic amenorrhea among all amenorrhea disorders ranges from 15% to 48%. It is not a result of a structural abnormality or organic disease, mainly related to various stress factors. FHA may occur at any age of life. FHA can be classified into the three groups: a) Various stress factors b) rapid weight loss, and c) extreme physical exercises. Psychological stressors such as emotional, familial and working problems can induce amenorrhea by reducing food intake. Psychological stressors can disrupt hypothalamus-pituitary activity which controls the ovarian functions. These cascades affect Gonadotropin Releasing Hormone (GnRH) secretion negatively via neuromodulators produced in the central nervous system. Emotional, cultural, cognitive and social factors may become major stressor agents when acute changes ocur. Consequently, failure of the reproductive function is reversible and become normal when reproduction is considered essential for those women. Adrenocorticotropic Hormone (ACTH) and cortisol levels are elevated due to response of stressors and activates lipolysis and glycogenolysis. Injection of Corticotropin-Releasing Hormone (CRF) intraventricularly reduces GnRH and Luteinizing Hormone (LH) release in animals. Central β-endorphin (βEP) levels increase as a result of CRH levels which is a potent inhibitor of GnRH and LH secretion. Patients with high levels of basal cortisolemia have poor response to ACTH stimulation. There are some neuro-steroids for modulation of CNS. These are; pregnenolone, pregnenolone sulfate, allopregnanolone, dehydroepiandrosterone and dehydroepiandrosterone sulfate.

FHA is characterized by reduced LH plasma levels as a result of stress-induced endogenous opioid hypertone. FSH plasma levels are typically results to be normal or low. FHA is a diagnosis of exclusion. A good anamnestic investigation is necessary for diagnosis. Menarche, menstrual cycle properties, time and duration of amenorrhea has to be asked. Other causes of amenorrhea (endocrine, metabolic and systemic diseases) should be excluded. Any stress situation induced by family or working problems, weight loss, eating disorders, physical training or activity should be asked to patient. Weight and body composition and body mass index should be noted. Other causes of amenorrhea such as hyperandrogenemia, hyperprolactinemia, hypoproteinemia need to be excluded. Hormonal profile especially LH, FSH, estradiol, androgens, cortisol, prolactin, thyroid hormones, thyroid autoantibodies and biochemical profile must also be evaluated. In some cases, additional tests are needed like the pulsatility study of LH and FSH, the GnRH test and the naloxone test for diagnosis.

Other causes of impaired gonadotropin secretion are; central nervous system or pituitary tumors, brain/pituitary radiation, pituitary apoplexy, head trauma, Cushing's disease, some drugs, chronic systemic illness, eating disorders, malnutrition, thyroid disorders, diabetes mellitus, sarcoidosis, hemochromatosis and histiocytosis. Syndromes such as, CHARGE, Prader-Willi, Bardet-Biedl and leptin deficiency/resistance also causes impaired gonadotropin secretion. If eating disorders are present, the quality of food has to be increased with more proteins. Psychological support might be also suggested. Opioid receptor blocker (naltrexone cloridrate) administration might be suggested for reversing opioidergic hypertone. Acetyl-L-Carnitine (ALC) is an another alternative treatment which modulates HPG axis function in hypogonadotropinemic patient. Gamma-aminobutyric acid (GABA) is another important modulator of stress or anxiety in central nervous system. It has been shown that, there is a rapid decrease in GABA levels as a response to acute stress. Pulsatile GnRH stimulation and exogenous gonadotropins are FDA approved treatments for fertility desired

women. In vitro fertilization is also an option. While investigating the causes of secondary amenorrhea, the history of patient should be asked in detail. Physiologic causes of amenorrhea like pregnancy, menopause and lactation should be ruled out firstly and physical examination should be perform in detail. Pelvic ultrasound examination is essential to exclude ovarian and uterine pathologies such as ovarian cysts and tumors. Laboratory findings are helpful for diagnosis. All of these steps are essential for accurate diagnosis.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

A case of crystal jelly ball ingestion with suicidal intention

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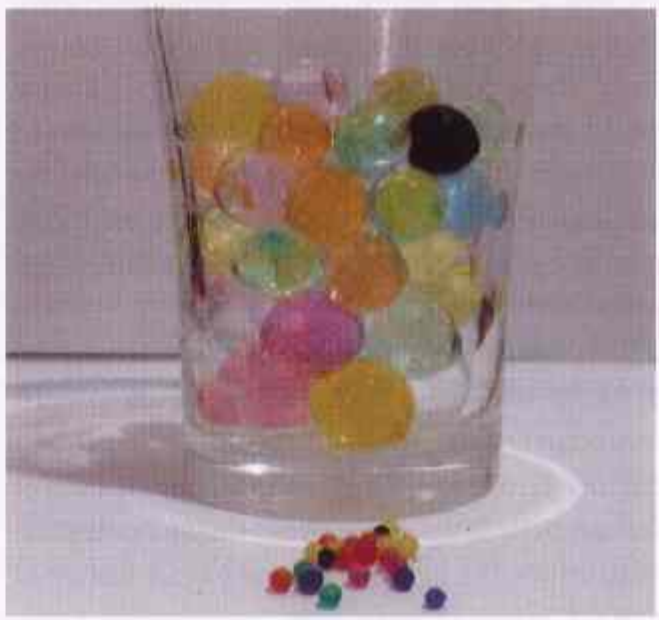
Abstract :
Crystal jelly balls are used for decoration purposes. Accidental ingestion of these jelly balls is reported in children due to its attractiveness. We present a case of ingestion of jelly balls by an adolescent with suicidal intention. Even though this patient passed undigested jelly balls safely, sinister complications like intestinal obstruction and intestinal perforation have been reported.

Keywords: Crystal jelly balls, jelly ball and suicidal intention

Introduction

Crystal jelly balls are colorful and attractive beads like structures which are used in decorations and has a capacity to absorb water to expand. They are also known as water beads, jelly beads, water jelly balls and water monkey(1) (2). It is a Superabsorbent polymer (SAP), a hydrogel which forms multiple hydrogen bonds in an aqueous solution thus widely used in potting plants and disposable diapers. High-density cross-linked SAP such as crystal balls are capable of retaining their shapes with water absorption(2). Therefore, accidental or deliberate ingestion can result disastrous consequences. We may be reporting the first patient who ingested jelly balls for self harm even though there are few cases of accidental ingestion in the literature.



Case report

A 17-year-old girl presented with an episode of non bilious vomiting with mild epigastric pain following four hours of self ingestion of twenty crystal jelly balls. She

passed four undigested jelly balls with vomitus. On examination, epigastric tenderness and marks of multiple parallel old cuts over left wrist suggestive of previous deliberate self harm attempts were detected. Other than that, she was not ill, pulse rate was 108 per minute with good volume and blood pressure was 110/80mmHg without any lung signs. Ultrasound scan of the abdomen done on admission did not revealed any evidence of intraluminal cystic structures. Patient was kept under observation without oral intake during ward stay for eighteen hours. She complained of abdominal distension while in the ward and bowels were not opened till eighteen hours of ingestion. Mild generalized abdominal tenderness was apparent at 15th hour. Abdominal x-ray after eighteen hours also did not show any evidence suggestive of intestinal obstruction. After twenty-four hours, she started to pass undigested jelly balls with stools. At the completion of 30th hour, she passed all the jelly balls. None of them had ruptured inside. Psychological counselling was arranged on discharge.

Discussion

Foreign body associated emergencies are common among paediatric practice including ingestion, choking and foreign body insertion to external acoustic canal. These types of presentations are rare among adults. Use of crystal jelly balls in children was banned in Poland, Italy and Malaysia following sinister consequences reported within recent years and Turkey announced jelly ball ingestion as a "public health problem"(1). (2). (3)

Intestinal obstruction is a common complication of foreign body ingestion especially in children and it may occur proximal to ileo-caecal valve, the narrowest part of intestine after Vermiform appendix. The size of foreign body is the major determinant in intestinal obstruction. The most fearful and unique feature of Jelly ball is its highly expansile nature, where it may expand even up to 400 times of its initial volume(4). The longer the duration it remains inside the body, the larger the expansion and can cause intestinal obstruction at any part of GIT(5). Therefore we can expect intestinal obstruction beyond ileo-caecal valve with these jelly balls in comparison to other foreign bodies. Several cases were reported with intestinal perforation following intestinal obstruction with jelly balls in children warranting surgical correction and fatal outcomes were not uncommon(6).(7). The risk of fatal outcomes is relatively late to other suicidal methods as it takes time to obstruct the intestine with expansion.

In our case, even though there was latency of passing these jelly balls but it did not resulted in intestinal obstruction. Latency could be due to reduced gastric motility as a result of keeping patient nil by mouth. Discouraging enteral feeding is an important step of management as it minimizes the water absorption from the gut. Still, use of drugs to increase gastric motility is controversial because it may aggravate existing intestinal obstruction as patient may develop peristaltic movements

Weather the jelly ball itself can be visualized by any mode of radiological investigations is a simple but important research question we might ask from experts in radiology to answer because jelly balls are radiolucent(4). One case report has mentioned the "double wall sign" or "gut signature sign" in intestinal obstruction with jelly balls. But, other lesions can also present in a similar way in radio imaging(8).

Conclusion

Ingestion of crystal jelly balls could be lethal both in children and also in adult population causing intestinal obstruction due to it's highly water absorptive and expansive properties. Developing a radiological diagnostic method in the context of jelly ball ingestion may be a simple but important study area.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE REPORT

Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome

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Abstract :

Female genital system develops from Müllerian ducts. It differentiates into upper two-thirds of the vagina, uterus, cervix, and fallopian tubes. The MRKH Syndrome is rare development disorder of the Müllerian ducts where the woman presents with primary amenorrhea due the failure of development of uterus and upper vagina. This case report is about a 20 years old girl presented with a history of primary amenorrhea. Upon investigation, the hormonal profile was normal. The ultrasound of the pelvis showed normal bilateral ovaries with query rudimentary uterus. The diagnostic laparoscopy was performed under general anesthesia and finding was normal tubes and ovaries with fibrous band like "uterus".

Keywords: MRKH Syndrome, Mullerian agenesis, Mullerian dysgenesis, Rokitansky syndrome

Introduction

Female genital system develops from Müllerian ducts (paramesonephric). It differentiates into upper two-thirds of the vagina, uterus, cervix, and fallopian tubes This organogenesis involves cell-to-cell communication, proliferation and differentiation, as well as interplay of several genes (such as HOX genes)1. MRKH syndrome patients have normal 46 XX karyotype, normal external genitals (vulva, labia majora, labia minor and clitoris) and regular hormonal profiles.2.Clinically, patients will have an imperforate hymen and a proximally obstructed vagina canal, which in turn leads to primary amenorrhea and cyclic pelvic pain at puberty 3.Additionally, they are either partially or entirely infertile. Majority of the reported cases are randomly distributed, but more incidence is observed in relatives/siblings/family members.4 hereby, signifying a possible genetic etiology.

Case Report

A 20 years old girl presented with a history of primary amenorrhea. She has cyclical lower abdominal pain which last for 3 to 4 days and settles without any analgesia. She did not complain of any gastrointestinal or urinary symptoms. She is otherwise healthy. There is no family history of similar problem.

she is 160 cm tall and 51.5 Kg weight and normal appearing female external genitalia and breasts (Tanner stage-5) and had normal axillary and pubic hair

development. Pelvic examination showed her vulva, labia minora and majora, and clitoris as normal and well estrogenized. The vagina was found to be blindly ending. There were no dysmorphic features. Vital signs within normal.

Upon investigation, the hormonal profile was normal, while ultrasound of the pelvis showed normal bilateral ovaries with query rudimentary uterus. The diagnostic laparoscopy was performed under general anesthesia and finding was normal tubes and ovaries with fibrous band like "uterus"

Discussion.

The MRKH syndrome is classified in 2 types: type I is characterized by an isolated absence of the upper two thirds of the vagina; type II is associated with other malformations. Upper urinary tract malformations are found in about 40% of cases,9 including unilateral renal agenesis (23%-28%), ectopia of one or both kidneys (17%), renal hypoplasia (4%), and horseshoe kidney and hydronephrosis. Skeletal abnormalities are found in 10%, while auditory defects are found in 2% to 10% of cases5,6,7

Patient usually undergoes puberty with normal thelarche and adrenarche, however, remain primary amenorrhea. Patients may report cyclic abdominal pain due to cyclic endometrial shedding without a patent drainage pathway. Because ovarian function is normal, patients experience all bodily changes associated with menstruation. There is usually Infertility, difficulty with intercourse, voiding difficulties, urinary incontinence, or recurrent UTIs and/ or vertebral anomalies (most commonly scoliosis). The degree of vaginal aplasia can vary from complete absence to a blind pouch. The shallower the canal, the greater the likelihood of the patient having dyspareunia or inability to have intercourse.

Differential diagnosis includes Gonadal dysgenesis, Androgen insensitivity syndrome, Agenesis of vagina and uterus, vaginal transverse septum, and Imperforated hymen. Treatment is usually delayed until the patient is ready to start sexual activity. The management depends upon the type and underlying abnormality. It may be either surgical or non-surgical, but the chosen method needs to be tailored to the individual needs and motivation of the patient and the options available. Non-surgical option in some cases is Franck's technique or perineal dilatation. The surgical techniques include various options like McIndoe technique, William vaginoplasty, Rotational flap procedure, Intestinal neovagina and Vacchietti technique.

In addition, it is important to manage psychological symptoms in women with Müllerian agenesis. This is because a young woman who discovers that she has a congenital malformation involving her reproductive organs may develop extreme anxiety about her feminity and physical image

Conclusion

When there is complaint of primary amenorrhea despite being young normal looking adolescent female with normal secondary sexual characters, this is enough to raise suspicion. Radiological studies including MRI and US plays a pivotal role in highlighting the exact anatomical details to decide about the management. The diagnostic laparoscopy can be used instead. The management is either surgical or non-surgical and should be tailored to the individual needs and motivation of the patient and the options available. It is still important to manage psychological symptoms in these women

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CASE SERIES

Coagulopathy and Bleeding in Dengue, Blood Transfusion is an Effective Intervention.

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Abstract :

Dengue is a viral infection which predominantly affects liver, vascular endothelium and immune system. Dengue haemorrhagic fever(DHF) the most severe form of dengue viral infection occurs in minority of dengue infected patients. Even though DHF often complicates the clinical course with fluid leak, the coagulopathy, liver impairment and bleeding (either frank or concealed) occur in most DHF patients who develop life threatening complication. We treated 500 DHF and 2000 dengue patients during the period of four moths from January 2017 to April 2017. There were no deaths. Furthermore, we never had patients who developed pre-shock or shock during this period. Out of 500 DHF 40 patients were received blood with good success.

Keywords: Dengue, coagulopathy, and blood transfusion

Introduction

Dengue is a viral infection which predominantly affects liver, vascular endothelium and immune system . Even though most infections are just dengue fever without much complication, the dengue haemorrhagic fever often complicates clinical course with severe and sometime dreadful complications such as fluid leak, shock and bleeding. Dengue haemorrhagic fever(DHF) the most severe form of dengue viral infection occurs in minority of dengue infected patients. Even though DHF often complicates the clinical course with fluid leak , the coagulopathy, liver impairment and bleeding(either frank or concealed) occur in most DHF patients who develop life threatening complication. The early detection of coagulopathy, liver impairment and bleeding will help to identify such patients who need meticulous management strategies including blood transfusion. The most effective available method to stop progression of coagulopathy and hypoperfusion induced liver injury in DHF is blood transfusion. The blood transfusion in dengue not only stop coagulation process but also reduce the fluid leak and organ hypoxia thus almost immediate improvement in the overall clinical picture. The blood transfusion in dengue has some additional benefits as well such as improves oxygen perfusion and improves oncotic pressure thus reduces fluid leak.

We treated 500 DHF and 2000 dengue patients during the period of four moths from January 2017 to April 2017. There were no deaths. Furthermore We never had patients who developed pre-shock or shock during this period. Out of 500 DHF we transfused 40 patients with blood.

CASE 1

22yr old girl admitted on the fifth day of DHF with early signs of leak and her profiles as follows (on 5th and 6th day)

PCV	40.1	38.4	43.7	37.6	35.6	40	38
PL	59 000	45000	39000	30000	30000	45000	67000
HR	90	90	98	100	92	88	72
BP	110/60	110/60	110/60	100/60	100/60	110/70	120/80
				BLOOD			

Initial fluid management was 90ml/hr(oral plus IV) given and then increased to 100ml .she had persistent tachycardia and was ill. Her APPT was 41compared to the control of 31. Her AST also was risen to the level of 149iu . She was suspected of concealed bleeding at 30th hour of critical period as there was PCV drop ,tachycardia , APPT rise without blood pressure reduction and urine out put droped. She was transfused with 5ml/kg of blood. Soon after blood transfusion her clinical ,biochemical and vitals improved drastically.

CASE2

25yr old girl admitted on the fifth day of DHF with clear evidence of leak and her profiles as follows (5th and 6th day)

PCV	43.2	45.3	44.7	44.2	46.2	46	40.7	38.3	39.5
PL	39 000	26000	24000	15000	15000	14000	15000	18000	15000
HR	98	98	100	100	100	100	110	110	88
BP	110/70	110/70	110/80	100/70	110/70	120/80	120/80	120/80	110/80
								BLOOD	

She is 65kg and initially fluid was given at the rate of 90ml/hr(oral plus IV) and then increased to 100ml she had persistent tachycardia and was ill but her BP, pulse pressure and urine output were normal. Her APPT was 103 on the day 6th day of fever compared to the control of 31which was on 36th hour of the critical period. Her AST also was risen to the level of 739iu however the INR was normal. Furthermore, she developed per vaginal bleeding 7 days before her expected date. The parameters were clearly pointed out that this patient developed bleeding due to coagulopathy and she was transfused with blood at the 36th hour of critical period and response to the transfusion was immediate and obvious. Her sense of well-being improved and vitals normalized and AST has come down to180 and APTT came down to 73. she had an uneventful recovery thereafter.

CASE-3

She is 23yr old girl admitted on the fifth day of DHF without the evidence of leak but the patient was ill(experienced fever and vomiting) and her profiles as follows

PCV	38	41.2	45 (6th d)	49.2 (6th d)	51.3 (6th	50 (6th	47 (7th d)	48.9 (7th d)	43 (7th d)	38 (7th d)
PL	66 000	37000	28000	25000	24000	22000	17000	18000	24000	35000
HR	98	98	100	100	100	100	102	100	100	98
BP	110/80	110/80	110/80	110/80	120/85	120/85	120/90	120/90	120/80	110/80
			BLOOD							

She is 58kg and initially fluid 100ml/hr(oral plus IV) given and then increased to 110ml for 4hours. she had persistent tachycardia and was ill but her BP, pulse pressure and urine output(.5ml) were normal. Her APPT was more than 2min on the day 6th of fever compared to the control of 31which was on 10th hour of the critical period. Her AST level was 834iu on admission. The INR was 1.62. Furthermore, she developed per vaginal bleeding on the second day of admission (before her expected date). The parameters were clearly pointed out that this patient developed bleeding due to coagulopathy and she was transfused with blood at the 10th hour of critical period and response to the transfusion was immediate and obvious. Her sense of well-being improved and vitals improved and AST has come down to572iu and APTT came down to 89. However, she continued to leak and managed with iv normal saline and oral fluids. she was discharged to home only on 9th day.

CASE-4

She is 18yr old girl admitted on the fifth day of DHF without the evidence of leak but the patient was ill and her profiles as follows

PCV	37.9	38.4	41.3 (6th d)	42 (8th d)	43.4 (6th	45 (7th d)	42.1 (7thd)	43.5 (9th d)	42 (10th d)
PL	55 000	49000	37000	25000	35000	34000	27000	35000	55000
HR	98	98	100	100	100	100	100	80	80
BP	110/80	110/80	110/80	110/80	120/85	120/90	120/90	120/80	110/80
							BLOOD		

After 12hours of admission she developed leak and the fluid was given at the rate of 90ml per hour and maintained at the same rate until PCV reached 45. then increased to 100ml per hour as there was tachycardia and marginal urine output(0.5ml/kg/hour). At the same time clotting profile were sent. As you see there was a drop of PCV 0f 3points and APTT was prolonged to 55. We transfused 250ml of blood suspecting concealed bleeding. Patient improved clinically as well as her vital signs. HR came down to 80/min and blood pressure was 120/80 with wide pulse pressure.

Discussion

Microvascular fragility is a common finding -demonstrated by a positive "tourniquet test1.

There are many changes related to coagulopathy;

- Vasculopathy
- Rise in atypical lymphocytes
- Thrombocytopenia
- Derangements of clotting factors
- Liver dysfunction-Dengue virus is a hepatophilic virus
- Activation of fibrinolytic system

Indicators of coagulopathy in dengue2;

- AST/ALT level- probably due to liver necrosis/ endothelial damage
- Low WBC with high atypical lymphocytes
- Prolonged APTT

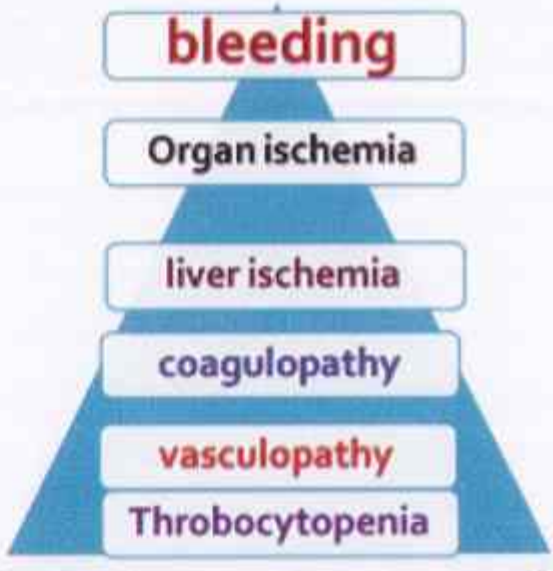
Coagulopathy in dengue is as high as 50% according to some studies but In some studies only 23% reported.

If you suspect coagulopathy in dengue ,the following laboratory tests will be helpful;

- Platelet count
- Prothrombin time
- Activated partial thromboplastin time
- Thrombin time
- Fibrinogen level
- Fibrin D-dimer
- Inhibitors levels

The pathogenesis mechanism of increased vascular permeability and coagulopathy is not well understood but it has been found cytokines, chemical mediators such as tumor necrosis factor (TNF), interleukin- 1 (IL-1), IL-2, IL-6, platelet-activating factor (PAF), complement activation products C3a and C5a, and histamine may have a role3.There are overproductions of cytokines and coagulopathy in Dengue Infection. Interleukin- 6 (IL-6) is one of several inflammatory mediators that responsible for this condition. APTT prolongation in DHF patients caused by a lack of intrinsic pathway which could be due to Impaired synthesis of coagulation factor, Synthesis of immune mediated (acquired) factor VIII inhibitors, Antibodies against dengue virus E protein bind to human plasminogen and inhibit plasmin activity or enhance plasminogen activation. Therefore, both coagulation and fibrinolysis are hyper activated in the acute stage of dengue virus infection4,

BLEEDING CASCADE IN DENGUE



The main reason for the bleeding in dengue is imbalance between coagulation and fibrinolysis.

We treated more than 1500 patients this year and out of this more than 400 were DHF patients and transfused to more than 60 patients. There were 90% of patients among blood transfused had prolonged APTT and almost 100% of patients had a significant rise (more than two fold) of AST. There were only four patients had elevated AST more than 1000u. Prevalence of coagulopathy was high among those who took NSAID.

Conclusion

APTT prolongation in DHF patients caused by a lack of intrinsic pathway which could be due to impaired synthesis of coagulation factor, Synthesis of immune mediated (acquired) factor VIII inhibitors, Antibodies against dengue virus E protein bind to human plasminogen and inhibit plasmin activity or enhance plasminogen activation.in our clinical practice we noticed that blood transfusion improved the coagulation defect. In future, need more study regarding this burning issue.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

IMAGE OF THE YEAR

de Winter syndrome

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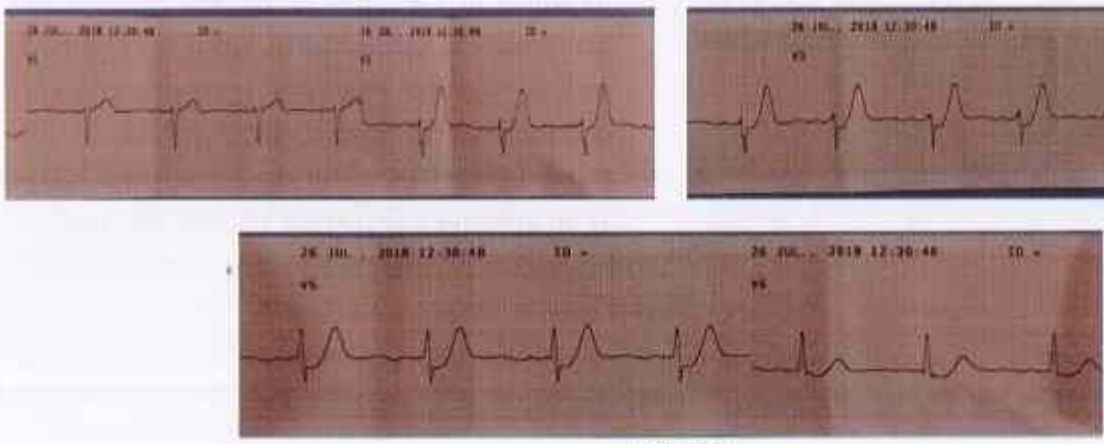
Case history

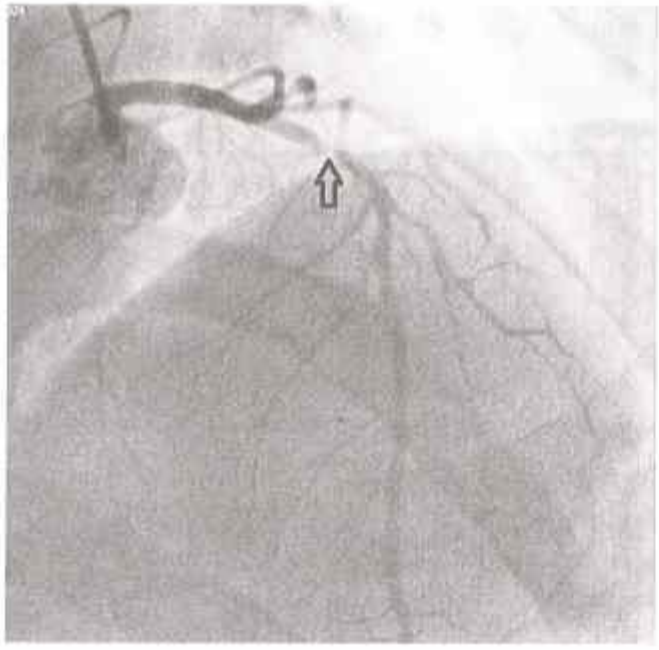
A 42-year -old gentle man presented with left sided chest pain. It was tightening nature, last for more than 30 minute. He was admitted at Base Hospital Kalmunai. On admission ECG was taken (Picture 1). Troponin I was significantly positive. Coronary angiography showed 99% occlusion at LAD artery. Angiogram reveled severe occlusion of LAD (picture 2). After stenting angiogram reveled patency of the LAD (picture 3).



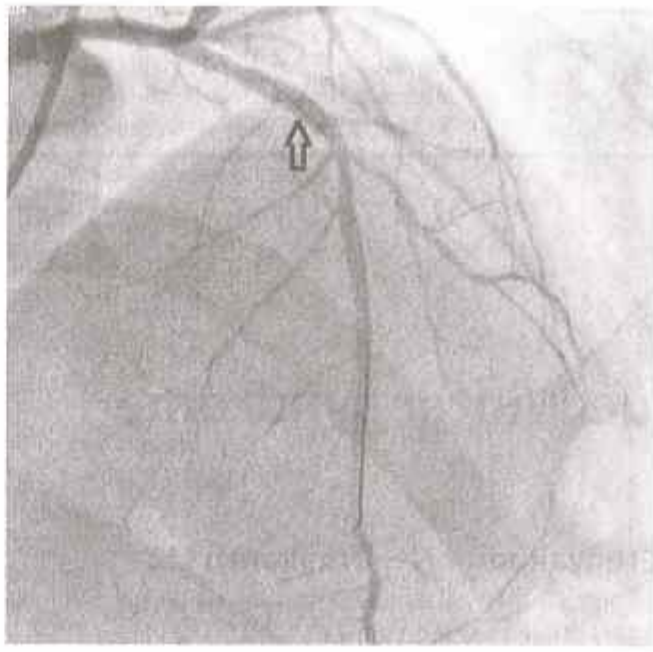
Picture 1

Introduction

It is obvious that, morbidity and mortality associated with ST-elevation myocardial infarction (STEMI) has been dramatically reduced after the introduction of reperfusion therapy either with fibrinolysis or percutaneous coronary intervention(PCI), small group of patients may, however, present with ST-T changes which are not typical of STEMI and failure to identify such patients may lead to delay in diagnosis and reperfusion therapy with catastrophic results(1) (2). The de Winter pattern on ECG was first recognized and reported by de Winter et al. in 2008(3). They found



Picture 2



Picture 3

this pattern in about 2% (30 of 1532) of patients with proximal LAD occlusion(4). The de Winter pattern should not be confused with hyperacute T-waves or Wellens' pattern on ECG. Hyperacute T-waves occur within minutes of coronary artery occlusion and progress rapidly to classical STEMI pattern. Patients with Wellens' syndrome have biphasic or inverted T-waves in leads V1 to V3 and represent critical stenosis of LAD which can develop extensive anterior wall infarction within days(2)(3).

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

LETTER TO THE EDITOR

Family Medicine and its unique aspects

Editor

Family medicine is the medical specialty which provides continuing and comprehensive health care for the individual and the family. It shares many areas of content with other clinical disciplines, incorporating knowledge to deliver unique primary medical care. Primary care is the backbone of the health care system and encompasses the functions including first-contact, continuity, comprehensive, coordinative and highly personalized types of care. It includes health promotion, disease prevention, health maintenance, counseling, and patient education in a variety of health care settings

What are its unique features?

It is the specialty in breadth that integrates the biological, clinical, and behavioral sciences of medicine. The scope of family medicine encompasses all ages, both genders, each organ system, and every disease entity. A primary care physician is a generalist physician who provides definitive care to the undifferentiated patient at the point of first contact and takes continuing responsibility for providing the patient's care. Family Physician is primarily responsible for providing comprehensive health care to every individual seeking medical care and arranging for other health personnel to provide services when necessary.

Family physicians devote most of their practice to providing primary care services to a defined population of patients and most cost-effective health care systems depend on a strong primary care base. Family physicians do not just treat patients; they care for people. This caring function of family medicine emphasizes the personalized approach to understanding the patient as a person, respecting the person as an individual, and showing compassion for his or her discomfort. The most challenging diagnoses are those for diseases or disorders in their early, undifferentiated stage, when there are often only subtle differences between serious disease and minor ailments.

Diagnosing a problem in its early, undifferentiated stage is much more difficult than after symptoms have progressed to the point that the diagnosis is evident. The family physician's relationship with each patient should reflect compassion, understanding, and patience combined with a high degree of intellectual honesty, while the longitudinal relationship evolves into a strong bond between physician and patient characterized by trust, loyalty, and a sense of responsibility.

Coordination and integration of all necessary health services (minimizing fragmentation) and the skills to manage most medical problems encountered while one of the essential functions of the family physician is the willingness to accept ongoing

responsibility for managing a patient's medical care. Patients especially want "a physician who listens to them, who takes the time to explain things to them, and who is able to effectively integrate their care" (Stock Keister et al., 2004) The primary care physician serves as the entry point for substantially all the patient's medical and health care needs.

Why it is essential now?

It is much more important to know what sort of patient has a disease than what sort of disease a patient has by Sir William Osler (1904). The physician must be thorough in approaching problems with a sense of humor. Continuity of care is a core attribute of family medicine, transcending multiple illness episodes, and it includes responsibility for preventive care and care coordination. Comorbidity, the coincident occurrence of coexisting and apparently unrelated disorders, is increasing as the population ages. According to World Health Organization, primary care is the best way of coping with the illnesses of the 21st century and that better use of existing preventive measures could reduce the global burden of disease by as much as 70%.

How it could be moved forward?

A major challenge in family medicine is the need to be alert to the changing stresses, transitions, and expectations of patients over time, as well as the family interactions on the health of individual patients.

Physicians who provide primary care should be trained specifically to manage the problems encountered in a primary care practice, While Patients want a physician who is attentive to their needs and skilled at addressing them and with whom they can establish a lifelong relationship.

According to Francis Peabody (1930), 'the treatment of a disease may be entirely impersonal; the care of a patient must be completely personal'.

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BATTICALOA MEDICAL JOURNAL
Volume 9, September 2018, Annually
The official publication of the Batticaloa Medical Association
ISSN 1800 - 4903

CLINICAL AND SCIENTIFIC LETTER

Therapeutic Apheresis at Teaching Hospital Batticaloa

Editor

Introduction: Therapeutic Plasma Exchange (TPE) and Therapeutic Red Cell Exchange (RCEx) are established treatment modalities in modern medicine. TPE is defined as a therapeutic procedure in which blood of the patient is passed through a medical device which separates plasma from other components of blood. The plasma is removed and replaced with a replacement solution such as colloid solution (e.g., albumin and/or plasma) or a combination of crystalloid/colloid solution. RCEx is defined as a therapeutic procedure in which blood of the patient is passed through a medical device which separates red blood cells from other components of blood. The patient's red blood cells are removed and replaced with donor red blood cells and colloid solution. TPE is the first line treatment for rare clinical conditions like thrombotic thrombocytopenic purpura but is being widely used as an adjunct therapy for number of neurological, renal, hematological and metabolic disorders. Use of RCEx is well established for patients with sickle cell disease aiming for primary and secondary stroke prevention and in sickle cell crisis situations.

Blood bank teaching hospital Batticaloa provides therapeutic apheresis service using haemonetics MCS+ machine which is also being used for production of apheresis platelet form volunteer blood donors. Discontinuous centrifugation is the technique used in the machine which draws in blood from a central or a peripheral vein into a disposable kit. Red cells are re-infused with replacement fluid via the same line after plasma being separated using an inbuilt centrifugation. During first eleven months since introduction of the service in October 2017 nineteen patients have undergone therapeutic apheresis and their clinical conditions, outcome and complications are summarized here.

Results: Out the 19 patients 14 underwent TPE and 5 underwent RCEx. Patient underwent TPE ranged from 15 to 73 years of age and five males and 9 females were in this group. Seven had neurological conditions, five had renal conditions and remaining two patients had metabolic conditions. Out of the five patients underwent RCEx two had sickle cell disease and others presented with propanil poisoning. Further details on RCEx and TPE are given in table 1 and 2 respectively.

Table 1. Summary on patients underwent RCEx

	age	sex	WD	Condition	Cycles	outcome
1	24	M	MICU	SCD Respirator Crisis	1	HbS dropped 60% to 16%
2	45	M	04	SCD 2^{ry} stroke prevention	1	Awaits HPLC report
3	45	F	MICU	Propanil Poisoning	1	Expired
4	46	M	MICU	Propanil Poisoning	1	Recovered
5	30	M	MICU/4	Propanil Poisoning	2	On treatment

Table 2. Summary on patients underwent TPE

Pt No	age	sex	WD	Condition	Cycles	outcome
1	29	F	MICU	GBS Bulbar palsy	11	Recovered
2	73	M	34	CIDP / Lower limb weakness	5	Improved
3	41	F	SICU	Myasthenia crisis	3	Recovered
4	60	M	34	Sensory Ganglionopathy	5	Not improved
5	61	F	1	?GBS not responding to IVIg	2	Discontinued
6	68	F	MICU	? GBS/MG muscle weakness	3	Discontinued
7	15	M	MICU	Multi organ failure DHF	3	Recovered
8	18	M	MICU	AHE / Wilsons Disease	6	Recovered
9	21	F	26	Hyper triglycerideamic pancreatitis	1	TG drop 4449 to 712
10	70	F	MICU	RPGN	2	Discontinued
11	58	F	35	AKI following viper bite	5	Recovered
12	53	M	34	AKI following viper bite	2	Recovered
13	59	F	35	RPGN	3	Treatment ongoing
14	17	F	18	Lupus Nephritis flare up	4	Treatment ongoing

	Neurological		Metabolic		Renal

Discussion: Patient number one who had 11 TPE procedures had them in tree admissions. She presented with lower limb weakness which later progressed into bulbar palsy needing ICU admission and ventilation. Initially she recovered with 4 TPE procedures. However subsequently she got readmitted 3months and 5 months later with similar symptoms needing ICU admission and ventilation in both occasions. She recovered after 4 and 3 TPE procedures after the second and third admission respectively.

CIDP patient presented with walking difficulty due to lower limb weakness was the oldest patient underwent TPE at 73 years. His weakness improved and walked without assistance with 5 TPE cycles done every other day. Due to lack of ICU beds TPE was done in the medical ward but he tolerated all cycles without complications.

Third patient was a known patient with bulbar myasthenia admitted for caesarian section at her third pregnancy and developed respiratory paralysis in the postnatal ward needing ICU admission and ventilator support. Increased pyridostimine dose, steroids and IVIg did not help to wean her off from ventilator. She got a rapid improvement with first TPE itself taken off from ventilator and send to normal ward after 3rd TPE.

Fourth patient with sensory ganglionopathy had tingling and numbness of both hands which did not improve even after 5 TPE cycles offered every other day. It is a challenge to assess the improvement in this type of neurological conditions since there is no objective method to measure the outcome.

The diagnosis had not been fully established in fifth and sixth patients who presented with lower limb weakness. The patient who has IVIG was offered TPE very late in the course of treatment. She developed DVT in lower limb where femoral line was in place and TPE was discontinued. TPE was discontinued in the sixth patient as well since no arrangements were made from the ward to continue TPE after she was discharged from the ICU.

Patient with Multi organ failure after dengue haemorragic fever had low GCS without any ICH in brain imaging. He regained consciousness taken out form the ventilator with 3 TPE cycles. Although it was

not a text book indication for TPE an immune medicated encephalopathy could have been the reason for the improvement. However there is no objective way to attribute the outcome totally to TPE.

Both patients with metabolic complications were referred by for TPE by the consultant gastro entomologist. The 18 year boy transferred from local hospital for deepening jaundiced developed acute hepatic encephalopathy needing ICU admission. Wilson disease was the tentative diagnosis since all infectious markers became negative. His deep hepatic coma improved since 3rd TPE cycle and further improved with total of 6 TPE cycles.

Acute pancreatitis could develop when triglyceride (TG) levels are more than 500 – 1000 mg/dl. Our patient presented with pancreatitis had a TG level of 4449mg/dl. Her body weight was around 60kg and total of 5534ml of blood was processed during 3 hours of TPE removing 2800ml of plasma reducing the TG levels to 712mg/dl. Since targeted outcome was to lower the TG levels below 1000mg/dl no further TPEs was offered.

Remaining five patients had renal conditions and all of them were offered TPE together with Haemodialysis. Two of them had AKI following viper bites and features of MAHA and responded to combination of treatment. Out of the two patients with RPGN TPE was discontinued in one patient who had repeated allergic reactions for plasma products used as the replacement and other patient is still on treatment. The 17 year girl with lupus nephritis had a flare up of the condition and treatment changed to cyclophosphamide. TPE was requested to gap the time until the medications become effective and she is still under treatment with normal creatinine levels and no dialysis.

Out of the five patients who received RCEx two had sickle cell disease needing exchange for an acute chest syndrome in one patient and other was a routine exchange for secondary stroke prevention.

Out of the three patients who had propanil poisoning the female patient presented very late after poisoning and expired without improvement. One male patient discharged with full recovery and other developed acute respiratory distress needing ICU admission two days after 2nd RCEx in spite of rapid transient improvement.

Way forward: Careful selection of patients is an important step for the success of therapeutic apheresis program. Having clearly defined objective parameters to measure the treatment outcome is equally important to determine the frequency and duration of treatments. Non availability of human albumin which is the recommended replacement fluid for many conditions increase the risk of transfusion related complications since large volumes of plasma are used for one patient. Lack of trained staff and not having a dedicated place for therapeutic apheresis procedures is also a challenge and must be address to ascertain the sustainability of the program.

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