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References to an article with 3 or less authors:

References to an article with more than 3 authors:

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Infections and Infectious Diseases have been a major cause of morbidity and mortality all over the world for many centuries. Nowadays many doctors whose work is in based in hospitals are of the opinion that as a community we are losing the battle against infections as newer, more resistant and virulent strains of bacterial and viral infections are appearing in clusters and sometimes in the form of mini-epidemics like the current Ebola virus infection in Africa. We now see more drug-resistant tuberculosis than we did a couple of decades back and many other multi-drug resistant nosocomial infections are a serious cause for concern, especially since there are very few new antibiotics in the research pipeline. Injudicious use of antibiotics by the medical fraternity has certainly compounded the problem. However, if you consider the scenario of a few decades back when infectious diseases were the main cause of mortality in India and occasionally pandemics would cause very high morbidity and mortality globally, then one must admit that the situation is very much better today. Outbreaks of new infections are usually quickly contained and their impact is limited. As a society we are now more vigilant and now have systems in place to quickly and effectively reduce the impact and scale of these infectious outbreaks. The life expectancy of the average Indian has almost doubled since Independence and the population has increased manifold, which is surely a reflection of the fact that we are winning the fight against infections.

If we were to compare infections with wars - until the 1950’s our civilization witnessed many wars, including the two world wars, where many countries participated in widespread destruction and death. But over the last few decades the numbers and scale of wars have come down. More importantly, as in the case of infections, the mortality and damage done by these conflicts has been minimized significantly. There are still local conflicts and wars, but they are largely contained, and the damage is very limited compared to the wars of past. Like dangerous nosocomial infections the scourge of terrorism keeps sprouting up and causing problems. But most countries have an effective machinery to combat and limit the impact of terrorism and the preventive steps initiated to tackle terrorism have been effective in containing the problem to some pockets of the world.

So overall whether it is mortality due to infections or wars- when one views the big picture – as a society we have made significant progress. But we need to beware in the coming decades as the resultant problems of increased longevity and an ever increasing population take a toll on the limited resources that Mother Earth has to offer.
Science has contributed enormously to our comfort and convenience in daily life. The manner in which our civilization has advanced in the last few years is due to tremendous contributions from various areas of science. However, it is wise to pause and reflect on how life is changing around us and how we should use scientific discoveries in a sensible and responsible manner. In this context the following two parables by Amma are noteworthy.

One day a scientist was driving along a road. Suddenly he noticed that a hen was running alongside his car. He increased the speed of the car to 50 Km/hr and still the hen was able to keep up. He then increased the speed of the car to 80 Km/hr and to his amazement the hen was still able to race alongside. The scientist was intrigued. He stopped the car and had a closer look at this amazing hen. To his great surprise he saw that the hen had 3 legs and that is how it could run at such supernormal speeds. His scientific curiosity was aroused and so he enquired in the area and found out the house where this hen belonged. He found an elderly couple in the house. He told them that he had come to enquire about the 3 legged hen that he had found on the roadside. The elderly couple told him that their son had done a PhD in Biotechnology and had conducted experiments to develop a new tastier breed of chicken. However, the result was this 3 legged hen. “And how does the new breed of hen taste?” enquired the scientist. “For that no one has been able to catch even one of the hens, as they are too fast with their 3 legs,” replied the elderly couple. This story symbolizes the state of many of our scientific experiments today which sometimes lose direction and run amok.

The second parable is about a bird watcher who noticed that the number of hummingbirds in his area had declined considerably. He asked a pair of hummingbirds why they were not breeding as before. The hummingbirds replied, “we went to your neighbor’s garden and saw a number of beautiful flowers, but when we went to suck honey from the flowers, we injured our beaks because the flowers were made of glass. Then we went to some nearby flats and saw a number of potted plants kept on the balconies of these flats. With great joy we flew there hoping to get some honey. But those plants were all made of plastic and the sharp ends of the leaves injured us. Your neighborhood looks beautiful both in the day and night and the artificial bright flowers never wilt, but unfortunately this is not an environment into which we would like our children to be born.” As our luxuries increase our environment becomes increasingly artificial and hostile to Nature. It is our minds that must be air-conditioned not our homes and offices. We must ensure that our scientific discoveries are used in a manner that maintains our harmony with Nature.
ABSTRACT

Sepsis or sepsis syndrome is a life-threatening medical condition characterized by an infection and the body’s overwhelming inflammatory response to that infection. Sepsis remains the primary cause of death from infection despite advances in modern medicine, including vaccines, antimicrobials, and critical care. It may lead to shock, multiple organ dysfunction, and death, especially if not recognized early and treated promptly. Sepsis is a major clinical issue in Emergency Departments (EDs), as it is commonly seen first in the ED and is associated with a high mortality rate. Between one third and one half of patients with sepsis die. In the developing world, sepsis accounts for 60-80% of lost lives per year in childhood, killing more than 6 million neonates and children yearly and is responsible for more than 100,000 cases of maternal sepsis. Every hour, about 50 people die from sepsis. This article briefly outlines the clinical features, early diagnosis, evaluation and treatment of sepsis in Emergency and critical care settings.

Keywords: Sepsis, Shock, Ionotropes, Multi organ dysfunction syndrome, Antibiotics, Fluids, Early goal directed therapy.

INTRODUCTION

Sepsis or sepsis syndrome is a life-threatening medical condition characterized by an infection and the body’s overwhelming inflammatory response to that infection. Sepsis remains the primary cause of death from infection despite advances in modern medicine, including vaccines, antimicrobials, and critical care. It may lead to shock, multiple organ dysfunction, and death, especially if not recognized early and treated promptly. In the developed world, sepsis and sepsis related problems are increasing by an annual rate of 8 - 13% over the last decade, and now claims more lives than any other disease. Sepsis causes more deaths than prostate cancer, breast cancer and HIV/AIDS combined. Globally, an estimated 20 - 30 million cases of sepsis occurs each year. Reasons are multiple for this increase in morbidity and mortality, like increase in number of diabetic patients, aged population1,4, HIV infection, cancer, cancer chemotherapy / radiation therapy, granulocytopenia, cirrhosis, alcohol dependence, increasing use of immunosuppressant drugs like steroids, Increased use of invasive devices such as surgical prosthesis, inhalation equipment, and intravenous catheters and urinary catheters Indiscriminate use of antimicrobial drugs and the development of multi drug-resistant and more virulent varieties of infections. Sepsis in trauma also contributes to a significant proportion of mortality and morbidity in the age group of 15-45 years. Infections are the second most important cause of death in trauma patients. Despite advances in trauma care, deaths due to septicemia are increasing8.

In the developing world, malnourishment, poverty, lack of access to vaccines and timely treatment all contribute to death. The incidence of sepsis is also increasing in number due to mainly hospital acquired infections.

Sepsis starts when inflammatory mediators released into the bloodstream to fight against the microorganisms and this mediators trigger inflammation throughout the body. This inflammation can trigger a cascade of changes that can damage multiple organ systems of body and lead to mortality.

Sepsis is a major clinical issue in Emergency Departments (EDs), as it is commonly seen first in the ED and is associated with a high mortality rate. Between one third and one half of patients with sepsis die1,2. In the developing world, sepsis accounts for 60-80% of lost lives per year in childhood, killing more than 6 million neonates and children yearly and is responsible for more than 100,000 cases of maternal sepsis3. Every hour, about 50 people die from sepsis.

Diagnosis of sepsis is often delayed because the clinical symptoms and laboratory signs currently used (fever, tachycardia, abnormal white blood cell count etc.) are not specific enough. Sepsis is under-recognized and poorly understood due to confusion about its definition among patients and healthcare providers, lack of documentation of sepsis as a cause of death in emergency room or ICUs in case of early death, inadequate diagnostic tools, and inconsistent application of standardized clinical guidelines to treat sepsis4. As sepsis is a time dependent illness, mortality increases with delay in starting appropriate treatment.

This review begins with a brief summary of the terminologies related to sepsis, and then addresses the fundamental clinical aspects of identification and resuscitation of the septic patient in ED.

DEFINITIONS

Sepsis has been defined as a clinical syndrome that results from a dysregulated systemic inflammatory response to an infection. There should be a presence of probable or documented evidence of infection
with systemic manifestations. Sepsis is characterized by the cardinal signs of inflammation (vasodilatation, leukocyte accumulation, increased microvascular permeability) of tissues.

Severe sepsis refers to sepsis-induced tissue hypoperfusion or organ dysfunction with any of the following thought to be due to the infection: Sepsis induced hypotension, Lactate above upper limits of laboratory normal, Urine output <0.5 mL/kg/hr for more than two hours despite adequate fluid resuscitation, Acute lung injury with PaO2/FiO2 < 250 in the absence of pneumonia as infection source, Acute lung injury with PaO2/FiO2 < 200 in the presence of pneumonia as infection source, Creatinine > 2 mg/dL, Bilirubin > 4 mg/dL, Platelet count < 100,000 microL–1 and Coagulopathy (INR > 1.5).

Septic shock is defined as sepsis-induced hypotension persisting even after adequate fluid resuscitation, which may be defined as infusion of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent)

Multiple organ dysfunction syndrome (MODS): MODS is the presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without inter-vention.

ARDS
Respiratory symptoms within one week of clinical insult and bilateral pulmonary oedema not related to cardiac failure or fluid overload
Patient should have moderate to severe impairment of oxygenation, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen (PaO2/FiO2) < 300 mm Hg.

COMMON ORGANISMS
Although septic shock can be caused by various viruses and fungi, most of the cases are due to bacterial infections predominantly due to gram negative bacteria. Common gram-negative bacteria causing septic shock are Escherichia coli, Klebsiella species, Enterobacter species, Proteus species and Pseudomonas aeruginosa. The most common obligate anaerobe to cause sepsis is Bacteroides fragilis. Approximately 45% of the cases of septicemia are due to gram-negative bacteria.

Common gram positive bacteria causing septic shock include Staphylococcus aureus, Streptococcus pneumoniae, Enterococcus species that are normal flora of the intestines, and Streptococcus pyogenes. The most common cause of neonatal sepsis is Group B Streptococcus (GBS). Approximately 45% of the cases of septicemia are due to gram-positive bacteria.

Approximately 10% of the cases of septicemia are due to fungi, mainly the yeast Candida.

CLINICAL FEATURES OF SEPSIS
General findings of sepsis: Since sepsis can start from different parts of the body, it can have many different symptoms. Symptoms of sepsis are usually nonspecific and include fever, chills, and constitutional symptoms of fatigue, malaise, anxiety, or confusion. These symptoms are not limited to infection and may be seen in a variety of noninfectious inflammatory conditions. Rapid breathing and a change in mental status, such as drowsiness, altered sensorium or confusion, may be the earliest findings of sepsis.

Other common findings include: Temperature > 38.3 or < 36ºC, Heart rate > 90 bts/min, Respiratory rate > 20 breaths/min, Significant fluid overload, and High blood sugar

Most of the patients with sepsis may have variety of lab findings suggestive of systemic inflammation like leukocytosis (WBC > 12,000 c/mm3) or leukopenia (WBC < 4000 c/mm3) or normal WBC with > 10 % immature cells and an elevated CRP.

Patients with bacterial infection will have increased plasma procalcitonin (PCT). PCT is a specific marker of bacterial infections. Normal value of PCT is < 0.25 µg/L. PCT levels in sepsis are generally > 1-2 µg/L and often reach between 10 and 100 µg/L in severe illnesses.

Hemodynamic changes like hypotension and tachycardia are seen in many patients. Arterial hypotension in sepsis is defined as SBP < 90 mmHg and or MAP < 70 mmHg, or an SBP decrease > 40 mmHg in adults.

Findings suggestive of organ dysfunction are seen in many sepsis patients like Arterial hypoxemia (arterial oxygen tension / fraction of inspired oxygen [PaO2/FiO2] < 300) (Ratio of PaO2 / FiO2 < 300), Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hours despite adequate fluid resuscitation), Creatinine > 1.5 mg/dL, Coagulation abnormalities (INR > 1.5 or aPTT > 60 seconds),Thrombocytopenia (platelets < 100,000 cells/mm3) and hyperbilirubinemia (due to liver disorder or hemolysis).

Hyperlactemia (> 1 mmol/L) and lactic acidosis are the key lab findings suggestive of low tissue perfusion, which is one of the most important complications of sepsis induced anaerobic metabolism. Serum lactate level ≥4 mmol/L is consistent with severe sepsis. There is some evidence that lactate levels carry prognostic value, Patients with a lactate of ≥4 mmol/L had a mortality of 40%, compared with <15% mortality for patients with a lactate of <2 mmol/L.

MANAGEMENT OF SEPSIS IN EMERGENCY DEPARTMENT
Diagnosis of septic shock: Hypotension is the most common indicator of tissue hypoperfusion. Hypotension
may not be seen in early phase of sepsis, so other features of hypoperfusion must be looked in early sepsis cases. Common signs of hypoperfusion are cool, vasoconstricted skin due to redirection of blood flow to core internal areas, tachycardia > 90/min, altered behaviour or restlessness, and oliguria or anuria.

Fluid management of septic shock: Crystalloids (Normal saline, Ringer’s lactate) are the treatment of choice. An initial bolus of 30 ml/kg crystalloid must be started in ED itself, then start an infusion of 2 litres over 30-60 minutes with target CVP of 8 - 12 cm H2O. 1 litre of crystalloid can expand the plasma volume by 300 ml where as 1 litre of colloid expands the plasma volume by 1000 ml (colloid like starch preparations are not recommended in sepsis patients, but 5% Albumin is a colloid that is safe for fluid resuscitation in severe sepsis). Most of the patients with septic shock requires 1 - 2 Litters of colloid or 4 - 8 L crystalloid to restore the circulatory volume. Colloids (Albumin) are better choice in patients with pulmonary edema.

Noradrenaline: After initial fluid correction, if BP is not improving adequately, patient should be treated with noradrenaline infusion. Noradrenaline infusion should be started at 0.05 to 3.3/kg/min. The combination of noradrenaline and dobutamine gives better outcome in septic shock therapy, especially patient has lactic acidosis.

Steroids: If the patient is in septic shock not responding to above strategies, initiate steroids in a dose of 200 /day of hydrocortisone IV (50 mg every six hours), continued for 5-7 days and tapered slowly depending on clinical response.

Antibiotics: Most appropriate antimicrobial must be started in one hour in ED after appropriate cultures have been obtained.

GOALS OF INITIAL RESUSCITATION (EARLY GOAL-DIRECTED THERAPY) IN FIRST 6 HOURS IN ED

- CVP 8 - 12 mmHg
- Central venous (superior vena cava) or mixed venous oxygen saturation (ScvO2 or SvO2) > 70 or 65%, respectively
- MAP≥65 mmHg
- Urine output ≥0.5 mL/kg/hour or about 30-50 mL/h
- Lowering of the serum lactate to near normal range

CONCLUSION

Sepsis and septicemic shock are major issues in patients admitted through ED. The knowledge about the clinical spectrum and timely interventions of complications are very critical in the management of this type of cases and an emergency physician should have solid grip on fine aspects of this subject for better clinical outcome. Rapid initiation of simple, timely interventions, including intravenous fluids, noradrenaline, steroids and antimicrobials, can reduce the risk of death by half. Early and effective management of sepsis in ED is cost effective, and reduces the number of hospital and ICU days for patients. Unfortunately, sepsis is still often overlooked and recognized too late.

ED – Emergency department, CVP- Central venous pressure, BP-Blood pressure, SBP – Systolic blood pressure, MAP – Mean arterial pressure, INR- International normalized ratio for a prothrombin time, aPTT - activated partial thromboplastin time.

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Acute CNS infections
Arun Grace Roy, Jalesh Panicker, Anand Kumar

ABSTRACT
Infections of the central nervous system (CNS) are important to recognize as they are treatable, and prompt diagnosis and treatment of the infection may mean the difference between recovery and death or profound disability. The clinical presentation can be similar in a majority of cases, but etiology can be varying, posing a challenge to the treating physician. Here, with this article, we try to bring an approach and treatment outline for common infections of the central nervous system.

INTRODUCTION
Infections of the central nervous system (CNS) commonly present in the emergency service. They are important to recognize as they are treatable, and prompt diagnosis and treatment of the infection may mean the difference between recovery and death or profound disability. However, the clinical presentations are distinct and identification of the pattern of clinical presentation helps in reaching a diagnosis and planning the appropriate investigations and treatment. These are summarized in table 1.

ETIOPATHOGENESIS OF CNS INFECTIONS
The brain is endowed with a blood brain barrier which prevents the entry of pathogens and inflammatory cells, providing an effective protection against infections. In the healthy individual, organisms can only reach the brain through haematogenous spread, extension from the juxta-cranial structures (middle ear cavity, paranasal sinus) or through neural pathways (e.g. olfactory nerves). However, iatrogenic factors can increase the risk for CNS infection by either causing a breach in the barrier, e.g. following neurosurgery, the presence of a foreign body, e.g. ventriculo-peritoneal shunt, or by medications that affect immunity or bacterial colonization, e.g. immunosuppressive drugs.

There are a variety of organisms that can cause an acute CNS infection and these are listed in table 2.

| Bacteria | Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes, Gram negative bacilli |
| Viral | Herpes simplex virus types 1 & 2, Japanese encephalitis, rabies, Western equine encephalitis, Eastern equine encephalitis (Triple E) and West Nile virus encephalitis |
| Fungus | Filamentous fungi (Aspergillus) and yeast species (Candida) |
| Parap Arsite | Plasmodium, amoebae, trypanosome |

There are several factors that can influence the type of organism infecting the CNS. However, it is known that for bacterial infections of the CNS, age, immune status, epidemiological trends and systemic infections are important factors. The type of bacteria causing meningitis varies according to age. In neonates, Gram-negative bacilli are the commonest cause, whereas during childhood, H. influenzae is the commonest. Recent reports, however, suggest that following vaccination programmes against H. influenza B, meningococcus may now be the most common cause for meningitis in this age group. In adults, pneumococcus is the commonest organism. Fungal and protozoal agents are rare causes of CNS infection.

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Most cases of bacterial meningitis begin with host acquisition of a new organism by nasopharyngeal colonization, followed by systemic invasion and development of a high-grade bacteraemia. Central nervous system invasion then occurs, although the exact site of bacterial entry into the central nervous system is unknown. Virulence factors are released by the bacteria. As part of the host immune response, inflammatory cytokines are released. This results in increased permeability of the blood-brain barrier, allowing proteins and neutrophils to enter into the subarachnoid space. There is, then, an intense subarachnoid space inflammatory response, which leads to many of the pathophysiological consequences of meningitis, including cerebral oedema and increased intracranial pressure. The pathology of encephalitis includes viral cytopathology (viral destruction of neurons), a para/postinfectious inflammation, or immune mediated response. Although neurons are primarily affected, vasculitis, meningitis, myelitis and radiculitis can be present.

**APPROACH TO THE PATIENT PRESENTING WITH AN ACUTE CNS INFECTION**

When a patient presents with an acute CNS infection, it is crucial to commence appropriate treatment at the earliest possible time. As in other areas of emergency medicine, history taking is an essential part of the evaluation. History and examination help to establish the syndromic diagnosis. It can also help in establishing the temporal sequence of events, which facilitates the diagnosis. The examination should be focused on establishing the extent of neurological involvement, and signs of a systemic source of infection. Neck stiffness, resulting from irritation of the meninges, is a nonspecific sign and may occur not only in meningitis, but also if the intracranial pressure is raised as in encephalitis, or even part of a systemic infection (meningism).

**ROUTINE INVESTIGATIONS**

Neutrophilic leucocytosis in the peripheral blood may be seen in pyogenic meningitis, and occasionally in acute tuberculous meningitis. ESR and C-reactive protein may be elevated in these conditions. Blood culture may be positive in up to 50% of patients with pyogenic meningitis. Chest x-ray may show pneumonia or changes suggesting tuberculosis.

**NEUROIMAGING**

Though lumbar puncture (LP) is the most essential test for the diagnosis and management of acute CNS infections, it is nowadays accepted practice to perform brain imaging before this invasive test, where available. CT imaging is often sufficient in assessing the risk of performing lumbar puncture in an acutely ill patient, although this cannot exclude raised intracranial pressure. Presence of focal lesions with mass effect would indicate increased risk of brain herniation from performing the test. Established brain abscess can be identified in CT imaging. Complications of meningitis, such as infarcts, may be seen in CT as well. Meningeal enhancement in a contrast enhanced CT scan suggests the presence of exudates.

However, in hospitals which lack an acute neuroimaging service, waiting for a CT scan may delay the lumbar puncture and thus the diagnosis. A brain scan is often unnecessary in uncomplicated meningitis and clinical features are helpful to determine the patient at risk who should have imaging before LP (table 3).  

<table>
<thead>
<tr>
<th>Age greater than 60 years</th>
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<tr>
<td>Immunocompromised state</td>
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<tr>
<td>History of CNS lesion</td>
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<tr>
<td>History of seizures within one week before presentation</td>
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<tr>
<td>Altered level of consciousness</td>
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<tr>
<td>Gaze palsy</td>
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<tr>
<td>Abnormal visual fields</td>
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<td>Facial palsy</td>
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Table 3: Clinical features that would suggest the need for imaging before performing lumbar puncture

Magnetic resonance imaging, though not often practical in the acute setting, provides additional information about the diagnosis. Presence of signal changes in the medial temporal and orbito-frontal regions would suggest herpes simplex encephalitis.

**CEREBROSPINAL FLUID**

Lumbar puncture is the most important investigation in acute CNS infections, and helps to confirm the diagnosis and identify the organism. CSF study should include cell count, protein, glucose and cultures (bacterial, fungal and mycobacterial), staining (gram, Giemsa, India Ink, acid fast bacilli), depending upon the suspected organism. CSF antigen detection, CSF antibody detection and DNA detection by PCR are various other useful investigations that could be seen in the appropriate setting. CSF abnormalities seen in various types of meningitis are given in table 4.
The CSF Gram stain can be positive in 60-90% of cases of untreated bacterial meningitis. The yield decreases to 20% if patient has received prior antibiotics. Latex agglutination tests for bacterial antigen detection and PCR are other investigations which are useful in bacterial meningitis. CSF AFB stain and AFB culture are useful investigations in suspected cases of tuberculous meningitis. An increased yield may be seen when using radiometric techniques in liquid media. CSF adenosine deaminase (ADA) may be elevated in tuberculous meningitis, though this may be elevated in other conditions such as neurobrucellosis, lymphoma with meningeal involvement, subarachnoid hemorrhage and sarcoidosis. PCR has a sensitivity of 56-90% and specificity of 88-100% in tuberculous meningitis. In herpes encephalitis, CSF DNA PCR has a sensitivity and specificity more than 95% compared with brain biopsy.

**ELECTROENCEPHALOGRAPHY (EEG)**

EEG may be useful in the setting of suspected encephalitis. Though the most common finding may be nonspecific slowing, EEG may demonstrate more specific abnormalities such as spike and wave discharges. EEG is essential when the possibility of status epilepticus is being considered. Presence of focal slowing or epileptiform discharges is of much more diagnostic value and in the temporal and frontal leads suggests herpes simplex encephalitis. The classical EEG finding in herpes simplex encephalitis is periodic lateralised epileptiform discharges (PLEDS).

**ACUTE PYOGENIC MENINGITIS EPIDEMIOLOGY**

In the United States and in other countries, epidemics of acute meningococcal meningitis are a common occurrence; in parts of sub-Saharan Africa (meningitis belt), meningococcal meningitis is endemic. In the United States, the overall incidence of meningitis is about 2 to 10 cases per 100,000 populations per year although the attack rates are very age-specific. The incidence is greatest in pediatric patients, especially infants, with attack rates in neonates at about 400 per 100,000, compared with 1 to 2 per 100,000 in adults and 20 per 100,000 in those less than or equal to 2 years old.

**CLINICAL FEATURES**

The classic triad of meningitis is fever, neck stiffness, and a change in mental status. Headache, which is holocranial, is another common symptom. Headache is usually abrupt in onset with nocturnal awakening and associated with nausea and vomiting, and photophobia and phonophobia.

In a study from the Netherlands, in adults presenting with community acquired acute bacterial meningitis, the sensitivity of the classic triad of fever, neck stiffness, and altered mental status is low, but almost all present with at least two of the four symptoms of headache, fever, neck stiffness, and altered mental status. About 20 - 30% of patients with meningitis do not have neck stiffness at presentation.

Often patients show features of raised intracranial pressure (ICP) due to capillary leak secondary to CNS inflammation. Alteration in CSF dynamics in meningitis can result in obstructive hydrocephalus. Clinical feature of raised ICP include declining level of consciousness, bradycardia, systemic hypertension and papilloedema.

A petechial or purpuric rash is almost exclusively seen in meningococcal disease but, particularly in the early phases of the disease, the rash may be erythematous or maculopapular in character. However, it must be remembered that as many as 50% of patients with proven meningococcal meningitis may not have a rash at presentation.

**MANAGEMENT OF ACUTE PYOGENIC MENINGITIS**

Treatment in a suspected case of meningitis is aimed at rapid diagnosis, specific antimicrobial therapy and
adjunctive therapy. In a suspected case, the emergency physician should have samples collected for blood culture, urgent lumbar puncture and commence appropriate antibiotics. If a physician requires imaging before LP, a blood culture should be sent and antibiotic and adjunctive therapy started, before sending patient for CT and then performing LP if required. Delay in treatment increases morbidity and mortality, so time should not be wasted for investigations. The choice of antibiotics depends on age and other associated factors like immune status, systemic diseases and epidemiological factors (tables 5, 6 and 7).

**USE OF STEROIDS IN PYOGENIC MENINGITIS**

<table>
<thead>
<tr>
<th>Clinical setting</th>
<th>Empirical therapy</th>
<th>Organism</th>
<th>Specific therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>age &lt; 3 months</td>
<td>Ampicillin+ gentamicin or Ampicillin+ 3rd generation cephosporin*</td>
<td>Group B streptococcus</td>
<td>Ampicillin + gentamicin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enterobacteriaceae</td>
<td>3rd generation cephalosporin + aminoglycosides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L. monocytogenes</td>
<td>Ampicillin + Gentamicin</td>
</tr>
<tr>
<td>3 months - 18 years</td>
<td>3rd generation cephosporin</td>
<td>N. meningitidis</td>
<td>Benzyl penicillin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S. pneumoniae</td>
<td>Benzyll penicillin or 3rd generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>H. influenzae</td>
<td>3rd generation cephalosporin or ampicillin + chloramphenicol</td>
</tr>
<tr>
<td>18 years – 50 years</td>
<td>3rd generation cephosporin</td>
<td>S. pneumoniae</td>
<td>Benzyll penicillin or 3rd generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alternatives – vancomycin + 3rd generation cephalosporin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rifampicin may be added to vancomycin</td>
</tr>
<tr>
<td>&gt; 50 years</td>
<td>Ampicillin+ 3rd generation cephosporin</td>
<td>S. pneumoniae</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L. monocytogenes</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gram negative bacilli</td>
<td>As above</td>
</tr>
<tr>
<td>Head trauma</td>
<td>Vancomycin + ceftazidime</td>
<td>Staph. aureus</td>
<td>Vancomycin + oxacillin</td>
</tr>
<tr>
<td>neurosurgical procedure</td>
<td></td>
<td>Staph. epidermidis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gram negative bacilli</td>
<td>Cefazidime + aminoglycoside</td>
</tr>
<tr>
<td></td>
<td></td>
<td>including pseudomonas</td>
<td></td>
</tr>
</tbody>
</table>
Table 5. Antibiotic recommendations for meningitis

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dose in children</th>
<th>Daily Dose in adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>20-30 mg/kg 8hrly intravenous</td>
<td>15mg/kg 8hrly intravenous</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>300mg/kg 6hrly intravenous</td>
<td>12gm 6hrly intravenous</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>150-300mg/kg 6hrly intravenous</td>
<td>8-12gm 6hrly intravenous</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>150 mg/kg 8hrly intravenous</td>
<td>6gm 8hrly intravenous</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>100mg/kg 12hrly intravenous</td>
<td>4gm 12hrly intravenous</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>60mg/kg 6-8hrly intravenous</td>
<td>30mg/kg 8hrly intravenous</td>
</tr>
<tr>
<td>Meropenem</td>
<td>120mg/kg 8hrly intravenous</td>
<td>6gm 8hrly intravenous</td>
</tr>
</tbody>
</table>

Table 6: Recommended dosages of antimicrobial therapy in patients with bacterial meningitis

<table>
<thead>
<tr>
<th>Organism</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria meningitidis</td>
<td>7days</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>7days</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>10-14 days</td>
</tr>
<tr>
<td>Streptococcus agalactiae</td>
<td>14-21 days</td>
</tr>
<tr>
<td>Aerobic gram-negative bacilli</td>
<td>21 days</td>
</tr>
<tr>
<td>Listeria monocytogenes</td>
<td>- / &gt; 21 days</td>
</tr>
</tbody>
</table>

Table 7: Duration of antimicrobial therapy for bacterial meningitis

VIRAL MENINGITIS AND ENCEPHALITIS

Epidemiologic studies estimate the incidence of viral encephalitis at 3.5-7.4 per 100,000 persons per year. Overall, viruses are the most common cause of encephalitis. The Center for Disease Control and Prevention (CDC) estimates an annual incidence of approximately 20,000 new cases of encephalitis in the United States, mostly mild in nature. Seasonal variation can affect the incidence of viral encephalitis. Japanese encephalitis is more common in rainy season, while arboviral encephalitis is prevalent during warm and/or wet seasons. Japanese encephalitis virus is the most common cause of epidemic encephalitis worldwide, causing encephalitis more often than meningitis. It is prevalent in Asia and Australia and affects children more than adults. Herpes simplex virus type 1 is the commonest cause of sporadic encephalitis. Enterovirus is the commonest cause of meningitis. Fever, neck stiffness and headache are the commonest symptoms in viral meningitis. Symptoms are less severe in comparison to bacterial meningitis.

In India, Japanese B Encephalitis is the commonest cause for epidemic encephalitis. Epidemiological studies have been carried out which show that there are several arboviruses that are responsible for encephalitis in India, e.g. West Nile virus, dengue hemorrhagic fever.

Encephalitis should be suspected when a febrile patient presents with altered mentation or level of consciousness. Seizures, both focal and general, are common manifestations of encephalitis. HSV encephalitis, which is the commonest, has a predilection for the temporal and orbitofrontal lobes resulting in memory impairment, behavioural change and altered sensorium.

Treatment is mainly supportive in viral meningitis, since it is a self-limiting disorder. Antipyretics and analgesics are the cornerstone of treatment. Oral or intravenous (IV) acyclovir can be tried in HSV 1&2, varicella and Epstein-Barr virus infection. IV acyclovir for
one week for severe HSV infection, and oral acyclovir 800mg five times a day, valacyclovir 1000mg TID and famciclovir 500mg TID in mild cases of HSV meningitis can be used. The experimental drug Pleconaril has been proven to be effective in enteroviral meningitis.

**HERPES SIMPLEX ENCEPHALITIS (HSE)**

Although a wide range of viruses have been reported to cause encephalitis, specific antiviral therapy for viral encephalitis is generally limited to disease caused by herpes simplex virus. Acyclovir is the treatment of choice for patients with herpes simplex encephalitis but morbidity and mortality remain high. In a retrospective multicentre trial of 93 adult patients, multivariate analysis also identified a Simplified Acute Physiology Score greater than 27 at hospital admission and a delay of greater than two days between hospital admission and administration of acyclovir therapy as independent predictors of poor outcome. The dosage of acyclovir in patients with normal renal function is 10 mg/kg intravenously every 8 h for 14–21 days. Recently, the use of higher dose acyclovir (20 mg/kg intravenously every 8 h for 21 days) in neonates with herpes simplex encephalitis has decreased mortality to 5%, with 40% of survivors developing normally. A negative CSF PCR result at the end of therapy was associated with a better outcome, suggesting that another CSF specimen should be subjected to PCR for herpes simplex virus at the end of therapy in patients who have not had the appropriate clinical response if the result is positive, antiviral therapy should be continued.

In patients with herpes simplex encephalitis, predictors of an adverse outcome include age of the patient (130 years), level of consciousness (Glasgow coma score, < 6), and duration of symptoms prior to starting acyclovir therapy (more than four days). The role of steroid in HSV encephalitis is controversial, since reports do not clearly document benefit in when steroid is added.

**TUBERCULOUS MENINGITIS**

Tuberculous meningitis (TBM) is still a major cause of serious illness in many parts of the world. It usually presents as subacute to chronic meningitis. But acute presentations in the form of acute meningitis, encephalopathy, raised intracranial pressure, seizures and acute focal deficits secondary to vasculitis are not uncommon. CSF examination shows normal to elevated CSF pressure, elevated protein (80-400mg/dl), low glucose (40mg/dl) and lymphocytic predominant (200-400 WBC/mm3) pleocytosis. Identifying the bacilli by smear and culture will establish the diagnosis. CSF TB PCR, which has been repeatedly used, has sensitivity of 70-75%. Neuroimaging in TB meningitis will show basal exudates and hydrocephalus. In suspected case of TB meningitis, evidence of infection, active or chronic, should be looked for in the chest and abdomen. The Mantoux test is another investigation that can help in the diagnosis.

Chemotherapy of TB meningitis include a regime of four drugs (rifampicin, INH, pyrazinamide, ethambutol/streptomycin) for two months or till the disease starts improving, followed by INH and rifampicin for at least ten months. The total duration of treatment should be a minimum of 1-1½ years. In multi-drug resistant TB and immunocompromised patients, five or seven drugs should be added, depending on the severity of illness. Steroids are indicated in TB meningitis in the presence of raised ICP, hydrocephalus, vasculitis, arachnoiditis, or markedly raised CSF protein.

**FUNGAL MENINGITIS**

It is a less common cause of meningitis compared to bacterial and viral meningitis. CNS manifestations of fungal infection can vary from meningoencephalitis, focal lesions, vasculitis, and raised intracranial pressure. Yeast species (cryptococcus) have a predilection to cause meningeal infection, while filamentous fungi (aspergillus) will cause parenchymal infection. Fungal infections are more common in immunocompromised patients, including patients on chronic steroid therapy.

Meningitis can be acute, subacute, or chronic. These are often associated with focal deficits, encephalopathy and raised ICP.

CT or MRI is indicated in suspected cases of fungal meningitis to look for hydrocephalus and focal lesions. Another clue to the aetiological agent is the presence of T2 hyperintensity in the basal ganglia in 40 % of cryptococcal infections.

CSF in fungal infection shows high opening pressure with elevated cell count, low sugar and elevated protein. CSF India ink preparation can show encapsulated yeasts in 50-75% of cryptococcal meningitis. Fungal culture, fungal antigen assay and antibody detection by radioimmunoassay are other useful investigations to detect the organisms. CSF pleocytosis is predominantly lymphocytic and rarely can be neutrophilic in aspergillus infections or eosinophilic in Coccidioides Immitis infection.

The successful treatment of central nervous system (CNS) fungal infections is highly dependent on the underlying immune status of the host, as well as on the prompt initiation of appropriate antifungal therapy. However, the diagnosis of these infections may be difficult, and proper therapy is often delayed. The standard antifungal agent for the treatment of CNS fungal infections has been amphotericin B. However, poor CNS penetration, fungal resistance, and toxicity often eliminate the effectiveness of amphotericin B. Because
of the problems associated with use of amphotericin B, newer liposomal preparations, as well as azole antifungal agents, have been developed. A new azole that is undergoing clinical trials is Ravuconazole. Flucytosine is often used as an adjunct to amphotericin B in patients with invasive infections by cryptococcus, candida and aspergillus. The duration of treatment is weeks to months depending on the response.

CEREBRAL MALARIA

Of all the four species of malaria that infect man, only plasmodium falciparum causes cerebral malaria. The transmission of plasmodium occurs through the bite of the female anopheles mosquito. In cerebral malaria, microvasculature of the brain is packed with red blood cells infested by the falciparum. The brain is swollen, with multiple micro-haemorrhages mainly in white matter. Microglial cells and macrophages surrounding the haemorrhagic foci are called Durcks granuloma.

WHO DEFINITION FOR CEREBRAL MALARIA

1. Unarousable coma / impairment of sensorium not attributable to any other cause in a patient with falciparum malaria. Coma should persist at least 30 minutes after a generalized convulsion to make the distinction from transient postictal coma.

2. Presence of asexual forms in peripheral blood smear or bone marrow smear

Fever is commonest clinical feature followed by encephalopathy. Focal deficits are rare. 50-60% of cases can have seizures. Fundus examination can show papilloedema, retinal ischaemia and hemorrhages. Severe cases may present with decerebrate or decorticate posturing.

Cerebral malaria is a neurological emergency requiring prompt diagnosis and treatment. It should be suspected in all cases of unexplained encephalopathy in malariaendemic regions. Diagnosis is by demonstration of malarial parasite in peripheral blood smears stained with Geimsa / Field stain. At least three peripheral smears repeated every 6-8 hours should be negative to exclude the diagnosis of malaria. The infection rate of red cells is usually high (greater than 10%). Antibody testing and PCR detection of DNA is now available.

WHO guidelines recommend the following range of anti-malarial medications, there being insufficient evidence to recommend any one over the other for severe malaria:

- Artesunate 2.4 mg/kg bw i.v. or i.m given on admission (time = 0), then at 12 h and 24 h, then once a day; artemether 3.2 mg/kg bw i.m given on admission then 1.6 mg/kg bw per day; for total 5-7 days

- Quinine 20 mg salt/kg bw on admission (i.v. infusion or divided i.m. injection), then 10 mg/kg bw every 8 h; infusion rate should not exceed 5 mg salt/kg bw per hour. Once patient is conscious or afebrile then quinine is given orally (10mg/kg every 8 hours) for 5-7 days. When the patient is on quinine, ECG monitoring for QT interval prolongation is recommended.

Anti oedema measures for raised ICP, anticonvulsants for seizures, and regular monitoring and treatment for hypoglycemia should be provided as required.

REFERENCES:


Dentofacial Effects of Rapid Maxillary Expansion

Navya Ashok, Sapna Varma NK, Ajith VV, Namitha Ramesh

ABSTRACT

Rapid maxillary expanders are orthopaedic devices commonly used to increase transverse width of maxilla in craniofacial abnormalities with maxillary constriction. Maxillary constrictions are associated with alterations in tongue posture, retroglossal airway narrowing, increased nasal resistance and can cause sleep disordered breathing. Though adenotonsillectomy is preferred treatment for sleep disordered breathing; there is persistence of sleep disordered breathing even after surgery. Orthodontic treatment should be considered as an adjunct to adenotonsillectomy in children with persistent or recurring sleep disordered breathing. In sleep disordered breathing, rapid maxillary expansion causes widening of the nasal fossa and releasing nasal septum, hence restoring normal airflow, by improving resting tongue posture and oro-pharyngeal space. This article outlines the effects of rapid maxillary expansion on skeletal, dental, airway and sleep parameters.

Keywords: RME-rapid maxillary expansion; MTD-maxillary transverse deficiency; OSA- obstructive sleep apnea; PSG-polysomnography

INTRODUCTION

Rapid maxillary expansion (RME) is an effective orthopaedic procedure used in growing patients to correct dental and skeletal maxillary transverse discrepancies. It has been proposed by Angell in 19th century. It was reintroduced in the middle of the last century by Andrew Haas. As early as 1920, Mesnard demonstrated radiographically that the mid-palatal suture could be separated using fixed appliance and that space would be filled with bone within 4-6 weeks. The incidence of maxillary transverse deficiency in the deciduous and mixed dentitions is estimated at 8% to 18% of patients having orthodontic consultations. This entity may occur in the primary dentition and manifest itself as a constriction of the lateral dimension of the upper arch. Different methods have been used to expand constricted maxillary arches. Depending on the basis of frequency of the activations, magnitude of the applied force, duration of the treatment, and patient age, different mechanics produce rapid, semi-rapid, or slow expansion.

The effects of respiratory function on craniofacial growth have been studied for decades, and most clinicians now understand that respiratory function is highly relevant to the orthodontic diagnosis and the treatment planning. The main characteristics of the respiratory obstruction syndrome is adenoid and tonsil hypertrophy, posterior cross bite, open bite, narrow external nares, and tongue thrusting. Infection and inflammation of the adenoids leads to upper airway obstruction, and the term ‘adenoid facies’ is often used to describe a possible aberrant craniofacial growth pattern related to mouth breathing characterized by lip incompetency, underdeveloped nose, increased anterior facial height, constricted dental arches, and proclined maxillary incisors with a high arched palatal vault.

An ENT surgeon evaluates nasopharyngeal airway either with endoscopy, CT or an MRI. Most 3D studies use multi-slice CT to evaluate the airway; this has the advantage of high-quality images to discern hard- and soft-tissue anatomies, but, because of the high radiation dose, it is restricted to patients with severe craniofacial deformities and those undergoing orthognathic surgeries. The factor, that determines the capacity for airflow is the minimal cross-sectional area of the passage. This narrowest portion can occur at any point along the nasopharyngeal trajectory and can only be accurately visualized by computed tomography. Orthodontists and otolaryngologists should combine efforts to determine the provision of an adequate and unrestricted respiratory airway to enhance the facial growth and development in specific patients.

Jean et al had reported improvement in nasal respiration with a reduction in mouth breathing following surgical removal of enlarged adenoids and tonsils. Evidence has demonstrated that nasal obstruction regardless of cause leads to mouth breathing which in turn leads to altered function resulting in altered facial form. Adeno and or tonsillectomy although preferred and cures sleep disordered breathing, two recent studies have documented persistence of sleep disordered breathing even after adenotonsillectomy in 75% children.

Prospective studies on children with rapid maxillary expansion have been shown to modify craniofacial anomalies and improve sleep disordered breathing in children. In presence of maxillary transverse discrepancies, orthodontic treatment should be considered as first line of treatment in children without...
adenotonsillar hypertrophy, and as an adjunct to adeno-
tonsillectomy in children with persisting/recurring
disordered breathing7.

The aim of the article is to present a comprehensive
review of the literature, including indications, diagnosis,
guidelines for case selection, a brief overview of the
techniques, limitations and effects of RME on skeletal,
dental, airway and sleep; to better aid the clinician in
the management of maxillary transverse deficiency.

INDICATIONS

- Maxillary transverse discrepancies that result in
either unilateral or bilateral posterior crossbite in-
volving several teeth with high arched palate. (fig1)
- Proclined upper anterior teeth with constricted
maxillary arch, with or without crossbite. (fig2)
- Class III malocclusion, borderline skeletal class III
ie; retrognathic maxilla with prognathic or normal
mandible. (fig3)
- Pseudo class III condition with constriction of arches
or cross-bite; caused due to shift of mandible due
to premature contact.
- Cleft lip and palate. (fig4)
- To gain arch length in patients who have moderate
maxillary crowding10

ETIOLOGY OF TRANSVERSE
DISCREPANCES

The causes of transverse discrepancies could be
either genetic or environmental. According to Graber,
Judith11,12 many constricted maxillary dental arches are
the result of abnormal function. Alterations in respiration
can cause posterior crossbites. The altered respiration
can lead to lowered tongue posture, rotation of the man-
dible, and less transverse development of the maxilla.
Patients with severe allergies and other respiratory issue
are at risk for developing maxillary constriction. Digit
habits that continue into the mixed dentition have also
been linked to the development of posterior cross bite
due to the increased amount of pressure from buccal
musculature.

MID PALATAL SUTURE

Mid palatine suture plays a key role and its patency
is vital for R.M.E. Closure of suture occur at 15 yrs of
age. Greater degree of obliteration occurs posteriorly
than anteriorly13. The optimal age for expansion is before
13 to 15 years.

Various shapes of mid palatal suture are
i. Infancy - Y-shape (fig5), ii. Juvenile - T-shape
iii. Adolescence - Jigsaw puzzle (fig6)
Dentofacial Effects of Rapid Maxillary Expansion

DIAGNOSIS

Unlike discrepancies in the vertical and the anteroposterior dimensions, diagnosis of maxillary transverse discrepancy is difficult; various methods are used for diagnosis.

Case history, clinical evaluation, model analysis, occlusograms, and radiographic measurements, PA cephalogram or 3D Computed tomography or cone beam computed tomography have been recommended for an accurate assessment.

CASE HISTORY

A detailed case history should be taken regarding any habits, family history, allergy, nasal obstruction or any sleep disturbances. A questionnaire regarding day time sleepiness, performance in school or academics, tiredness, oral breathing and night time restless sleep should also be recorded.

2 D RADIOGRAPHS

Rapid maxillary expansion has been analyzed using two-dimensional posteroanterior (PA) cephalograms, lateral cephalograms or occlusal radiographs. This analysis first identifies dental and skeletal landmarks on PA cephalograms. After identification of landmarks, linear measurements are taken by connecting the bilateral landmarks. It is also possible to measure patency of airway from lateral cephalograms. However, the disadvantage of using cephalograms is the fact that they are a two dimensional representation of a three-dimensional object and problems that result from difficulties encountered in landmark identification.

3 D CT/CBCT

Traditionally, most research in airway patency have been done using 2-D imaging technique. With the advent of 3-D imaging techniques clinician is able to visualize the craniofacial region and thereby helping in accurate diagnosis and treatment planning. Garret et al14 stated that Volumetric 3-D CT scanning provides a useful method for assessing skeletal and dental changes after rapid maxillary expansion.

Most 3D studies of the airway uses multi-slice CT to evaluate the airway; this has the advantage of high-quality images. With the decreased ionizing radiation and shorter imaging time of CBCT, evaluation of the craniofacial complex at various levels without the superimposition of structures can be done. The total radiation from a CBCT scan is approximately 20% of conventional CTs and equivalent to a full mouth periapical radiographic exposure. Measurements made in Dolphin 3D (Dolphin Imaging & Management Solutions) are clinically accurate for craniofacial analyses. When 3D scan is done for evaluation of tonsils, adenoids or upper airway obstruction, an additional X ray exposure like 2-D lateral cephalograms or OPG can be avoided for diagnosis and treatment planning in orthodontics. CT evaluation constitutes a useful supplement for orthodontic diagnosis and gives an image of changes taking place in all dimensions.

POLYSOMNOGRAPHY

Patients with transverse deficiency usually exhibit obstructive sleep apnea. Repeated episodes of upper airway obstruction during sleep is characterised by OSA15. Apneic episodes are characterized by upper airway closure and progressively increasing respiratory efforts driven by chemoreceptor and mechanoreceptor stimuli, which then provoke arousal from sleep and reopening of the airway. Diagnostic tests are needed to guide treatment recommendations. The severity of apnoea - hypopnoea index (AHI) and oxygen saturation (SpO2) are significantly correlated with the width of the airway space at the base of the tongue and hypopharynx. Sleep testing is performed to establish the diagnosis16, 17.

The current “gold standard” test for OSA is complete overnight polysomnography (PSG) performed in a sleep laboratory. This test involves recording of the electroencephalogram, electrooculogram and submental electromyogram for sleep - wake staging, pulse
oximetry, determination of airflow with an oronasal thermistor or through nasal pressure, determination of body position with mercury switch or video recording, recording of sound (snoring) with a microphone, and detection of periodic limb movements with leg electromyography electrodes. The basis of therapeutic intervention with oral appliances in the obstructed pediatric airway is to expand the maxilla and/or advance the mandible. Pirelli et al evaluated children with maxillary constriction, oral breathing & OSAS and demonstrated that RME is a valid treatment for OSAS in children. At 4 month follow up there was a significant decrease in AHI & arousal index.

**TYPES OF RAPID MAXILLARY EXPANSION DEVICES**

1. Tissue borne
2. Tooth borne: Banded – Hyrax or Biedermann type. Bonded - Minne Expander or Isaacson type (Fig 7)

![Banded RME](image1.png)

![Bonded RME](image2.png)

Ufuk et al reported the use of full occlusal coverage palatal expansion appliances that limits the vertical effects of inter-occlusal forces resulting in the release of the maxilla, it also plays an important role in expansion and protraction. They also suggested that this device could provide control of the vertical dimensional changes that occur in vertically growing patients during maxillary expansion.

**ACTIVATION**

Young growing patients - 2 turns each day for 4-5 days & later one turn/day till desired expansion achieved. (Fig 8)

![Activation](image3.png)

Although it may be possible to accomplish expansion in older patients, the results are neither as predictable nor as stable. Proffit and Burdon supported this opinion by suggesting that the feasibility of palatal expansion in the late teens and early twenties is questionable. Surgically assisted RME combined with fixed orthodontic treatment has been suggested to overcome this problem. An increase in maxillary width of up to 10 mm can be achieved by R.M.E. Rate of expansion is 0.2 to 0.5 mm per day with active expansion is completed in 2-4 weeks, leaving little time for the cellular response of osteoclasts and osteoblasts seen in slow expansion. Expansion should stop when the maxillary palatal cusps are level with the buccal cusps of the mandibular teeth.

**SKELETAL AND DENTAL EFFECTS OF RME**

One of the most common changes accompanying RME is the opening of a diastema between the maxillary central incisors (Fig 9). It is estimated that during active suture opening, the incisors separate approximately half
the distance the expansion screw has been opened. Following this separation, the incisor crowns converge and establish proximal contact. The mesial tipping of the crowns is due to the elastic recoil of the trans-septal fibers of periodontal ligament. Once the crowns of incisors contact, the continued pull of the fibers causes the roots to converge toward their original axial inclinations. This takes about 4 months. Posterior teeth shows buccal tipping and limited extrusion. (Fig 10). Expansion occurs when the force applied to the teeth and the maxillary alveolar processes exceed the limits needed for orthodontic tooth movement (Fig 11). It is seen that the two halves of the maxilla rotated in both the sagittal and frontal planes. Haas suggested when the mid-palatal suture opens, the maxilla always moves forward and downward. Skeletal changes in downward and anterior displacement of maxilla may be minimized or negated with the use of the bonded appliance.

**EFFECTS OF RME ON NASAL VOLUME**

The use of maxillary expansion has been extended for the correction of nasal obstruction, as it has been suggested that nasal width and volume increases by RME. RME treatment causes a significant increase in nasal cavity volume and maxillary transverse dimensions (Fig 12). Herhy et al evaluated patients requiring RME treatment for constricted maxillary arches who have significantly higher nasal resistance than other orthodontic patients and non-orthodontic subjects. The RME procedure reduced the nasal resistance of those treated to a level which was not significantly different.
from that of subjects with maxillary arches of normal dimensions. RME is not only an effective method for increasing the width of narrow maxillary arches but also reduces nasal resistance from levels associated with mouth breathing to levels compatible with normal nasal respiration. White et al.\textsuperscript{28} evaluated on nasal airway resistance prior to expansion, immediately after expansion (approximately one month), after a retention period of approximately 4 months and approximately one year after initiation of treatment. Findings indicate an average reduction in nasal airway resistance and was stable throughout the post treatment observation period (maximum one year).

**EFFECTS OF RME ON AIRWAY**

Total airway volume enlargement occurs by expansion of the palate volume. Long-term findings of study conducted by De Fellippe et al with RME; concluded that nasal airway resistance was stable, whereas mean nasal cavity volume and minimal cross-sectional area (MCA) increased. MCA is the narrowest cross-sectional area of upper airway. 61.3% of subjects reported subjective improvement in nasal respiration\textsuperscript{29}. RME caused relatively greater enlargement of the retropalatal airway than the oropharyngeal airway. According to Tso et al, the range of the MCA in healthy adults varied from 90 to 360 mm\textsuperscript{2}\textsuperscript{30}. With RME it is possible to obtain nearly normal value of MCA of upper airway for children with sleep disordered breathing (Fig13).

Low dose CT report on skeletal and dental effects of a patient treated with RME (Table 1). After treatment with RME on the same patient, MCA of upper airway increased from 61.8 mm\textsuperscript{2} to 89.1 mm\textsuperscript{2}.

**Fig 13 MCA of upper airway before and after RME**
EFFECTS OF RME ON SLEEP PARAMETERS:

After RME there is an increase in sleep efficiency, base line oxygen saturation, arousal index reduced and increase in total sleep time. Maria et al evaluated OSA patients treated with RME. At 12 month follow up, PSG showed significant decrease in apnea hypopnea index showing improvement in sleep17.

Sleep parameters evaluated by comparing PSG recordings which is taken before and after RME of the same patient. (Table2).

RETENTION AND RELAPSE AFTER RME:

Expansion through maxillary suture widening by rapid maxillary expanders has been claimed to promote stability after retention. The application of a fixed retainer immediate to RME, then followed by an intermittent removable retention appliance is highly recommended. Hershy et al27 concluded that reduction in nasal resistance achieved with the expansion procedure was not lost after 3 months of retention. In mixed dentition stage; a retention plate with clasps on molars is fitted and retention phase should be for 6 months31. Retention period of atleast 5 months is necessary to permit adequate mineralisation of suture and to minimise relapse tendency after expansion32.

CONCLUSION:

There is an enhanced orthopaedic response to maxillary expansion procedures during deciduous and mixed dentition periods. RME proves to be promising in the treatment of MTD*. The primary consideration ultimately involves determination of appropriate expansion protocol which would promote orthopedic movement of maxillary segments while maintaining tissue integrity. In addition to orthopaedic movements, RME also increases nasal cavity volume, reduces airway resistance and improves sleep disordered breathing. So for beneficial results it is important that pediatric sleep specialists, otolaryngologists and orthodontists should provide a multidisciplinary management for children with naso-respiratory problems, sleep disordered breathing and orthodontic anomalies.

<table>
<thead>
<tr>
<th>Lateral limits of maxillary base</th>
<th>PRE TREATMENT(T0)</th>
<th>POST TREATMENT(T1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxillary alveolar width</td>
<td>7.69mm</td>
<td>8.16mm</td>
</tr>
<tr>
<td>Nasal cavity width</td>
<td>4.66mm</td>
<td>5.30mm</td>
</tr>
<tr>
<td>Width of maxillary molars (crown)</td>
<td>2.93mm</td>
<td>3.20mm</td>
</tr>
<tr>
<td>Width of maxillary molars (root)</td>
<td>4.62mm</td>
<td>5.38mm</td>
</tr>
<tr>
<td>Width of maxillary base (canine slice)</td>
<td>5.75mm</td>
<td>5.75mm</td>
</tr>
<tr>
<td>Minimal constricted area of upper airway</td>
<td>4.95mm</td>
<td>5.05mm</td>
</tr>
</tbody>
</table>

Table 1: CT report of skeletal and dental changes with RME

<table>
<thead>
<tr>
<th>PSG</th>
<th>T0</th>
<th>T1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep efficiency</td>
<td>84.10%</td>
<td>87.25%</td>
</tr>
<tr>
<td>Arousal index</td>
<td>8.05 events per hour</td>
<td>6.22 events/hr</td>
</tr>
<tr>
<td>Baseline O2 saturation</td>
<td>97%</td>
<td>98.4%</td>
</tr>
<tr>
<td>Total time slept</td>
<td>365min</td>
<td>397min</td>
</tr>
</tbody>
</table>

Table 2: PSG report of a patient treated with RME

REFERENCES:
1. Book Rapid Maxillary Expansion ;Donad J Timms; Chicago
5. Judith D. Lampasso and James G. LampassoAllergy, Nasal


Reliability of Fine Needle Aspiration Cytology in salivary neoplasms: surgeon’s perspective

Bini Faizal*, Janhvi Jayesh Bhate*, Hiran K.R**

ABSTRACT

Fine needle aspiration (FNA) is used by surgeons as an initial clinical tool to differentiate between benign and malignant tumors of the salivary glands. The surgical intervention is planned depending on cytology. Not infrequently, this springs some surprises when the histopathology reports a malignancy.

The aim of this study is to evaluate the efficacy of FNA and cytology on salivary neoplasms and its influence on treatment outcome. A retrospective study was conducted in 120 patients who underwent surgery for FNA-proven salivary neoplasms at our institute. FNA was found to have a sensitivity, specificity and diagnostic accuracy of 66%, 97.1% and 70% respectively. FNA has a reliable sensitivity and specificity. However, limitations were encountered with specific lesions especially some cystic and malignant lesions which resulted in modification of treatment.

INTRODUCTION

Salivary gland tumors are uncommon, amounting to approximately 3-10% of neoplasms of the head and neck region. However, a wide variety of tumors in these glands and insufficient tumor cells in aspiration cytology make the diagnosis difficult in some patients. The general rule in salivary gland neoplasms is: ‘smaller the gland, higher the rate of malignancy’. Thus, the rate of malignancy increases from 20%–25% in the parotid gland to 40%–50% in the submandibular gland and to 50%–81% in the sublingual glands and minor salivary glands. Nearly 80% of benign parotid neoplasms are pleomorphic adenomas (PA). While PA is the most common benign tumor for both parotid and submandibular glands, the malignant tumors correspondingly are mucoepidermoid and adenoid cystic carcinomas.

Fine needle aspiration (FNA) still remains the mainstay of evaluation of salivary neoplasms. While a malignant neoplasm is treated with urgency, benign lesions are, to some extent, treated depending upon the convenience of the patient. The variation in morphology and the complex histology of salivary glands make cytology reporting more challenging and hence needs expertise in the field. The relative rarity of salivary lesions makes it more difficult for the pathologist to acquire diagnostic expertise. The lack of knowledge on the part of the clinician regarding the grey areas in cytology makes the matter complicated. There is an argument that a salivary neoplasm is always treated by surgery and hence, the hue and cry over discrepancies in FNA is undue. But a proper pre-operative planning is always better than a revision surgery. The converse is also true when a total parotidectomy performed for a malignant neoplasm turns out to be only a pleomorphic adenoma on histology. An adequate parotidectomy with a cuff of normal salivary tissue would have sufficed in such cases and an aggressive surgery could have been avoided.

The accuracy of cytological diagnosis depends on the expertise of the cytopathologist, technician, the site of lesion, the adequacy of sample and the sampling method. The false positive diagnosis is rarely made by an experienced and well trained pathologist. The cytologist may make some false negative diagnoses. The false negatives and false positives are pointers towards limitations and pitfalls in cytological interpretation in the material. The use of multiple FNA facilitates the yield of generous cellular samples that allow the utilization of ancillary techniques in cases of difficulty in interpretation.

Pleomorphic adenoma (PA) should always be the first differential in salivary neoplasm. The presence of all three elements, namely, three dimensional cohesive clusters of ductal cells, background of singly lying plasmacytoid myoepithelial cells and dense fibrillary brightly metachromatic stroma with partially obscured entrapped myoepithelial cells should be looked for. Some diagnostic problems do occur in differentiating pleomorphic adenoma from adenoid cystic carcinoma (ACC), basal cell adenoma (BCA), nerve sheath tumors and mucoepidermoid carcinoma (MEC) as the composition of three elements constituting a pleomorphic adenoma.

*Dept. of ENT, AIMS, Kochi.
**Dept. of Pathology, AIMS, Kochi.
can vary considerably. Liberal repeat aspirations with multiple sampling performed from different parts of the tumor reduce diagnostic error. FNA is comparable to intraoperative frozen section in salivary tumors. Diagnosis of carcinoma ex PA may be elusive in FNA.

The sensitivity of diagnosing PA by FNA cytology is up to 94%-26, 27. In benign tumors, the cells interdigitate intricately with the fibrillary connective tissue associated with them. This is in contrast to the sharp digitate junctions with the fibrillary connective tissue material that forms the spheres and cylinders of ACC. Plasmacytoid myoepithelial cells are the most helpful cytomorphologic feature for distinguishing PA from ACC. Lowhagen et al. advocate that if the cribriform structures appear together with any features of PA, a diagnosis of PA should be given. The cytologic identification of ACC rests on adequate sampling and careful inspection of all material to rule out the possibility of benign PA or basal cell adenoma (BCA). It should be noted that inflammatory masses of the salivary glands may mimic epithelial neoplasms at cytology because desquamated cells frequently populate the former.

Core biopsy is a relatively new technique which offers certain edge over FNA. The aspiration is done with an 18 gauge needle. The sample obtained is greater and there is preservation of tissue architecture. The capsular invasion may be visible to differentiate a monomorphic adenoma and adenoid cystic carcinoma. Moreover immunohistochemistry is likely to be more reliable. Core biopsy causes more morbidity than FNA. In a metaanalysis by Schmidt et al, the specificity estimates of FNA and core needle biopsy are comparable. However, core biopsy has better sensitivity. So CNB could be a useful adjunct in the event of a negative biopsy by FNA. There is more evidence of needle tracking by core biopsy which is worrisome.

MRI is the preferred modality of investigation in salivary neoplasms. A T1 weighted MR image usually maps the tumor well in terms of margins, extent and infiltration against a background of hyperintense (fatty) gland. If coupled with contrast enhanced fat saturated sequences, apart from showing perineural infiltration, bone and meningeal infiltration also will be clearly seen. This is possible because in fat saturation images, the bone marrow is hypointense. The hyperintense tumor is seen well in such instances.

However, no histologic distinction is possible with T1 weighted enhanced and non-enhanced images. T2 weighted imaging is found to be a reliable predictor (73%) of a salivary neoplasm. General dictum is that a hyperintense tumor on T2 is benign and a tumor with low to intermediate intensity is malignant. Addition of contrast helps in differentiating a cystic and solid lesion for example between a cyst and PA. Exceptions to this general rule are Warthin’s, chronic sialadenitis and radiation adenitis which might appear hypointense in T2. Malignant tumors which appear hyperintense are MEC commonly, occasionally ACC and rarely adenocarcinomas. So, a 25% error is expected if signal intensity is relied upon solely to predict histologic diagnosis. CT attenuation does not help in histologic diagnosis other than for differentiating between solid and cystic lesions and lipomas.

Ultrasonography (US) correctly differentiates between malignant and benign tumors in 90% of cases based on tumor margin. Malignant tumors show more vascularity in color Doppler. PA shows a hypoechoic area with peripheral vascularity. Limitations with US will be poor delineation of the deep lobe of parotid with skull base, parapharyngeal and retropharyngeal extension and overlapping of mandible. Small well delineated parotid mass may appear benign in US. An ultrasound guided FNA will increase the positive yield by avoiding cystic and necrotic areas and targeting solid areas. CT, MRI and ultrasound have very high sensitivity (88-98%) but poor specificity (52- 57%) in differentiating benign from malignant lesions. Nuclear scintigraphy may be helpful in Warthin’s and oncocytoma due to their increased tracer uptake in Technetium pertechnate imaging. Studies show that PET scan is also not effective.

Against this background, the present study was undertaken to determine the efficacy of FNA and the alertness required by the surgeon in analyzing the patient prior to surgery.

MATERIALS AND METHODS

Aim of the study:

The study was performed to determine the accuracy of FNA in diagnosing salivary gland diseases. An analysis was done to see whether any further treatment was required after histopathology. The possible grey areas in reporting cytology was analyzed.

Source of data:

A retrospective study was conducted in the Departments of ENT and Pathology of a tertiary care center from January 2007 to July 2012. A total of 120 cases of major salivary gland neoplasm with preoperative FNA and postoperative histopathology were selected. The data was collected from the Pathology and Surgery registers of the hospital.

Inclusion criteria: All major salivary gland histopathology with preoperative FNA were included in the study.

Exclusion criteria: None

Study design: Retrospective study.
Sampling:

All patients had undergone surgery after FNA. A few patients had to undergo further treatment depending on HP. Data was analyzed by two independent reviewers. Where there was discrepancy between FNA and HP, the possible reason was discussed with the pathologist. Whether the wrong FNA affected the treatment plan was also analyzed.

Statistical analysis: We compared the histopathological findings with the preoperative cytology of the FNAC specimens. We calculated the sensitivity, specificity, positive predictive value (PPV) negative predictive value (NPV), and overall accuracy of FNAC for diagnosing benign and malignant salivary gland diseases. Data was analyzed using SPSS 11.0 software for Windows. Based on the Chi square method, sensitivity and specificity of FNAC in differentiating between benign and malignant lesions was calculated. The measurement of agreement (Kappa score value) was 0.660 corresponding to P value <0.001, which was statistically significant. This showed that there was moderate agreement between FNAC and HP.

Observation, results and analysis:

<table>
<thead>
<tr>
<th>HP — FNA Crosstabulation: Contingency table</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>HP Malignant Count</td>
</tr>
<tr>
<td>% within HP</td>
</tr>
<tr>
<td>Benign Count</td>
</tr>
<tr>
<td>% within HP</td>
</tr>
<tr>
<td>Total Count</td>
</tr>
<tr>
<td>% within HP</td>
</tr>
</tbody>
</table>

Table 1- Percentage of malignant and benign lesions on FNA and HP

Out of 120 cases of salivary gland samples studied, FNA diagnosed 85 as benign and 35 as malignant (Table-1). Seven lesions were benign cystic lesions but no specific categorization was possible. Histopathology categorized 50 cases as malignant and 70 as benign. Of the 50 cases who received a histological diagnosis of malignant tumor; cytological diagnosis was concordant in 33 instances and discordant in 17. A total of 70 patients received a histological diagnosis of benign disease; of these 63 were neoplastic lesions, 7 cases were non-neoplastic chronic inflammatory disease of the salivary glands.

Pleomorphic adenoma was found to be the most common benign disease (33.3%) and Mucoepidermoid carcinoma (20%) was the commonest malignant neoplasm in FNA (Table-2). The pattern was the same in HP with Pleomorphic adenoma (25.8%) and Mucoepidermoid carcinoma (30%) respectively (Table-3). Of the 36 cases of MEC, 23 cases were correctly diagnosed by FNA, 13 were diagnosed correctly only after HP. Two cases diagnosed as malignant on FNA were later proven to be benign on histopathology. One was a case of Warthins tumour which was misdiagnosed as Acinic cell carcinoma and another was a case of pleomorphic adenoma which was misdiagnosed as Ca. ex-pleomorphic adenoma. There were two cases of Lymphoma which were misdiagnosed on FNA, one as Warthins tumour and another as mucoepidermoid carcinoma. Overall, FNA helped in the correct diagnosis of 33 malignant lesions; but among the benign lesions there was a misdiagnosis of 17 lesions which were later proven malignant on HP (Table-4).

Of the 17 cases which were proved as malignant only after histopathology, 7 required adjuvant radiotherapy in the postoperative period. Four patients had to undergo revision surgery which included complete excision of the involved gland along with neck dissection in cases which were found to have suspicious nodes on USG neck proven by FNA, followed by adjuvant radiotherapy. There were two cases of lymphoma which were misdiagnosed as a benign lesion (chronic sialadenitis) and another as MEC. Both patients after histopathology were evaluated fully for lymphoma and later treated with chemotherapy. Remaining four patients were kept on close observation and regular follow up since R0 resection with adequate margins away from the tumour had been attained. Recurrence has not been reported in these patients till date.

DISCUSSION

In our study, FNA was found to have a sensitivity of 66% and a specificity of 97.1%. The positive predictive value was 94.2% and the negative predictive value was 80% with an accuracy of 70.83% in diagnosing major salivary gland pathologies (Table-5). Our study was comparable to other studies in terms of sensitivity and specificity (Table-6)23,28. There was a significant number of patients who required further treatment either in the form of surgery, radiotherapy or chemotherapy. A revision parotidectomy puts the facial nerve at risk and the further unplanned treatment increases the stress for the patient.

Strength of the study: Though mismatch between FNA and histopathology has been known before, our study helped in finding out the clinical relevance in terms of patients requiring modification of treatment. The treatment modifications were significant necessitating caution in FNA reporting.

Limitations of the study: The FNA was done in the standard way with a 23 gauge needle; probably, an 18 gauge core biopsy gives better results.
### FNAC Diagnoses of Major Salivary Gland Lesions

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
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<tbody>
<tr>
<td><strong>BENIGN</strong></td>
<td></td>
<td></td>
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<tr>
<td>Pleomorphic adenoma</td>
<td>40</td>
<td>33.3</td>
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<tr>
<td>Warthins tumour</td>
<td>29</td>
<td>24.1</td>
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<tr>
<td>Chronic sialadenitis</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Benign cystic lesion</td>
<td>7</td>
<td>5.8</td>
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<tr>
<td>Lymphoepithelial cyst</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Oncocytoma</td>
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<td>0.8</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>85</td>
<td>70.8</td>
</tr>
<tr>
<td><strong>MALIGNANT</strong></td>
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<td></td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>24</td>
<td>20</td>
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<tr>
<td>Acinic cell carcinoma</td>
<td>5</td>
<td>4.1</td>
</tr>
<tr>
<td>Salivary duct SCC</td>
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<td>1.6</td>
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<tr>
<td>Adenoid cystic carcinoma</td>
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<tr>
<td>Adenocarcinoma</td>
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<tr>
<td>Ca. Ex-pleomorphic adenoma</td>
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<td>0.8</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td>35</td>
<td>29.1</td>
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</table>

| **GRAND TOTAL**      | 120   | 100 |

Table 2: Incidence of major salivary gland lesions

### Histopathological Diagnoses of Major Salivary Gland Lesions

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<tr>
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</thead>
<tbody>
<tr>
<td><strong>BENIGN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>31</td>
<td>25.8</td>
</tr>
<tr>
<td>Warthins tumour</td>
<td>25</td>
<td>20.8</td>
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<tr>
<td>Chronic sialadenitis</td>
<td>7</td>
<td>5.8</td>
</tr>
<tr>
<td>Basal cell adenoma</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Lymphoepithelial cyst</td>
<td>2</td>
<td>1.6</td>
</tr>
<tr>
<td>Lipoma</td>
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<td>0.8</td>
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<tr>
<td>Intraparotid lymph nodes</td>
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<td>0.8</td>
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<tr>
<td>Oncocytoma</td>
<td>1</td>
<td>0.8</td>
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<tr>
<td>Salivary duct cyst</td>
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<td>0.8</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td>70</td>
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<td><strong>MALIGNANT</strong></td>
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<td>Mucoepidermoid carcinoma</td>
<td>36</td>
<td>30</td>
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<tr>
<td>Acinic cell carcinoma</td>
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<tr>
<td>Adenoid cystic carcinoma</td>
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<td>Lymphoma</td>
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<tr>
<td>Salivary duct SCC</td>
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<td>Adenocarcinoma</td>
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<td>0.8</td>
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<tr>
<td><strong>TOTAL</strong></td>
<td>50</td>
<td>41.6</td>
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| **GRAND TOTAL**      | 120   | 100 |

Table 3: Incidence of salivary lesions on HP
### TABLE OF DISCORDANT LESIONS

<table>
<thead>
<tr>
<th>HISTOPATHOLOGY DIAGNOSIS (n=)*</th>
<th>MISDIAGNOSIS ON FNAC</th>
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<tbody>
<tr>
<td>Mucoepidermoid carcinoma (13)</td>
<td>Pleomorphic adenoma</td>
</tr>
<tr>
<td></td>
<td>Warthins tumor</td>
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<tr>
<td></td>
<td>Chronic sialadenitis</td>
</tr>
<tr>
<td>Acinic cell carcinoma (1)</td>
<td>Benign cystic lesion</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma (1)</td>
<td>Pleomorphic adenoma</td>
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<tr>
<td>Oncocytoma (1)</td>
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</tr>
<tr>
<td>Intraparotid lymph nodes (1)</td>
<td>Benign cystic lesions</td>
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<tr>
<td>Basal cell adenoma (1)</td>
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<td>Pleomorphic adenoma (3)</td>
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<td>Ca.ex pleomorphic adenoma</td>
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<tr>
<td>Warthin’s tumor (4)</td>
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<td>Warthins tumor</td>
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<tr>
<td>Basal cell adenoma (1)</td>
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<tr>
<td>Nodal marginal zone lymphoma (1)</td>
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</tr>
<tr>
<td>Diffuse B-cell lymphoma (1)</td>
<td>Mucoepidermoid carcinoma</td>
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Table 4: Discordant lesions

*(n=) *number of cases

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Accuracy</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
<th>Corresponding confidence interval (%)</th>
</tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>66%</td>
<td>97.1%</td>
<td>94.2%</td>
<td>80%</td>
<td>70.83%</td>
<td>23.1%</td>
<td>0.35%</td>
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<tr>
<td>Specificity</td>
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<td>Negative predictive value</td>
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<tr>
<td>Positive likelihood ratio</td>
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<td>Negative likelihood ratio</td>
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</table>

Table 5: Statistical analysis of FNA

<table>
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<tr>
<th>First author</th>
<th>No. of cases</th>
<th>Diagnostic accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tr>
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<td>87.7%</td>
<td>68.2%</td>
<td>87.7%</td>
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<tr>
<td>Piccioni</td>
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<td>81%</td>
<td>99%</td>
<td>93%</td>
<td>98%</td>
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<tr>
<td>Iqbal M</td>
<td>49</td>
<td>96.4%</td>
<td>62.5%</td>
<td>96.97%</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Stow N</td>
<td>104</td>
<td>92.3%</td>
<td>86.9%</td>
<td>92.3%</td>
<td>96.8%</td>
<td>86.6%</td>
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<tr>
<td>Rehman H</td>
<td>50</td>
<td>78%</td>
<td>53.28%</td>
<td>88.57%</td>
<td>72.7%</td>
<td>79.9%</td>
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<tr>
<td>Vaidya S</td>
<td>58</td>
<td>96.55%</td>
<td>81.82%</td>
<td>100%</td>
<td>100%</td>
<td>95.9%</td>
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<tr>
<td>Our study</td>
<td>120</td>
<td>70.83%</td>
<td>66%</td>
<td>97.1%</td>
<td>94.2%</td>
<td>80%</td>
</tr>
</tbody>
</table>

Table 6: Comparison with other studies
CONCLUSIONS

FNA is accurate in the diagnosis of salivary neoplasms in most of the cases. A core biopsy FNA may yield a more specific result and may match with histopathology though more studies on these lines are yet to come. A core biopsy in case of scanty aspirate or multiple aspirates may improve the yield. Moreover, in case of cystic lesions, FNA guided by ultrasound will be more representative. A surgeon should correlate the inputs from FNA and radiology and use his clinical judgement to avoid postoperative surprises from histopathology. A dedicated pathologist to report exclusively on FNA would be ideal.

ACKNOWLEDGEMENTS

Department of General Surgery, Head & Neck Surgery, AIMS

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Effect of social skill group training in children with Attention Deficit Hyperactivity Disorder


ABSTRACT

Background: Attention-deficit hyperactive disorder (ADHD) is a developmental neurobiological disorder affecting academic, social and emotional adjustment in children. Children with ADHD have problems in the areas of peer relations, emotional factors, and scholastic performance. Through social skills training, children can be taught to be less aggressive and impulsive, to manage anger, and to behave in a more socially acceptable way. Aim: To see the effects of social skills training in a group of ADHD children. Objectives: To minimize behavior problems and improve positive behaviour in children with ADHD through group training of social skills. Method: Through purposive random sampling, 31 children between ages 7 and 10 years (average age = 8 years, SD = 1.16) who were referred to Clinical Psychology Department from the Pediatric Neurology Division, with a diagnosis of ADHD, were selected for the study. Strength and Difficulties questionnaire (SDQ) was used to assess the variables under study. Ten weekly social skills training sessions were conducted for the group. Paired-samples ‘t’ test was used for analyzing the pre and post results of intervention. Results: After the training, most parents reported improvements in their child’s overall behavior. The post intervention assessment showed greater improvement in the areas of emotional problems, peer relations, conduct problems and prosocial behavior. Conclusion: There is significant improvement in the areas of emotional management, peer relations, conduct problems and prosocial behaviour in children with ADHD through social skills group training.

Key Words: ADHD, Social skill training, MISIC

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common behavioral disorders of childhood. Children with ADHD exhibit developmentally inappropriate levels of inattention, impulsivity, and/or motor activity. Apart from academic and behavior problems, these children often have significant social problems. They exhibit problems in the areas of peer interaction, emotional regulation, and prosocial behaviours. These social problems are associated with a greater risk for developing problems later in life. Disrupted and discordant relationships are more common in the families of young people with ADHD(1). It is known that children with ADHD have difficulties in affective components such as a motivation and mood regulation(2, 3, 4). This is the fundamental basis for the children’s problems with social skills, and these problems are closely related ADHD(5, 6).

Psychological therapies such as psycho-educational input, behavioural therapy, cognitive behavioural therapy in individual and group formats, interpersonal psychotherapy, family therapy, school-based interventions, social skills training and parent management training to encourage the development of coping strategies are being used for managing the behavioural disturbance of ADHD(7). Social skills training was developed in the early 1970s and according to Jacobs (2002) its aim is to teach the micro skills of social interaction such as eye contact, smiling and body posture. Children and young people who have ADHD often present with difficult family relationships and may have poor social skills and peer relationships. Social skills are described as the behaviours and skills necessary to engage in developing and maintaining constructive social relationships. Social skills training uses techniques from cognitive and behavioural approaches and is conducted within groups.

METHOD

Participants

The participants were selected by purposive random sampling. The sample comprised of 31 children aged 7 to 10 years (M = 8, SD = 1.16), referred from Pediatric Neurology to the Department of Clinical Psychology with a diagnosis of ADHD, for behavioural intervention. Those children who had gross neurological, sensory, or motor impairment, as well as a history of seizure disorder were excluded. Other exclusion criteria were an IQ score less than 80, and a score below 12 in the Swan ADHD rating scale.

Measures

The SWAN rating Scale for ADHD: It is used to assess the severity of ADHD. The questionnaire contains 18 items, each item rated in a 4 point scale. The total score determines the severity of ADHD symptoms. Psychometric properties for the SWAN were adequate, with high internal consistency and moderate test-retest reliability.

Malin’s Intelligence Scale for Indian Children (MISIC): It is an adaptation of the Wechsler Intelligence Scale for Children. It is used to assess the cognitive abilities of children aged 6 to 15 years. This battery comprises of 11 subtests through which an IQ score is obtained. The test-retest reliability of the battery is high and it has adequate congruent validity.
### Variables

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal</th>
<th>Borderline</th>
<th>Abnormal</th>
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</thead>
<tbody>
<tr>
<td>Emotional problems</td>
<td>0-4</td>
<td>5</td>
<td>6-10</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>0-2</td>
<td>3</td>
<td>4-10</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>0-5</td>
<td>6</td>
<td>7-10</td>
</tr>
<tr>
<td>Peer problems</td>
<td>0-3</td>
<td>4</td>
<td>5-10</td>
</tr>
<tr>
<td>Pro-social behaviour</td>
<td>6-10</td>
<td>5</td>
<td>0-4</td>
</tr>
<tr>
<td>Total</td>
<td>0-11</td>
<td>12-15</td>
<td>16-40</td>
</tr>
</tbody>
</table>

Strength and Difficulty Questionnaire – Parent Version (SDQ-P): This questionnaire developed by Goodman (1997) is a 25-item, 3-point rating scale which assesses the child on five dimensions – Emotional problems, Hyperactivity, Conduct problems, Peer problems and Pro-social behaviour. A total cut-off score of 11 with individual cut-offs for each of the 5 dimensions was used. Reliability and validity coefficients are adequate. The range of scores for each variable is as follows:

**Procedure**

A baseline assessment was done to all participants using the SWAN rating scale for ADHD, and MISIC. SDQ-P was given to parents of all participants before the intervention. The intervention consisted of ten weekly training sessions of two hours duration. Participants were trained in groups of 10 with an exception in one group where there were 11 members.

Many interactive games were used for observation and documentation of each participant’s behavior. Behaviour certificate and contingency management were used to reinforce and maintain the behaviours. The behavior of the therapist included unconditional positive regard and empathy. Therapist also provided structure and limit of the group training through rules and agreements.

Different themes were included in group training. Emotional Understanding and regulation was trained through activities for reading cues from others’ facial expression, drawings, cartoon, animation and self recording charts of own emotions. Activities for recognition of anger, postponing response, ignoring provocation, breathing exercise, and time out techniques were used for Anger management. Behaviour chart given to parents for recording and reinforcing target behaviour. Empathy and emotional bonding were made to understand through discussions about their own experiences and related emotions. Role play, visual prompts, contingency management, and cognitive exercises were used for reducing Impulsivity. Specific exercises and modeling were given for reducing impulsive responses like giggling on other’s performance and blurring out answers. Attention enhancement worksheets and homework assignment were given. Peer Problems were addressed through role play of verbal and nonverbal communication techniques. To improve pro-social behaviour children and therapist jointly developed stories and the themes were based on emotional understanding of another person and helping behavior. Children were also taught to self-record pro-social behaviours. Parental counseling was given for marking on behavior chart and prompting specific behaviour.

**RESULTS AND DISCUSSION**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention</th>
<th>Mean</th>
<th>SD</th>
<th>t values</th>
<th>Sig. (2 tailed)</th>
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<tr>
<td>Emotional problems</td>
<td>Before</td>
<td>3.61</td>
<td>1.564</td>
<td>6.445</td>
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<tr>
<td></td>
<td>After</td>
<td>2.45</td>
<td>1.121</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conduct problems</td>
<td>Before</td>
<td>3.52</td>
<td>1.503</td>
<td>7.045</td>
<td>.000</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>2.19</td>
<td>1.078</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>Before</td>
<td>7.39</td>
<td>1.520</td>
<td>7.042</td>
<td>.000</td>
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<tr>
<td></td>
<td>After</td>
<td>5.71</td>
<td>1.532</td>
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</table>
The results indicate a significant decrease in emotional problems, conduct problems, hyperactivity, and peer problems in children with ADHD through social skills group training. An increase in pro-social behaviour is also noted as a significant result of the training. Parents reported significant improvement in overall behaviour in home setting and less complaints from class teacher. Parents rated improvement in emotional regulation by reporting exhibition of less anger, and saying sorry after the unpleasant events.

Studies have already shown that there is no measurable difference between the pro-social skills of children with ADHD as compared to children without this disorder. Therefore, it is very likely that children with ADHD already know the pro-social behaviors, but do not perform them as they should. Through the social skill training, children were taught about the meaning, necessity and consecutive positive feeling of pro-social behaviour. Group training allowed participants to watch other children’s behaviour of same age group. Improved real life interaction with peers generalized into different settings such as school, play ground, and home. Effect of getting reinforcement in group and appreciation from group members and therapist facilitated the generalization and maintenance of improved behaviours.

Impaired sustained attention and inability to wait and give appropriate responses are the main reasons for peer rejection. Attention enhancement worksheet on daily basis as home work and behavioural rehearsal helped to improve inattention, hyperactivity and impulsivity. Participants working together to solve personal problems or share information increased group cohesion, good peer relations and pro-social behaviour. Participant’s motivation gradually changed from extrinsic to intrinsic through the realization of subjective positive feeling, less complaints from others, and appreciations.

This study also supports the growing idea that ADHD must be treated through a multi-modal approach and that medicine alone cannot meet all the needs of students with the disorder.

**CONCLUSION**

Through social skills group training, a significant improvement was observed in emotional regulation, conduct problems, hyperactivity, peer problems and pro-social behaviour in children with ADHD. There was a qualitative report of improvement – less anger, friendlier, and helping mentality in participants – by parents.

**REFERENCES**

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Cerebral venous thrombosis in Nephrotic syndrome

Thanu S., V.N Unni, Anil M, Rajesh R., George K

ABSTRACT

Cerebral venous thrombosis is one of the rare complications of nephrotic syndrome. We report a girl with nephrotic syndrome who presented with headache and vomiting with no neurological signs. Magnetic resonance imaging with magnetic resonance venogram showed cerebral venous thrombosis and she was started on anticoagulants. A high index of suspicion and radiological investigations are needed for prompt diagnosis and management of this condition.

Key Words: Cerebral venous sinus thrombosis, nephrotic syndrome, magnetic resonance venography.

INTRODUCTION

Nephrotic syndrome is associated with a hypercoagulable state due to multiple factors like decreased levels of antithrombin, protein S, and plasminogen (due to urinary losses), increased platelet activation, hyperfibrinogenemia, and the presence of high molecular weight fibrinogen moieties in the circulation. Thromboembolism is one of rare complications of nephrotic syndrome. The most common sites include the renal vein, deep leg veins, inferior vena cava and femoral/iliac artery. Other reported sites include cerebral and brachial arteries as well as mesenteric, portal and hepatic veins. Cerebral venous thrombosis can present with headache, vomiting, cranial nerve defects and motor weakness. A high index of suspicion is required when patients present with various neurological manifestations. Delay in diagnosis or initiation of therapy can lead to permanent neurological deficits.

CASE REPORT

A 6 year old girl was admitted with complaints of headache and vomiting since 3 days. She was diagnosed to have steroid responsive nephrotic syndrome at the age of 3 years. She was an infrequent relapser and was on Prednisolone 40mg daily at the time of presentation as she was in relapse. Mother gave history of child getting up from sleep with headache and crying for few minutes and then going back to sleep since 3 days. The child also had recurrent vomiting, not associated with food intake. However, she did not give any history of fever, visual disturbances or motor weakness.

On examination, child was irritable and crying. Pedal edema was present. Blood pressure was: 84/50 mmHg, Height: 106 cm, Weight: 16 Kg, BSA: 0.69 sq.m. Neurological examination did not reveal any signs of meningeal irritation, focal neurological deficits or papillodema. Investigations showed Hb: 14.6g/dl, serum albumin: 1.35g/dl, urine protein: 3+, normal urine microscopy, S.creatinine: 0.7mg/dl, S.Cholesterol: 330mg/dl. Ultrasound abdomen with Doppler showed normal kidneys and renal vessels as well as inferior vena cava. MRI brain was normal, MR venogram showed superior sagittal and bilateral transverse sinus thrombosis (Fig 2a and 2b). She was started on unfractionated Heparin. Concurrently she was started on Warfarin and dose was adjusted to keep INR between 2 and 3. Heparin was stopped after 5 days and she was continued on Warfarin. After six days, child became active and her headache gradually subsided. On follow up after 6 weeks, child is in remission and is being continued on Warfarin and tapering dose of steroids.

Fig 2a: Magnetic resonance venogram showing thrombosed superior sagittal sinus (arrow head)

Fig 2b: Magnetic resonance venogram showing thrombosed transverse sinus on right and left (arrows)
DISCUSSION:

As early as 1840, renal vein thrombosis was recognized to be associated with nephrotic syndrome. Since then, it is recognized that any major blood vessel may develop a thrombus. The overall incidence of thromboembolism in nephrotic syndrome is said to be 3%.[10] Cerebral venous thrombosis is one of the rare complications of nephrotic syndrome. It can be easily missed because of its variable presentation. However, because of increasing clinical awareness and more sensitive imaging techniques, cerebral venous thrombosis is being diagnosed more frequently. Clinical findings in cerebral venous thrombosis occur due to two mechanisms. i) Increased intracranial pressure due to impaired venous flow. ii) Focal brain injury from venous ischemia/infarction or hemorrhage. Headache is the most common symptom of cerebral venous thrombosis.[1,11] It is usually diffuse and increases in intensity over 2-3 weeks. Isolated headache without focal neurological findings or papilledema occurs in 25% of patients with cerebral venous thrombosis and presents a significant diagnostic challenge. Clinical presentation of cerebral venous thrombosis varies with site of thrombosis. The various manifestations are given in the figure 1.[17]

![Clinical presentation of cerebral vein thrombosis](image)

Maintenance of hemostasis involves a number of processes including platelet activation and aggregation, activation of clotting cascade, termination of clotting cascade through a variety of inhibitors and dissolution of clot by plasmin.[1,3,11] Thrombosis in nephrotic syndrome occurs from preferential loss of proteins involved in the inhibition of systemic hemostasis or increased synthesis of factors promoting thrombosis or by activation of hemostatic system by the glomerular disease.[3,13] The abnormalities include increased level of fibrinogen, factor V, Von willebrand factor, Factor VIII, alpha-1 macroglobulin, which are thought to be due to increased hepatic synthesis of the factors stimulated by hypoalbuminemia; decreased level of anti-thrombin III, plasmin, factor XI, XII, alpha-1 anti-trypsin, protein S and protein C are likely to be due to urinary loss of these proteins.[12] Other factors predisposing to thrombosis are intravascular volume depletion, exposure to steroids, increased blood viscosity associated with hemoconcentration due to use of diuretics.[2,3,4] While venous thromboembolism is far more common, arterial thromboembolism also may occur in patients with nephrotic syndrome. In contrast to venous thrombi, which are composed predominantly of fibrin and red cells, arterial thrombi are composed predominantly of platelets.[14] Thrombosis can occur in aorta, renal, femoral, mesenteric, cerebral, carotid and brachial arteries.[1,3,14,15,18] From various studies it is found that the median time to thromboembolic events is about 71 days after the diagnosis of nephrotic syndrome.[11] Multivariate analysis demonstrated that the risk of thromboembolic events is greater in children older than 12 years of age and increases with increasing urinary protein excretion.[12] Infants with congenital nephrotic syndrome are at increased risk for renal vein thrombosis. Otherwise renal vein thrombosis is rare in children compared to adults.[11]

Our patient had superior sagital and bilateral transverse sinus thrombosis. An MRI with venogram is very sensitive and should be done to define the extent of thrombus. Advantage of MRI with MRV is visualization of both superficial and deep venous system with good definition of brain parenchyma.[1,2,16] T2 weighted images with MRV are considered to be the more sensitive sequences.[18]

The aim of anti-coagulation therapy is to prevent thrombus growth and to help in recanalisation. Initially unfractionated heparin (UFH) or low molecular weight heparin (LMWH) is started, and concurrently oral anti-coagulants (Warfarin) should be initiated. UFH or LMWH can be stopped after 5 days and Warfarin dosage is adjusted to keep PT INR between 2.0 to 3.0. Our patient was started on unfractionated Heparin along with Warfarin. Her headache and irritability gradually improved over a period of 1 week. Anticoagulation should be continued for 3-6 months and a repeat MR Venogram is required to assess the venous thrombus.[1,4] Controversy exists regarding intiation of prophylactic anticoagulation in children with nephrotic syndrome even though there is high risk for developing venous thrombosis.[5,14] Prophylactic anticoagulation is not recommended unless the patient had a thromboembolic event previously or albumin concentration less than 2g/dl, fibrinogen level more than 6g/l or antithrombin III level less than 70% of normal.[12] High risk patients have been treated with low dose aspirin although there are no trials that demonstrate their efficacy in thrombus prevention in children with nephrotic syndrome.[14]
CONCLUSION

A high index of suspicion is required to rule out cerebral venous thrombosis in nephrotic syndrome patients who present with non specific symptoms like headache and vomiting. MRI with MR Venogram is the most sensitive imaging modality to rule out cerebro venous sinus thrombosis. Prompt initiation on anti-coagulants and regular follow up would help in preventing neurological sequelae.

REFERENCES

Dysphagia and vocal cord palsy
Renuka Balu, Sachin Suresh, Unnikrishnan Menon

ABSTRACT

Dysphagia is a common symptom, with a variety of possible causes, and associated symptoms. A patient with this symptom could therefore present in different out-patient departments in an Institution. Occasionally, investigating the associated symptom could lead to an unsuspected diagnosis.

In this case report, we present a case of carcinoma thyroid, which was incidentally recognised on investigating for asymptomatic vocal cord palsy, in an adult male referred from Gastroenterology for throat findings. Relevant discussion and literature review are also presented.

INTRODUCTION

Dysphagia can occur due to a variety of causes depending on the age of the patient. Based on the predominant associated symptoms, the patient may consult different specialties, like Gastroenterology or ENT, for the initial evaluation. Hence, the investigation protocols would vary as per the focus of the concerned specialty. This may lead to the overlooking of certain unusual causes of dysphagia.

We present the case report of such a patient with dysphagia with incidental evaluation in ENT resulting in an unexpected diagnosis. Relevant literature search is discussed.

CASE REPORT

A 46 years old man presented with symptoms suggestive of acid reflux for the past 8 years and dysphagia, more for solids, since 3 months. He had undergone prior evaluation under a Gastroenterologist. Upper gastro-intestinal endoscopy was done 5 years back and it was reported as normal. He was put on proton pump inhibitors, but symptoms persisted. He was re-evaluated by Gastroenterology in our institution and a repeat endoscopy was also found to be normal. He was referred to ENT department as part of evaluation for symptoms of GERD. On detailed history taking, the patient gave history of occasional voice change without causing much functional limitation. A prior ENT evaluation 3 years back for voice change was reported as unremarkable.

Routine neck examination revealed presence of a vague swelling in the left side of neck, which was not moving with deglutition. It had a woody feel on palpation. There was no clear evidence of lymph node enlargement. On further evaluation, the maximum phonatory duration was found to be 7 seconds. Indirect laryngoscopy showed evidence of left vocal cord palsy; it was immobile in the paramedian position with compensation from right side. The left pyriform fossa was not opening up. Hypopharynx and arytenoid was found to be congested.

A CT scan from base of skull to upper mediastinum was then obtained, as part of protocol evaluation of left vocal cord palsy. This showed an infiltrative poorly enhancing mass lesion with intra-lesional vascular channels arising from the left lobe of the thyroid gland (Fig. 1). The lesion measured 57 mm x 47 mm transaxially and 61 mm caudo-cranially. Medially, the lesion was found to be displacing the trachea towards the right, compressing the airway for a length of 3.6 cm. There was extension into the trachea-esophageal groove with compression of the esophagus. Laterally, the lesion was infiltrating...
the carotid sheath encasing the left common carotid artery 360 degrees, displacing the left internal jugular vein laterally. Inferiorly, the lesion was extending up to the top of manubrium. There was posterior extension into the pre-vertebral space without any vertebral bony changes. Bilateral level II and left level III - 8.5 mm (FDG non-avid) lymph nodes were noted. PET scan confirmed the findings of a FDG-avid infiltrative poorly enhancing mass lesion arising from the left lobe of the thyroid gland with extensions to surrounding structures as described in the CT scan (Fig. 2).

Ultrasound-guided FNAC showed poorly differentiated carcinoma appearing to arise from thyroid. Subsequently, a trucut biopsy done was done which showed infiltrative neoplasm of the thyroid. Immunohistochemistry was positive for HMWCK and CK19 and negative for TTF1 and thyroglobulin. CD5 showed nonspecific positivity.

In view of the extensive infiltration into the carotids and pre-vertebral space, the patient was advised neo-adjuvant chemotherapy followed by CTRT.

**DISCUSSION**

The etiology of dysphagia is varied. The possibilities depend on the age of the patient and associated presenting symptoms. In view of the protean presentation, patients with dysphagia may be evaluated by varied protocols by different specialties. The protocol for evaluation thus may be biased according to the concerned specialty and this may lead to overlooking of certain less common causes associated with this symptom.

The presence of subtle voice symptoms, obtained by leading questioning prompted us to perform an indirect laryngoscopic examination. This was the turning point in the diagnostic approach to this patient. The detection of unilateral vocal cord palsy on the left side prompted a detailed check for the underlying cause. Unilateral vocal cord paralysis can be due to malignancy (25%, commonest being carcinoma lung), surgical trauma (20%), inflammatory causes (13%), neurological disorders or idiopathic1. The CT scan confirmed a highly infiltrative form of thyroid malignancy as the cause in our patient which was eventually confirmed by PET scan and biopsy. Unfortunately, the diagnosis in this case was made at a late stage when the malignancy had already become extensively infiltrative precluding a surgical resection.

Compressive symptoms are common among patients with thyroid disease which range from mild, presenting with neck pressure or globus sensation to severe, characterized by significant dysphagia or dyspnoea2. Thyroid enlargement associated with goiter can lead to some compressive symptoms owing to proximity to the esophagus. This situation is most likely to occur in patients who have substernal extensions of their goiter in which the goiterous mass occupies the narrowed space in the thoracic inlet3-5.

More ominous are thyroid malignancies. Although the majority of these do not directly lead to dysphagia, it is not uncommon that extracapsular extension of thyroid tumors involves the tracheoesophageal junction and thus the course of the recurrent laryngeal nerve, leading to vocal cord paralysis, and secondary dysphagia due to pressure effects6. The highly malignant forms of thyroid cancer such as the anaplastic variety directly invade surrounding structures. These patients may present with rapid onset of dysphagia as the tumors invade the cervical esophagus and surrounding neuromuscular structures. This was the case in our patient. Hence, a high index of suspicion has to be maintained in the initial evaluation so that such malignancies can be diagnosed before they become extensively infiltrative.

**CONCLUSIONS**

A careful survey for associated symptoms, however subtle, and a high index of suspicion for underlying infiltrative conditions need to be considered in the evaluation of patients with dysphagia. Thyroid lesions are an important but often overlooked cause of dysphagia, particularly when associated with voice symptoms. This case report highlights this point and illustrates the need for a comprehensive approach in evaluation of such patients.
REFERENCES


Sinonasal malignancy in a patient on hemodialysis

R Gaba*, VN Unni*, NV Seethalekshmi**, A Mathew*, R Rajesh*, G Kurian*

ABSTRACT

The risk of malignancy increases in end stage renal disease. The exact mechanisms are not known but is likely to be multifactorial. One possible cause is the increased susceptibility of dialysis patients to viral infections. We report a case of chronic kidney disease stage 5 D who presented with right sided nasal obstruction. On nasal endoscopy, he was detected to have a mass in right maxillary sinus and endoscopic biopsy showed squamous cell carcinoma. He underwent right total maxillectomy and the excisional biopsy showed well differentiated squamous cell carcinoma. Sinus malignancy is extremely rare in patients on hemodialysis, and to the best of our knowledge, there are no published cases so far.

Key Words: Chronic kidney disease, maxillary sinus carcinoma, squamous cell carcinoma

INTRODUCTION

Increased risk of cancer is described in the end-stage renal disease (ESRD) and kidney transplant populations. For every 10 ml/min decrement in eGFR, the risk for cancer increases by 29%. Chronic kidney disease (CKD) stage 3 or above may be an independent risk factor for the development of cancer among older men.

Maxillary sinus cancer is a rare neoplasm and constitutes a small percentage (0.2%) of all human malignant tumors, and only 1.5% of all head and neck malignant neoplasms. In patients on hemodialysis, maxillary sinus malignancies must be extremely rare, with no published case reports so far (to the best of our knowledge).

CASE REPORT

A 53 year old man, known to have type 2 diabetes mellitus, systemic hypertension, diabetic retinopathy, diabetic nephropathy and chronic kidney disease stage 5, had been on maintenance hemodialysis for the past one year. He presented with complaints of right sided nasal obstruction for two months, which got aggravated during the last 3 weeks. There was no history of nasal discharge, epistaxis, post nasal drip, trauma, headache or facial pain. On nasal endoscopy, he was detected to have a mass in the anterior wall and the floor of the right maxillary sinus. Computed tomography of para nasal sinus showed a hypodense soft tissue lesion with air foci within it involving the entire right maxillary, anterior and posterior ethmoid, sphenoid and frontal sinuses extending into nasal cavity and nasopharynx. Nasal endoscopic biopsy showed squamous cell carcinoma. He underwent right total maxillectomy and the excisional biopsy was consistent with well differentiated squamous cell carcinoma.

DISCUSSION

Cancer risk in CKD begins at a GFR of 55 ml/min, and increases linearly as the eGFR falls, reaching a maximum three-fold increased risk with GFR ≤ 40 ml/min per 1.73 m², which is similar to the increase in risk seen in dialysis population and kidney transplant recipients.

A recent study showed a significant relationship between increasing levels of albumin-creatinine ratio and increased risk for cancer.
Table 1 Sites and type of malignancy in different renal diseases

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sites of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerulonephritis&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td>Analgesic nephropathy&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Kidney, urinary tract</td>
</tr>
<tr>
<td>Acquired renal cysts&lt;sup&gt;21&lt;/sup&gt;</td>
<td>Kidney</td>
</tr>
<tr>
<td>Transplant&lt;sup&gt;22&lt;/sup&gt;</td>
<td>Non-Hodgkin’s lymphoma, Kaposi’s sarcoma, Cervix (in situ tumors), Vulva, Perineum</td>
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</table>

The risk for cancer in patients with impaired kidney function is multifactorial in etiology. Patients on maintenance dialysis are more susceptible to viral mediated cancers such as human papilloma virus associated cancers: cervical cancer and carcinoma of the tongue<sup>8</sup>. There is also an increased risk for renal cell carcinoma and cancers of transitional cell epithelium, because of the higher frequency of acquired cystic disease of the kidneys and analgesic abuse<sup>9</sup> (Table 1). There is a relationship between vitamin D deficiency, which is common among people with moderately reduced kidney function and risk for prostate, breast, and colon cancer<sup>10</sup>. CKD is also a pro-inflammatory state, and there is an association between chronic inflammation and risk for cancer<sup>11</sup>. Elevated levels of epidermal growth factor receptor (EGFR) and transforming growth factor-alpha (TGF-alpha) in chronic kidney disease may be factors associated with carcinogenesis<sup>12</sup>.

Viral infections and their relationship to sinus malignancy is being studied. Studies show that elevated levels of epidermal growth factor receptor and transforming growth factor-alpha are associated with inverted papilloma carcinogenesis. Human papilloma virus and Epstein Barr virus infection are involved in malignant transformation of inverted papilloma<sup>13-15</sup>.

Sinonasal malignancies occur more in men, who are affected 1.5 times more often than women; eighty percent of these tumors occur in people aged 45-85 years<sup>16</sup>. About 60-70% of sinonasal malignancies occur in the maxillary sinus<sup>17</sup>. The annual global incidence of maxillary sinus cancer is 0.5–1.0 case per 100,000 population<sup>18</sup>. In India, incidence of maxillary sinus malignancy is 0.3 per 100,000 population. Squamous cell carcinoma constitutes over 80% of all malignancies that arise in the nasal cavity and paranasal sinuses. Incidence of sinonasal malignancy in patients on maintenance hemodialysis is not known.

Squamous cell carcinoma of maxillary sinus has varied presentation; nasal mass or obstruction, rhinorrhea, epistaxis, cranial neuropathies, pain, facial asymmetry, proptosis, visual disturbances and paresthesias can all be the manifestations. Histologic examination reveals sheets, ribbons, and individual squamous, polyhedral, or round-to-ovoid cells with various degrees of keratinization.

The mainstay of treatment of maxillary sinus malignancy is surgical resection (maxillectomy) followed by radiotherapy. Several studies have shown the superiority of post operative radiotherapy over pre-operative radiotherapy, radiotherapy alone and chemo-radiation. As most of the cases of maxillary sinus malignancy are locally invasive at the time of diagnosis, post-operative radiotherapy is recommended. For tumors involving lymph nodes, nodal dissection is advised. Non-resectable tumors are managed with chemo-radiation.

Survival rates with treatment for patients with maxillary sinus cancer average about forty percent at five years. Five year survival is around 80% in early stage tumors with treatment. Patients with unresectable tumors treated with radiation alone have a five year survival of less than 20%.

**CONCLUSION**

This case report intends to highlight the occurrence of a rare malignancy whose incidence in absence of published data, is unknown in the dialysis population. The presentation is quite innocuous; so a high index of suspicion is needed for diagnosis. Owing to the association between viral infections and sinonasal malignancy and due to the fact that patients on maintenance dialysis are highly susceptible to viral infections, the incidence of sinonasal malignancy is likely to be higher in dialysis population than general population.

**REFERENCES**


Acute Urinary Retention – A Typical Presentation

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ABSTRACT

We report the case of a 75 years old man who presented to ER with acute urinary retention and pain in the urethra for the previous 3 hours. Examination revealed a mobile mass in the urethra, which turned out to be a leech.

The presentation, management and literature review of ‘Urethral hiriduniasis’ has been described in this case report.

CASE PRESENTATION

A 75 year old man presented to our ER with acute urinary retention and pain over the penis for the last 3 hours. He was apparently normal till going for fishing in the morning. During fishing in the river, he felt a tingling sensation over his urethra with some uneasiness. There was no history of decreased urinary output, abdominal pain or fever. There was no past history of any difficulty in initiating micturition or flow of urine. He had no known co-morbidities. He was an occasional smoker.

On initial examination, heart rate was 75 bpm and blood pressure was 120/70 mm Hg. Abdomen was soft and non-tender; bladder was palpable.

On examining the urethra, a mobile mass was found to obstruct the urethral orifice. Initially, an attempt to remove it manually with a blunt forceps was tried but the mass slipped inside.

On flushing the mass with saline, a blackish mass suddenly popped out of the urethra (Fig 1). Then, 3% NS was used to flushed the urethra, following which, a huge leech came out immediately (Fig 2). The patient was then observed for an hour in the ER, during which there was no hematuria or dysuria. He was discharged on oral ciprofloxacin 500 mg BD for 7 days with analgesics.

DISCUSSION

Leeches are invertebrates of the phylum annelida and class hirudinea. Leech is a sanguinivorous hermaphrodite. The body is soft, elongated, verniform, dorsoventerally flattened, and slippery. Their posterior and anterior suckers serves as organ of locomotion and provide firm adhesions to the host’s body at the time of feeding.

Leeches rest at the edges of ponds and swim with amazing accuracy towards a wave. Leech bites of skin are common. The parasite can enter anatomical orifices like urethra, anus, vagina, nose and oral cavity/throat. Rectal, vaginal and urethral bleeding, hemoptysis, chronic headache, dysphagia, hoarseness, inspiratory stridor, dysphagia, laryngeal stridor are all known complications.

Leech saliva contains many chemicals including hirudin, hyaluronidase, collagenase, fibrinase, hementin, plasminogen activators, bdellins, egllins, eleastase, cathepsin B, antihistamine and apyrase. These secretions serves to maintain access to blood and prevent clotting. Bleeding following leech bite can last for about 24 - 48 hrs. But cases of intense urologic bleeding has been reported. Hamit et al has reported two cases of urethral bleeding and one case even required blood transfusion.

Infection is a common complication varying from 2.4 -20%. The intestinal flora of leech contains aeromonas hydrophlia and areomonas veroni biovar sobria making digestion of sampled red blood corpuscles easier. Most common germ is aeromonas hydrophila. Aeromonas produce betalactamase that induces resistance to penicillin & 1st generation cephalosporin. Third generation cephalosporin and fluroquinolones are effective.

Accidental entry of leeches per urethra has been reported even before. It has been successfully managed with saline irrigation in many studies. In failed cases, cystoscopic removal has been reported.

Banu et al have studied 117 pediatric patients presenting with accidental entry of leech per urethra. They irrigated the urethrae of all these children using catheter with saline. In 57 patients, spontaneous expulsion occurred; cystoscopic removal was done in rest of the patients.

Alam S et al have studied the efficacy of saline irrigation for the management of hematuria following accidental entry of leech per urethra into urinary bladder in 43 children. They found it to be a relatively simple, safe and inexpensive method of removing the leech.

Most available reports were on vesical hiriduniasis. Only one case of leech obstructing the urethra was reported by Rashid Ahmad et al. They tried removal with a pair of forceps but failed; later, it was removed cystoscopically.
CONCLUSION

Urethral hiriduniasis is an emergency and needs immediate attention. It can cause pain, bleeding and infection. Saline instillation can be tried initially, which is usually successful. If this fails, the leech has to be removed cystoscopically.

Manual removal should be never attempted as it can cause more trauma. Patient should be discharged with oral fluoroquinolones as there is a chance of subsequent infection.

REFERENCES

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