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Acute Pancreatitis -- The Quest for the Cause

Prof. Premashish Kar*

Acute pancreatitis is one of the most common cause of medical emergencies presenting with significant morbidity and mortality throughout the world1 Other less common causes that include are endoscopic retrograde cholangiopancreatography (ERCP), abdominal surgery, trauma, hypertriglyceridemia, hypercalcemia, drug induced, autoimmune, genetic, ischemic, various infections, congenital pancreatic divisum, microlithiasis of the gall bladder.

The different causes finally determine the management and allow elimination of precipitants and prevention of disease recurrence. The different causes also influence the natural history and the occurrence of different complications. Hereditary pancreatitis may be associated with the development of pancreatitis carcinoma. Though in most of the cases of acute pancreatitis a battery of tests including serum amylase, serum calcium and triglyceride levels, abdominal ultrasonography, and CT abdomen are carried out yet in 40% of the cases the exact etiology is not established who have a high mortality and 50% 2,3 of them experience recurrent pancreatitis which may progress to chronic pancreatitis with irreversible morphologic and functional changes.

It is felt in that further evaluation of pancreatitis may disclose evidence of potential etiology such as unrecognized gallstone disease, CBD stone, and chronic pancreatitis. Alcohol intake and biliary tract disease account for majority of the cases (90%) in USA while in UK alcohol account for 8.32% of the attacks of acute pancreatitis4,5. The management is mainly conservative with surgery reserved for patients with biliary pancreatitis and those developing complications secondary to acute disease. For those developing pancreatitis necrosis there is a trend towards delaying necrosectomy. For successful management of acute pancreatitis a team approach comprising of physicians, surgeons and interventional radiologist should be monitoring the course of the disease.

REFERENCES:

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Original Article

A Study of Non Obstructive Pancreatitis in a Tertiary Care Center of North East India

P Dihingia*, A Dutta**, P Goswami**, S Das***, M Debbarma***, N Jain***

Abstract

**Background:** Acute pancreatitis is a potentially fatal disease of multiple etiologies. Whereas pancreatitis due to obstruction (Gall stone, Stricture, growth etc) of the biliary tract is treated in the department of surgery, those with non obstructive pancreatitis is treated in the department of medicine. **Aims and Objectives:** We aim to study these non obstructive pancreatitis that came to our department during last one year. **Materials and Methods:** We randomly selected patients with acute pancreatitis with non obstructive pathology coming to our tertiary care hospital over a period of two years and studied them in respect to their clinical presentation, laboratory, radiological results and outcome. **Results and observations:** 42 cases (35 men, 7 women) were studied. The average age was 47.6 years with 48.2 years for men and 44.7 years for women. 32 (76%) patients were alcoholic of which 29 (91%) were men and 3 (9%) were women. 14 (33%) cases had recurrent pancreatitis. 2 patient had hypertriglyceridemia, 1 had organophosphorous poisoning, , 1 had mumps and 6 (14%) had idiopathic pancreatitis. 11 (26%) patient had diabetes mellitus of which 8 were alcoholic, 2 had idiopathic pancreatitis and one had hypertriglyceridemia. 13 patients had chronic liver disease with portal hypertension, splenomegaly with ascites whereas another 11 patient had fatty liver on ultrasonography of abdomen. **Conclusion:** We concluded that alcohol is the most common cause of non obstructive acute pancreatitis in north eastern India. The mortality was higher in patients with other co morbidities, especially chronic liver disease with complications. Elderly patients had a severe course and increased mortality.

**KEYWORDS:** Acute Pancreatitis, Non gallstone pancreatitis, Alcoholic pancreatitis.

**INTRODUCTION:**

Acute pancreatitis is a potentially fatal disease of multiple etiologies which is frequently diagnosed in patients coming to the emergency department with abdominal pain. Whereas pancreatitis due to obstruction (Gall stone, Stricture, growth etc) of the biliary tract is treated in the department of surgery and those with non obstructive pancreatitis is treated in the department of medicine. We aim to study these non obstructive pancreatitis that came to our department during last one year.

**MATERIALS AND METHODS:**

Patients with acute pancreatitis coming to our hospital from January 2014 to December 2015 were randomly selected (every alternate Saturday and every Wednesday) and included in the study. Children below 12 years and patients with obstructive pathology (gall stone and malignancies) were excluded from the study. Diagnosis was ascertainment by clinical examination, laboratory results (increased serum amylase and lipase) and imaging studies (ultrasonography of abdomen and contrast enhanced CT Abdomen). Severity was assessed clinically by Acute Physiology and Chronic Health Evaluation scoring system (APCHE) and CECT scan.

**RESULTS AND OBSERVATIONS:**

42 cases were included in the study which included 35 (83%) men and 7 (17%) women. 10 patients were below 40 years of age, 16 were in the age group of 41-50 years, 12 were in the age group of 51-60 years and 4 were above 60 years of age. The average age was 47.6 years with 48.2 years for men and 44.7 years for women.

**Fig 1 : Demographic profile of the patients**
32 (76%) patients were alcoholic of which 29 (91%) were men and 3 (9%) were women. 14 (33%) cases had recurrent pancreatitis. 2 patient had hypertriglyceridemia, 1 had organophosphorous poisoning, 1 had mumps and 6 (14%) had idiopathic pancreatitis. 11 (26%) patient had diabetes mellitus of which 8 were alcoholic, 2 had idiopathic pancreatitis and one had hypertriglyceridemia. 13 patients had chronic liver disease with portal hypertension, splenomegaly with ascites whereas another 11 patient had fatty liver on ultrasonography of abdomen. 2 patients had old healed lesions in lung suggestive of past Koch’s lesion.

Fig 2 : Etiological classification of the cases

The average hemoglobin percentage was 8.2 (+ 1.7) gm%. Serum amylase was 537 (+ 32) U/L and lipase was 793 (+293) U/L at presentation. The average total count was 15,842 (+784). 14 (33%) cases had mild pancreatitis and all of them had favorable outcome, whereas 28 (67%) had severe pancreatitis. 4 (14%) cases of severe pancreatitis expired and 24 (86%) survived. Complications were seen in 9 (21.4%) cases with pseudocysts in 3 cases, pleural effusion in 4 cases, hemorrhagic pancreatitis in 2 cases. The average hospital stay was 5.6 days with a maximum of 16 days and a minimum of 4 days. 4 (9.5%) patients expired during hospitalization.

Fig 3 : Severity and Complications

DISCUSSIONS:
Amboldi A et al with 288 cases of acute pancreatitis (AP), during a twenty-year period (1975-1996) showed that in 61% of cases the AP was associated with biliary illness, and in 13% of cases with alcohol abuse. Roseano M et al from Italy showed in a series of 244 patients affected by AP (168 mild, 76 severe) mean age was 64.4 years (range 17-94 years old). As regard as etiology is concerned, 166 are biliary pancreatitis, 42 alcoholic, 27 idiopathic, 9 iatrogenic. Of the 69 non biliary pancreatitis 60% were alcoholic. In our study we found much more number of alcoholics.

Banday IA et al from Jammu and Kashmir found out that out of 50 cases, 33 (66%) male and 17 (34%) females, cholelithiasis was found to be most common etiological factor for acute pancreatitis in 40% cases. Alcoholic pancreatitis was seen in 36% of cases. Together cholelithiasis and alcoholism accounted for 76% of cases. Pleural effusion was the most common extra-pancreatic complication, 28 patients (56%), followed by ascites. Majority of patients were categorized as severe pancreatitis (44%). 38% patients were grouped into moderate pancreatitis and 18% were categorized in mild pancreatitis. Baig SJ et al from Kolkata Medical College showed that although gallstones have largely been implicated as a common cause of acute pancreatitis, alcoholism was the main etiological factor in eastern India comprising 41.1%, gallstones in 23.5%, trauma in 17.6%, idiopathic in 11.7% and post-endoscopic retrograde cholangiopancreatography in 5.8%. Our study further emphasizes the role of alcohol as the cause of acute pancreatitis in north eastern India as 76% of non obstructive acute pancreatitis were caused by alcohol, with 83% in men and 43% in women.

Amboldi A et al saw that the overall mortality has been 7.2%, ranging from 45.4% in 17 severe necrotic hemorrhagic AP to 2.1% for the mild one. Roseano M et al found an overall mortality rate of 2.8% (0.6% in the mild AP and 7.8% in the severe AP). In the surgical group the mortality rate was 18.1%. Baig SJ et al had a mortality rate of 4.4% due to multi organ failure. We found a mortality rate of 9.5% which was much higher than these studies but many of our patients had decompensate chronic liver disease with complications.
Losurdo G et al showed that elderly patients usually undergo a severe AP course, but without increase of mortality. We also had 4 patients above the age of 60 years, all of whom had a severe course and one expired.

CONCLUSION:
Alcohol is the most common cause of non obstructive acute pancreatitis in north eastern India with numbers much higher than reported in international and national studies. The mortality was higher in patients with other co morbidities, especially chronic liver disease with complications. Elderly patients had a severe course and increased mortality.

REFERENCE:
Prevalence of metabolic syndrome in COPD and its association with severity of disease

B Hazarika*, S Choudhury**, Raghavendra M K***, J Sarma****

Abstract
Background: COPD patients would be at risk for the metabolic syndrome since these patients are limited by respiratory symptoms and adopted to a sedentary lifestyle, increasing their risk for weight gain and insulin resistance. Thus this study is an attempt to find out the prevalence of metabolic syndrome in association with the severity of COPD. Objective: To study the Prevalence of metabolic syndrome in COPD and its association with severity of disease. Materials and Methods: It is a cross sectional study carried out on 129 diagnosed COPD patients (GOLD criteria) as well as 103 apparently healthy non smoker volunteers (control group). In all patients Fasting lipid profile, FBS, PPBS, HBA1C, BMI, Waist/Hip ratio was done. NCEP ATP III criteria was used for diagnosis of metabolic syndrome. Results: During the study period, out of 129 COPD patients, 61 (47.28%) patients were diagnosed with metabolic syndrome as compared with 103 control group in which 18 (17.47%) were diagnosed with metabolic syndrome. Conclusion: Thus from this study we can conclude that, the prevalence of metabolic syndrome is high in COPD patients. Early recognition of metabolic syndrome can prevent the potential life threatening cardiovascular complication and development of diabetes mellitus.

Key words: Chronic obstructive pulmonary diseases, metabolic syndrome, syndrome X.

INTRODUCTION:
Chronic obstructive pulmonary disease (COPD) is characterized by persistent airflow limitation that is usually progressive and associated with chronic airway inflammation. The overall prevalence of COPD is estimated to be 4 - 5% in our country1. It has been recognized as a major cause of morbidity worldwide and is likely to be the third leading cause of death by the year 20202. It occurs most commonly in tobacco smokers and is characterized by an increase in the annual rate of decline of forced expiratory volume in 1 s (FEV1).

COPD has been associated with several extrapulmonary systemic manifestations such as diabetes mellitus, osteoporosis, metabolic syndrome, cardiovascular disease and lung cancer3,4. Metabolic syndrome, also called insulin resistance syndrome or syndrome X is a cluster of risk factors that is responsible for much of the excess cardiovascular disease morbidity among overweight and obese patients and those persons with type 2 diabetes mellitus5.

The major characteristics of metabolic syndrome include insulin resistance, abdominal obesity, elevated blood pressure, and lipid abnormalities (i.e., elevated level of triglycerides and low levels of high-density lipoprotein cholesterol). Several etio-pathogenic mechanisms have been proposed as a possible link between COPD and metabolic disorders that include systemic inflammation, adipose tissue inflammation, medications and physical inactivity6,7.

So the aim of this work is to study the Prevalence of metabolic syndrome in COPD and its association with severity of disease.

MATERIALS AND METHODS:
The present study is carried out on 129 diagnosed COPD patients (GOLD criteria) as well as 103 apparently healthy non smoker volunteers (control group). All the patient were recruited from the department of pulmonary medicine, Guwahati Medical College, Guwahati, Assam, India in the period between January 2014 to July 2015 after taking their written informed consent prior to participation in the study.
All patients and controls were analyzed for clinical and laboratory findings, including full history taking, clinical examination, routine laboratory investigations including complete blood picture with differential white cell count, erythrocyte sedimentation rate, complete liver and kidney functions test, serum uric acid, lipid profile including HDL-cholesterol, triglycerides, and ECG. 2D ECHO has also been done in all patients.

Body weight, height, and waist circumference were obtained in all participants. Waist circumference was measured by a single observer using an inelastic tape at the midpoint between the lowest rib and the iliac crest.

Blood pressure was taken from both arms and the higher measurement was used for analysis. Participants were asked to fast for 12 hours before blood sampling. Serum triglycerides were measured by a Lipase-Glycerol kinase method. HDL-C was assessed by oxidase method.

Standard pulmonary function tests in the form of spirometry was done for all COPD patients and control group. Based on the spirometry finding all COPD patients were classified into mild, moderate, severe and very severe category.

NCEP : ATP III criteria was used to diagnose metabolic syndrome. Three out of the following five criteria must be present for diagnosing metabolic syndrome.

1. Waist circumference (WC > 102 cm men or > 88 cm in women)
2. Fasting blood glucose > 100 mg/dL (5.6 mmol/L) or previously diagnosed type II diabetes
3. Serum triglyceride > 150 mg/dL (1.7 mmol/L) or specific treatment for this lipid abnormality
4. Serum high density lipoprotein (HDL) d’ 40 mg/dL (1.03 mmol/L) in men or d’ 50 mg/dL (1.29 mmol/L) in women or specific treatment for this lipid abnormality
5. Systolic blood pressure e’ 130 mmHg and/or diastolic blood pressure e’ 85 mmHg or treatment of previously diagnosed hypertension.

Data are reported as mean ± SD or proportions and 95% confidence intervals. Statistical analysis was performed by using unpaired t test and Fisher exact test. A value of p < 0.05 was considered statistically significant.

Baseline characteristics of all the subjects participated in the study were summarized in Table:2. COPD patients and control participants were matched for age, gender. There were no statistically significant differences between the Patient and control group regarding age (p value = 0.5264), diastolic blood pressure (p value = 0.2107) and triglycerides (p value = 0.158) and high density lipoprotein cholesterol (p value = 0.099).

There were statistically significant differences between the 2 groups regarding body mass index (p value < 0.001), waist circumference (p value = 0.0216), systolic blood pressure (p value = 0.0120), fasting blood glucose (p value <0.0001) and the incidence of metabolic syndrome were more common in COPD group of patient compared with healthy group.

According to our result it was found that, presence of metabolic syndrome is more common in COPD patients compared to healthy group of patients. Our result also shows that presence of metabolic syndrome is more common in moderate group of COPD patients.

During the study period, out of 129 COPD patients, 61(47.28%) patients were diagnosed with metabolic syndrome as compared with 103 control group in which 18(17.47%) were diagnosed with metabolic syndrome (Table:3).
Prevalence of metabolic syndrome in different GOLD grading of COPD has also been studied. In this study out of 129 COPD patients mild, moderate, severe and very severe COPD was found to be 16, 56, 35, and 22 respectively. Metabolic syndrome in mild, moderate, severe and very severe COPD was 43.75%, 64.28%, 34.28% and 27.27% respectively (Table:4).

The prevalence of metabolic syndrome in both male and female COPD patients is also studied. Out of 100 male COPD patients, 49(49%), and out of 29 female patients 12(41.37%) were diagnosed with metabolic syndrome (Table:5).

In control group, out of 103, 18(17.47%) were diagnosed with metabolic syndrome.

Out of 81 control males, 13(16.04%) were diagnosed with metabolic syndrome. In case of female controls, out of 22, 5(22.72%) were diagnosed with metabolic syndrome.

**DISCUSSION:**

COPD is a complex disease with multiple systemic comorbidities and complications. Systemic inflammation and physical inactivity have been identified as relevant extrapulmonary marker of the severity of COPD, as both conditions are related to exacerbations, hospitalizations, and mortality in this patient population. When COPD and metabolic syndrome coexists, the comorbidities such as diabetes, hypertension, cardiovascular diseases are more common when compared to general population.

The main finding of our study is that presence of metabolic syndrome is more common in COPD patients (47.28%) compared to healthy group of patients (17.47%). Our result also shows that presence of metabolic syndrome is more common in moderate group of COPD patients (64.28%). The study done by H. Hosny et al. also finds that the presence of metabolic syndrome was more common in COPD group of patient compared to healthy group. Similar finding is also observed in the study done by Marie-Kathrin Breyer et al. Our study also finds that presence of diabetes is more common in Grade III and IV COPD patients. This can be explained by the diseases progress in severity, patients use more medications in the form of steroids and also in COPD patients adipose tissue inflammation will be present, which leads to whole body insulin resistance and then development of diabetes.

It is important to emphasize that COPD result in sedentary lifestyle and physically inactive condition, which could explain the higher prevalence of the metabolic syndrome in COPD patients compared to the control participant. COPD is an important risk factor for cardiovascular disease, increasing the risk by two- to three-fold. It is recognized that patients with the metabolic syndrome are at increased risk for cardiovascular events. Thus, in COPD patients, the presence of the metabolic syndrome might explain the increase in incidence of cardiovascular diseases.

**CONCLUSION:**

Thus our study concluded that prevalence of metabolic syndrome is more common in patients with Grade II COPD. Early recognition of metabolic syndrome can prevent the potential life threatening cardiovascular complication and development of diabetes mellitus.

**Abbreviations:** COPD=Chronic obstructive pulmonary diseases, GOLD= Global Initiative for Chronic Obstructive Lung Disease NCEP= National Cholesterol Education Program, BMI= body mass index.

**REFERENCES:**


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Name of person described in article or shown in photograph: ____________________________________

Subject matter of photograph or article: ______________________________________________________

Title of article: _________________________________________________________________________

Medical practitioner or corresponding author: ________________________________________________

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4. I can withdraw my consent at any time before publication, but once the Information has been committed to publication it will not be possible to withdraw the consent.

Signed: ___________________________ Date: ___________________________

Signature of requesting medical practitioner/health care worker:

________________________ Date: ___________________________
Clinical Profile of Snake Bite in Upper Assam

M Gogoi***, A Sarma***, S Gogoi***, N Jain***

Abstract

Background: Envenoming resulting from snakebite is an important public health hazard in many regions. It is common in rural areas. Hence, delay access to life saving anti-venom is a concern. The objectives of this study were to know about common types of snakes in local areas, clinical features, complications, and mortality rate in snakebite victims admitted in a tertiary care centre (Assam Medical College & Hospital, Dibrugarh).

Materials and Methods: This descriptive study was conducted in the Department of Medicine in Assam Medical College & Hospital, Dibrugarh, from 1st April 2015 to 31st October 2015. Eighty-five cases with history of snakebite were analysed. Whole Blood Clotting time (WBCT) and neurological examination were the main bedside procedures to assess the degree of envenomation.

Result: A total of Eighty-five (85) cases from both genders, from 14 to 68 years age were studied. There were 55 poisonous and 30 non-poisonous cases. Among the poisonous cases, 48 (87.3%) viper bites (haemotoxic) having haemostatic abnormalities and 7 (12.7%) elapid (neurotoxic) bites presented with neuroparalytic symptoms, of which 1 case expired following respiratory failure. Most cases were from Dibrugarh and neighbouring districts and few from neighbouring state of Arunachal Pradesh. Almost all victims had localized oedema at the site of bite. Fang/teeth marks were noted in 72 (84.7%) cases. Majority (84%) were bitten on the legs below knee. One patient had acute renal failure (ARF) and septicemia. One case of viper bite was presented with sub-arachnoid haemorrhage. 1 case of elapid bite needed assisted ventilation. 4 patients (5.5%) had adverse effects after anti-venom administration and needed intravenous hydrocortisone, promethazine and subcutaneous adrenaline. The average dose of anti-venom was 10 vials for both viper and elapid bites. Overall mortality rate was 1.3%.

Conclusion: In this part of country poisonous snake bite is common Viper bite (Haematotoxic) is more common than elapid (neurotoxic) bite. Average antivenom requirement is comparatively high (10 vials). Rare presentation like subarachnoid haemorrhage is also observed.

INTRODUCTION:

Snake bite is a common medical emergency encountered in South-Asia. India is estimated to have the highest snakebite mortality in the world¹. Snake bite is one of the accidental cause of morbidity and mortality in India. Among various venomous snakes, in India most of the deaths occur due to Russell’s viper (Daboia russeli) and saw-scaled viper bite (Echis carinatus)²,³. The estimated total of 45,900 national snakebite deaths in 2005 constitutes about 5% of all injury deaths and nearly 0.5% of all deaths in India.⁴ Viperine bite is usually associated with coagulopathy in the form of local cellulitis, mucosal and cutaneous bleeding, acute kidney injury and rarely intracerebral hemorrhage. The largest numbers of fatal snakebites occur in South Asia and Africa. In South-Asia, there are 25,000–30,000 deaths each year from snakebite⁵. Snakes bite millions of people annually, creating ‘one of the neglected health problems of the tropics’ due to a lack of antivenoms.⁶

Contributing to this in developing nations, there are also deficiencies in the management of complications, transportation, hospital equipments and public knowledge of appropriate first aid, which result in a mortality rate of one hundred fold higher than in developed countries⁷. The victims of snake bites are mainly of the rural population, who are bitten during field work and when sleeping outdoors⁸. Only cases of snakebite with severe envenomation reach the healthcare centres.
AIMS AND OBJECTIVES:
This study was conducted to identify the type of common snakes, clinical features, complications and outcome of snake bite in this region.

MATERIAL AND METHODS:
This descriptive study was carried out in the Department of Medicine in Assam Medical College & Hospital, Dibrugarh, from 1st April 2015 to 31st October 2015. Eighty-five cases with history of snakebite, from Dibrugarh, neighbouring districts and neighbouring state of Arunachal Pradesh were studied. Patients included were those with the presence of fang marks and presence of neurological symptoms, swelling, cellulitis, bleeding or blister formation at local site. Data were recorded with reference to the type of snake (whenever possible), age and sex of the person bitten, site of bite, place and time of bite, time of arrival at hospital, symptoms and signs, type of treatment received before referral, in-hospital treatment and duration of hospital stay. The time after snakebite before the first dose of anti-venom, the amount of anti-venom received and adverse effects were recorded.

RESULTS:
A total of Eighty five cases of snake bite were included in the study from the period of 1st April 2015 to 31st October 2015. There were 55 poisonous and 30 non-poisonous cases. Among the poisonous cases, 48 (87.3%) viper bites (haematotoxic) having haemostatic abnormalities and 7 (12.7%) elapid (neurotoxic) bites presented with neuroparalytic symptoms, of which 1 case expired following respiratory failure. Majority of victims of snakebite were from Dibrugarh (41 cases), Sivasagar (22 cases), Tinsukia (18) and Arunachal Pradesh (4 cases). Out of 85 cases, 52 (61.3%) were men, 33 (38.7%) were women. The male to female ratio was 2:1. Age group between 20-25 yrs were mostly bitten. The most frequently bitten site was the legs below knee (80%). From the history and estimation of CT, it was believed that a total of 55 patients (64.7%) had bites by poisonous snakes.

The haemostatic abnormalities (attributed to viper bites) were seen in 48 (87.3%) and neuroparalytic features (hallmark of cobra and krait bites) were evident in 7 (12.7%) cases. There were 30 patients who had no symptoms of both neuroparalytic and haemostatic dysfunction. Of the 48 patients with viper bites, one patient (1.75%) developed acute renal failure and septicemia and one patient manifested with sub-arachnoid haemorrhage.

Among 7 patients with neuroparalytic features, one patient required assisted ventilation but the patient died of acute respiratory distress syndrome (ARDS) from neurotoxin, who couldn’t receive snake antivenom. Twenty three (23) victims (27.1%), were given antivenom immediately if the clotting time was prolonged or if ptosis was evident. Remaining victims, 62 cases (72.9%) were treated on arrival who didn’t require anti snake venom but they were monitored regularly for deterioration. Medical referral records were available with 15 (17.6%) cases indicating receipt of inj tetanus toxoid and analgesic. Two patients (2.3%) had received treatment before coming to hospital with anti snake venom. 58 cases had tourniquet tied above the site of bites. No case reported with incision and drainage performance outside. Twenty three (23) victims (27.1%) with signs of systemic envenomation had received equine polyvalent anti-venom. One vial when reconstituted gives 10 ml. Anti-venom was withheld in 62 (72.9%) cases in the absence of systemic envenomation. The maximum dose of anti-venom given for viper bites was 30 vials and 20 vials for neuroparalytic snakebite. Of the 23 patients that received anti-venom, 4 (17.4%) patients had an adverse reaction to anti-venom (i.e., anaphylaxis in 2 patients, pyrexial reaction in one and urticaria in one patient) and they were treated with intravenous hydrocortisone, promethazine and subcutaneous adrenaline. No side-effects of this therapy were noted. The average duration of hospital stay in snakebite victims was 4 days (range 1–16 days).

Table 1: Demographic profile of patients studied.

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<th>Gender</th>
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<td>77.7</td>
</tr>
<tr>
<td>Mean ± SD in Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>5.20 ± 3.43</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4.13 ± 2.53</td>
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</tbody>
</table>
DISCUSSION :

Snake bites are the common cause of morbidity and mortality in tropical countries. In India, there are 216 species of snakes, of which only four are venomous snakes (cobra, krait, Russell’s viper and saw scaled viper). Snake bites are very common in Assam particularly in the tea-garden areas among rural dwellers, farmers working bare footed in fields or sleeping out-doors. Most snakebites occur during the monsoon season probably because of flooding of the habitat of snakes and their prey. Our study, is in conformity with the fact from another south Indian study, where snake bites abound during the months of October to December (33%) and May to July (67%)9. Severity of Snake bite depends upon degree of envenomation. Mild viperine envenomation presents with local swelling, cellulitis, blister formation. Severe cases were associated with local as well as systemic manifestation like gingival bleeding, epistaxis, hematuria, sub-conjunctival hemorrhage, gastrointestinal and cerebral hemorrhage. Myoglobinuria from muscle damage can cause renal failure. Cardiotoxin present in venom may cause arrhythmia, hypotension, impair contractility. The neurological manifestation includes drowsiness, confusion, fainting, dizziness, blurred vision, loss of muscle coordination and convulsions.

During this study, 50% of recipients of ASV had received it within few hours of bite. Only 1 victim died during this study i.e compared with a national death rate of 4.1 per 100,000 populations. Whereas one of the victim manifested with sub-arachnoid haemorrhage. Hence, though rare, sub-arachnoid haemorrhage may occur in case of haematotoxic snake bite like viper. The overall mortality rate during this study was 1.3%. Whereas case
fatality rates greater than 20% have been reported in hospitalized victims in Nepal. One study from South India reported a mortality rate of 4%.

CONCLUSIONS:
Snakebite mainly affects the rural men of developing countries. Snake bite is an occupational hazard and there is a need of awareness among farmers and labourers regarding wearing of foot wears. There is a need to educate the public about the hazards of snake bite, early hospital referral and treatment. Availability of anti-venom at primary healthcare centre and rapid transportation facilities may change the morbidity associated with snakebites. Early administration of the polyvalent anti-venom has reduced morbidity and mortality but is associated with anaphylaxis in small group of patients. There is need to educate the rural population about the hazards and treatment of snake bites. Also, randomized controlled trials are needed to investigate the issue of rationale of anti-venom treatment.

A RARE CASE OF SUB-ARACHNOID HAEMORRHAGE FOLLOWING SNAKE BITE:
Case History: A 40 year old female, hailing from Seujpur area of Dibrugarh Town was presented to hospital in Emergency Department with history of snake bite over the left foot and mid thigh. She reported 1 hr after the bite with the complaint of pain and swelling over the dorsum of left foot (bite area). Tourniquet was applied above the ankle for a short period but swelling progressed increasingly, which after about 8 hours involved up to the mid left leg. No swelling occurred over the thigh. There was no history of drowsiness, breathing difficulty, or bleeding manifestations. She was a known hypothyroidism on regular medication with Thyronorm (100 ug).

On examination, pulse rate was 90/min, BP 140/90 mmHg and respiratory rate 16/min. She was afebrile. Systemic examination were normal. Local examination showed 2 fang marks over the dorsum of left foot and over the left mid-thigh. There was no local swelling or redness or tenderness over the thigh but the left foot was swollen, inflamed with raised local temperature without oozing of blood. She was conscious, alert and oriented to time, place and person. No ptosis present.

On admission, the whole blood clotting time was <20 mins and single breath count >20. She was kept under close monitoring over night. After 6 hours the WBCT was >20 min and the local swelling increased up to the mid left leg. The PT was 23 sec(control 11.5 sec). Hence, she was started on ASV (anti snake venom) 10 vials according to guidelines with prior institution of inj hydrocortisone and avil. No reaction occurred. Meanwhile, the patient has been on continuous monitoring for vitals, neurological symptoms like ptosis, drowsiness, respiratory rate, O2 saturation and other haematological and bleeding manifestation. On the other hand, she was kept on antibiotic coverage along with fluid and nutritional support. Left lower limb was kept elevated at foot-end and avoided mobilization.

On the 3rd day, bruise developed over her upper limbs and the serial WBCTs were >20 mins and PT 31.6 sec with INR 4.69. Hence, again she was given ASV for another 7 vials. In the meantime, she has received 1 unit of 0+ve whole blood and 4 units of FFP transfusion. On the other hand, she complained of both frontal and occipital headache with pain in back of neck. ENT and Ophthalmology opinion were taken. Fundoscopic examination revealed hypertensive changes with mild blurring of disc margin with swelling of the disc. X-ray PNS showed maxillary and frontal sinusitis and x-ray cervical spine showed early degenerative changes of c-spine. Meanwhile, the NECT scan of brain revealed acute focal sub-arachnoid haemorrhages along left side basal prepontine and inter peduncular cistern. The repeat PT...
was 17 sec and INR 1.87 and the patient was given another 5 vials of ASV. From 9th day onwards the 6 hrly WBCT were all < 20 mins and PT and INR values came down to normal range.

At discharge all symptoms were subsided and the limb swelling subsided and her blood parameters were within normal limits. A repeat NECT scan brain revealed a sub-arachnoid - haemorrhages in the basal cistern measuring 1.1 x 1.0 x 0.9 cm. but CT-Brain angiography revealed normal appearance of major intracranial arteries without evidence of aneurysm or active vasospasm.

DISCUSSION:

Intracerebral haemorrhage following viper bite is a rare complication. Ischaemic infarction involving different arterial territories following viper envenomation has been described. So far, to our knowledge one case of sub-arachnoid haemorrhage following viper bite has been reported. The systemic haemorrhagic manifestations are due to disseminated intravascular coagulation with consumption of clotting factors. Though fibrin degradation product and D-dimer could not be estimated the elevated PT and activated partial thromboplastin time level suggested disseminated intravascular coagulation, which might be the cause of haemorrhage. Moreover, any possibility of vascular abnormality had been ruled out in our case in the CT-angiography study. Hence, sub-arachnoid haemorrhage could be attributed to viperine snake bite. It is extremely rare to bleed only at subarachnoid space, due to disseminated intravascular coagulation hence we are reporting the case.

REFERENCES:

Stem Cell and Regenerative Medicine

A K Sen*, R M Doley**, D S Timung***

INTRODUCTION:
Stem cell biology is a rapidly expanding field that explores the characteristics and possible clinical applications of a variety of stem cells that serve as the progenitors of more differentiated cell types. Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine. Patient-derived stem cells can also be used as disease models and as a means of testing drug efficacy.1,2,3

DEFINITION:
Stem cells are the blank, unspecialized immature cells that have the remarkable unique potential to produce unaltered daughter cells (self-renewal) and to generate into many different specialized cell types (potency) in the body serving as a sort of repair system of the body. They can divide without limit to replenish other cells for as long as the person or animal is still alive. When a stem cell divides, each “daughter” cell has the potential to either remain a stem cell or become another type of cell with a more specialized function.1,2,3,4,5,6

Origin of the term ‘stem cells’:
The word “stem cell” were first used by eminent German biologist, Hackel, 1868 to describe the origin of multi-cellular organism from a unicellular organism i.e fertilised egg.7,8. In 1886, William Sedgwick uses the term “stem cells” to describe the parts of a plant that grow and regenerate.9. June 1, 1909 — Russian academic Alexander Maximow lectures at the Berlin Hematological Society on a theory that all blood cells come from the same ancestor cell. This introduces the idea of blood stem cells that are multi-potent, or have the ability to differentiate into several types of cells9.

Stem Cell Characteristics:
These are blank cells’ (unspecialized), capable of dividing and renewing themselves for long periods of time (proliferation and renewal) and has the potential to give rise to specialized cell types (differentiation), self renewing (has the ability to continuously divide) and has the ability to repair (return function to damaged cells in living organism,) and has the ability of stem cells from one tissue to generate specialized cell type of another tissue (Plasticity) e.g hematopoietic cells may give rise to skeletal, myocardial and hepatic cells.2,3

Stem cells are unique in the fact that they can regenerate an infinite number of times, can be grown in culture indefinitely, are classified as pluripotent and are able to differentiate into specialized cells as when needed. On division, one daughter cell replenishes a whole compartment, and the other remains fully “stem.”2,3

Source of Stem cells:
Stem cells may be derived from- autologous, allogenic or xenogenic sources. Histocompatibility is prerequisite for transplantation of allogenic stem cells. Fetal tissue is the best current tissue source for human neural stem cells. Autologous – Stem Cells: Sources of the patient’s own stem cells (autologous) are either the cells from patient’s own body or his or her cord blood. For autologous transplants nowadays stem cells from the peripheral blood rather than the marrow are collected.

Allogenic – Stem Cells: Sources of stem cells from another donor (allogenic) are primarily relatives (familial-
allogenic) or completely unrelated donors (unrelated-allogenic). The stem cells in this situation are extracted from either the donor’s body or cord blood.

Xenogenic - Stem Cells: Stem cells from different species are transplanted, e.g. striatal porcine fetal ventral mesencephalic (FVM) xenotransplants for Parkinson’s disease. This has no major ethical concerns and a large amount of tissue is available, however life long immunosupression and risk of rejection are the major limitations.

Classification of stem cells:
(A) According to potency
- Totipotent: Each cell can develop into a new individual. E.g. Stem Cells produced from fusion of an egg and sperm and cells from early embryo.
- Pluripotent: Cells can form any cell types. E.g cells derived from inner cell mass of the blastocyst.
- Multipotent: Stem cells that can produce only cells of closely related family of cells e.g hematopoietic stem cells can differentiate into RBC, WBC etc...
- Oligopotent: Stem cells that can differentiate to only few cells e.g lymphoid stem cells.
- Bipotent: Dual differentiation. E.g oval cells can differentiate into hepatic and biliary epithelium.
- Unipotent: Stem cells that can produce only one cell type.

(B) According to their Origin
- Embryonic stem cells: isolated from the inner cell mass of the blastocyst of the discarded embryos after IVF (in vitro fertilization) or from aborted embryos.
- Fetal stem cells: obtained from aborted fetal gonadal tissue.
- Cord blood stem cells: obtained from the remaining blood in the umbilical cord after delivery, these cells contain a big deal of hematopoietic stem cells.
- Adult stem cells: are multipotent stem cells present in few numbers in many sites (bone marrow and niches) of human body.

Embryonic stem cells:
- These are derived from embryos, developed from eggs that have been fertilized in vitro and then donated for research purposes with informed consent of the donors. The embryos from which human embryonic stem cells are derived are typically four or five days old and are a hollow microscopic ball of cells called the blastocyst. The blastocyst includes three structures: the trophoblast, blastocoel, and the inner cell mass.

Embryogenesis and Differentiation:
- Specific regions of the embryo give rise to the specific organ systems.
  - Ectoderm generates the outer layer of the embryo and produces the surface layer (epidermis) of the skin and forms the nerve.
  - Endoderm becomes the innermost layer of the embryo and produces the digestive tube and its associated organs including the lungs.
  - Mesoderm becomes sandwiched between the ectoderm and endoderm and generates the blood, heart, kidney, gonads, bones, and connective tissues.

Embryonic Stem Cell Properties:
- They are derived from 4-5 day old embryos (Prior to implantation in uterus), has indefinite proliferative capacity (“immortal”) making a stem cell line and has the ability to become any cell type in the body. They are the only cells that definitely can become heart muscle cells and other clinically important cell types.

Sources of Embryonic Stem Cells:
1. In Vitro Fertilization (IVF): Here sperm is obtained from male. Ovum is removed from ovary of female. Ovum and sperm are then combined in test tubes/Petri dish. Fertilized eggs (zygotes) are allowed to divide for a few days. Blastocysts are then transferred to uterus of woman.
2. Nuclear Transfer or reprogramming: The process of reversal of terminally differentiated cell to totipotent or pluripotent cell is called nuclear transfer. It offers another potential way to produce embryonic stem cells. In animals, nuclear transfer has been accomplished by inserting the nucleus of an already differentiated adult cell into enucleated oocyte.

Embryonic Human Stem cells have Been Grown into the following cell-types:
- Smooth Muscle
- Pancreas
- Heart Muscle
- Liver
- Nerves
- Lymph Nodes
- Kidney
- Yolk Sac
- Bone
- Endoderm
- Cartilage
- Retinal (Eye) Cells
- RBC & WBC

Stem cells in adults:
The history of research on adult stem cells began about 40 years ago. An adult stem cell is an undifferentiated cell
found among differentiated cells in a tissue or organ. It can renew itself, and can differentiate to yield the major specialized cell types of the tissue or organ. It maintain and repair the tissue in adult in which they are found. Some use the term somatic stem cell instead of adult stem cell.

In the 1960s, researchers discovered that the bone marrow contains at least two kinds of stem cells-hematopoietic stem cells, that forms all the types of blood cells in the body and bone marrow stromal cells, was discovered a few years later. Stromal cells are a mixed cell population that generates bone, cartilage, fat, and fibrous connective tissue. In 1960s, scientists who were studying rats discovered two regions of the brain that contained dividing cells, which become nerve cells. Scientists agreed that the adult brain does contain stem cells that are able to generate the brain’s three major  cell types—astrocytes and oligodendrocytes, which are non-neuronal cells, and neurons, or nerve cells.

Sources of adult stem cells:
The adult tissues reported to contain stem cells include—(1) Bone marrow, (2) Peripheral blood, (3) Blood vessels, (4) Skeletal muscle, (5) Skin, (6) Brain and (7) Liver.

Other sources of stem cells:
This has become possible with the appearance of two miracles-Induced pluripotent stem cells (IPSC) and Stimulus-triggered Acquisition of pluripotency (STAP).

Induced pluripotent stem cells: In the year of 2007, Professor Shinya Yamanaka and his research team said that adult differentiated cells can be transformed into pluripotent cells and they published their results of transforming adult human fibroblasts into pluripotent cells by defined factors. It is the direct conversion of terminally differentiated cell to Embryonic Stem like cells i.e IPS cells by transiently overexpressing a combination of key transcription factors.

Stimulus –Triggered Acquisition of pluripotency (STAP): The newest breakthrough in the field of stem cell research was declared by the beginning of the year (2014) by the valuable research of Haruko Obokata. Here, adult cells like lymphocytes were exposed to strong external stimulus like transient low pH resulting in pluripotency.

Types of Adult stem cells and their differentiation:
A. Hematopoietic stem cells-RBC, B lymphocytes, T lymphocytes, Natural killer cells, Neutrophils, Basophils, Esinophil, Monocyte, Macrophages, and Platelets.
B. Bone marrow stromal cells (mesenchymal stem cells-bone cells (osteocytes), cartilage cells (chondrocytes), fat cells (adipocytes), and other kinds of connective tissue cells such as those in tendon.
C. Neural stem cells in the brain give rise to its three major cell types: nerve cells (neurons) and two categories of non-neuronal cells— astrocytes and oligodendrocytes.
D. Epithelial stem cells :Absorptive cells, Goblet cells, Paneth cells, and Enteroendocrine cells.
E. Skin stem cells- keratinocytes, which migrate to the surface of the skin and form a protective layer and the follicular stem cells can give rise to both the hair follicle and the epidermis.

Difference between embryonic and adult stem cells:
1. Embryonic stem cells can reproduce almost limitlessly. Adult stem cells can only reproduce a limited number of times before they become “senescent”. Adult stem cell “lines” are not normal cells and usually have cancerous properties.
2. Embryonic stem cells can make any of the more than 200 different cell types and tissues. Adult stem cells are only capable of making a limited number of cell types (e.g. blood cells).

Advantages of adult stem cells: Autologous (in some cases), no tissue rejection, no ethical concerns, no teratoma formation, easy to obtain (bone marrow aspirate) and widely available.

Disadvantages /criticism of adult stem cells- Some “plasticity” or “transdifferentiation” may be simply a result of cell fusion and not as “pluripotential” as embryonic stem cells.

Stem cell technologies:
1. Cloning technologies
2. Induced Pluripotent Stem cells

The Promise of Stem Cell Research
Applications of stem cells:

Given their proliferation and differentiation capacities, stem cells has great potential for the development of novel cell-based therapies. However, recent studies suggest that dysregulation of stem cell properties may be the cause of certain types of cancer.

1. Basic research
   - Stem cell theory of cancer
   - Role of signals in gene transcription and differentiation of stem cells

2. Biotechnology:
   - Specific cell lines to test new drugs and decrease animal testing.
   - Development efficative antitumor drugs

3. Cell based therapy:
   - Regenerative therapy for many diseases like Parkinsonism, Alzheimer’s, spinal cord injury, stroke, burns, heart diseases, diabetes, liver disease etc.

REGENERATIVE MEDICINE:

Damage to an organ results in proliferation, differentiation, and migration of various cell types. Thereby releasing cytokines and chemokines and remodeling of the extracellular matrix resulting in reconstruction. Endogenous stem and progenitor cells are among the cell populations that are involved in these injury responses. Normally, an equilibrium is maintained in which endogenous stem cells intrinsic to the tissue, replenish dying cells. The goal of stem cell therapies is to promote cell replacement in organs that are damaged beyond their ability to self-repair.

General strategies for stem cell replacement:

Three different therapeutic concepts for cell replacement:

One approach - direct administration of stem cells. The cells may be injected directly into the damaged organ, where they can differentiate into the desired cell type. Alternatively, stem cells may be injected systemically since they have the capacity to home in on damaged tissues by following gradients of cytokines and chemokines released by the diseased organ.

Second approach - transplantation of differentiated cells derived from stem cells. For example, pancreatic islet cells can be generated from stem cells before transplantation into diabetic patient, and cardiomyocytes can be generated to treat ischemic heart disease.

A third approach - stimulation of endogenous stem cells to facilitate repair. E.g. Therapeutic stimulation of hematopoietic system, where factors such as erythropoietin, G-CSF, and GM-CSF are used to increase production of specific blood elements.

Sources of stem cells for tissue repair:

- Embryonic Stem (ES) cells,
- Induced Pluripotent Stem (iPS) cells,
- Umbilical-cord blood stem cells (USCs),
- Organ-specific somatic stem cells
- Somatic stem cells

Stem Cell Therapy:

It is similar to the process of organ transplantation only the treatment consists of transplanting cells instead of organs. Stem cells can be used to generate healthy and functioning specialized cells, which can then replace diseased or dysfunctional cells. Bone marrow transplants are an example of cell therapy in which the stem cells in a donor’s marrow are used to replace the blood cells of the victims of leukemia. To graft new skin cells to treat serious burn victims, and to grow new corneas for the sight-impaired. The goal is for the healthy cells to become integrated into the body and begin to function like the patient’s own cells.

Disease specific applications of stem cells:

1. Ischemic Heart Disease and Cardiomyocyte Regeneration:
   Heart has the capacity for low levels of cardiomyocyte regeneration. Cardiac stem cells and adult bone marrow stem cells may be used. Stem cell therapy may deliver cells either systemically or locally. The cells must survive, engraft, and differentiate into functional cardiomyocytes. Some employ intramyocardial, transendocardial, intravenous, intracoronary, and retrograde coronary venous injections. Transplantation may use different cell types, including ES cells, HSCs, MSCs, USCs, and ASCs.

2. Diabetes: Islet cell and pancreas transplantation success-proof of cell based therapies for type 1 diabetes. Demand for donor pancreas far exceeds the number available. Maintenance of long-term graft survival is a problem. A renewable source of stem cells capable of regenerating pancreatic islets has been sought. Hence, the
concept for cell-based therapies for type 1 diabetes. Different cell types in use includes iPSC cells, ES cells, hepatic progenitor cells, pancreatic ductal progenitor cells, and MSCs. Clinical trials of MSCs, USCs, HSCs, and ASCs in both type 1 and type 2 diabetes are ongoing.

3. Nervous System: Sources of stem cells-Human ES or iPS cells, Multipotent stem cells resident in brain and Fetal neural stem cells. Fetal neural stem cells—amyotrophic lateral sclerosis (ALS), stroke, and several other disorders. Trials of stem cells - spinal cord injury, multiple sclerosis, epilepsy, Alzheimer’s disease, ALS, acute and chronic stroke, traumatic brain injury, Parkinson’s disease. In Parkinson’s disease, the major motor features of the disorder result from the loss of a single cell population: dopaminergic neurons within the substantia nigra. Employs stem cells with ability to migrate and disperse within tissue and the potential for engineering regulatable release of dopamine. Both ES cells and MSCs can facilitate remyelination after experimental spinal cord injury (SCI)^1,2.

4. Alzheimer’s disease: Stem cells could, however, be genetically modified so as to deliver substances to the Alzheimer brain, to stop cells from dying and stimulate the function of existing cells. A recent clinical trial (Phase I) has shown this approach to be of some benefit to patients with Alzheimer’s disease, by slowing down the progression of the disease^1.

5. Leukaemia and cancer: Bone marrow transplant has been used successfully to treat diseases such as leukemias, lymphomas, aplastic anemia, immune deficiency disorders, and some solid tumor cancers^1.

BMT can be used to replace diseased, nonfunctioning bone marrow with healthy functioning bone marrow, regenerate a new immune system, replace the bone marrow and restore its normal function after high doses of chemotherapy and/or radiation and replace bone marrow with genetically healthy functioning bone marrow to prevent further damage from a genetic disease process (such as Hurler’s syndrome and adrenoleukodystrophy).

6. Liver disease: Liver transplantation is currently the only successful treatment for end-stage liver diseases^1. The shortage of liver grafts limits its application. Potential sources of stem cells for regenerative strategies include endogenous liver stem cells (such as oval cells), ES cells, MSCs, and USCs. The available evidence suggests that transplanted HSCs and MSCs can generate hepatocyte-like cells in the liver only at a very low frequency.

7. Drug Testing: Stem cells could allow scientists to test new drugs using human cell line which could speed up new drug development. Only drugs that were safe and had beneficial effects in cell line testing would graduate to whole animal or human testing. It would allow quicker and safer development of new drugs.

8. Rheumatoid arthritis: EU-funded researchers have developed a new potential treatment for rheumatoid arthritis, based on adult stem cells from body fat, or adipose tissue^8. The results of initial clinical trials are encouraging, and with a large number of patients all over the world the benefits could be staggering. Adipose-derived stem cells have been shown to have potent anti-inflammatory and repair-promoting capabilities, and show promise of use for a wide range of therapeutic applications.

9. Stem cells – Blindness: In clinical trials at Moorfields Eye Hospital in London, surgeons restored eye sight for six patients who lost their sight after chemical accidents and genetic diseases. The patients went under successful stem-cell transplant. Bone Marrow Stem Cells May Cure Eye Disease: Bone marrow stem cells can switch roles and produce keratocan, a natural protein involved in the growth of the cornea—the transparent, outer layer of the eyeball. This ability of marrow cells to “differentiate” into keratocan-producing cells might provide a means for treating abnormal corneal cell growth in people.

10. Limbal stem Cell therapy: The treatment is known as limbal stem cell therapy, and the patients who received the treatment suffered from chemical burn or genetic disease know as aniridia. By replacing the limbal stem cells, the cornea begins to clear up as the cells are replaced with the healthy transparent layer again^19.

Tissue Engineering: A new branch in Medicine

The approach to tissue engineering contain the combination of three dimensional scaffold with live and functional cells. Stem cells proving the ideal tool as they are capable of rapid proliferation and they can be induced to differentiate into multiple lineage. Human embryonic are capable of differentiation to endoderm, mesoderm, or ectoderm tissue types. Adult stem cells generate a relatively muted immune response^1.
Cryopreservation:

It is a process where cells or whole tissues are preserved by cooling to low sub-zero temperatures, such as (typically) 77 K or “196 °C (the boiling point of liquid nitrogen). At these low temperatures, any biological activity, including the biochemical reactions that would lead to cell death, is effectively stopped.

CryoBanks India:

CryoBanks has 80 counselling centres across the country manned by bio-tech graduates, who visit households and hospitals to create awareness and market the concept. India is the seventh largest and second most populous country in the world with approximately 20 million births per year representing one of the largest birth markets in the world.

Obstacles of Stem Cell Research:

- How to find the right type of stem cells?
- How to put the stem cells into the right place?
- Will the stem cells perform the desired function in the body?
- Differentiation protocols for many cell types have not been developed.

Biblical Argument: The Bible indicates that God recognizes human beings as persons prior to development in the womb. Bible defines murder as being intentional and premeditated. ESC research destroys embryos that are considered as ensouled human beings.

Ethical debate: Harvesting ES cells destroys the blastocyst”This is murder”. ES cell research requires human cells. Could create a commercial market for human cells”This devalues life”

CONCLUSION:

Stem and progenitor cell research is a complex and very exciting field that promise fantastic curative discoveries in numerous areas from cancer to diabetes to neurogenerative diseases. Both adult and embryonic stem cells should be studied. Ethical concerns need to be taken into account. Appropriate guidelines are needed to ensure appropriate conduct of the research.

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INTRODUCTION:
Hyponatremia is defined as serum [Na⁺] of less than 135 mmol/l and equates with a low serum osmolarity once translocational hyponatremia and pseudohyponatremia are ruled out. True hyponatremia develops when normal urinary dilution mechanisms are disturbed. This may occur by three mechanisms. First, hyponatremia may result from intra-renal factors such as a diminished glomerular filtration rate (GFR) and an increase in proximal tubular fluid and Na⁺ reabsorption, which decrease distal delivery to the diluting segments of the nephron. Hyponatremia may also result from a defect in Na⁺ Cl⁻ transport out of the water-impermeable segments of the nephrons (the thick ascending limb of Henle [TALH] or distal convoluted tubule). Most commonly, hyponatremia results from continued stimulation of vasopressin secretion by non-osmotic mechanisms despite the presence of serum hypo-osmolality.

Most patients with a serum Na⁺ concentration above 125 mmol/l are asymptomatic and should be treated if symptomatic. Below 125 mmol/l, headache, yawning, lethargy, nausea, reversible ataxia, psychosis, seizures, and coma may occur as a result of cerebral edema. Rarely, hypotonicity leads to cerebral edema so severe that there is increased intracerebral pressure, tentorial herniation, respiratory depression, and death. Neurological symptoms associated with hyponatremia is designated as “hyponatremic encephalopathy”2. Hyponatremia-induced cerebral edema usually occurs with rapid development of hyponatremia, typically in hospitalized postoperative patients receiving diuretics or hypotonic fluids. Untreated severe hyponatremia has mortality up to 50%. Neurologic symptoms in a hyponatremic patient call for immediate attention and treatment.

TREATMENT OF HYponatremia:
Correction of hyponatremia is associated with markedly improved neurological outcomes in patients with severely symptomatic hyponatremia. Usually symptoms, degree and duration of hyponatremia determine the treatment. Acutely hyponatremic patients (hyponatremia developing within 48 hours) are at great risk for development of permanent neurologic sequelae from cerebral edema if the hyponatremia remains uncorrected. Patients with chronic hyponatremia are at risk for osmotic demyelination if the hyponatremia is corrected too rapidly. Hyponatremia can be classified based on serum sodium concentration hyponatremia as ‘mild’ (130-135mmol/l), ‘moderate’ (125-129) and ‘severe (<125mmol/l)’ or based on the time of development of hyponatremia acute <48 hrs and chronic >48 hours and most importantly based on clinical symptoms as moderately symptomatic and severely symptomatic hyponatremia. Classification based on volume status, patients with hyponatremia may be hypovolaemic, euvolaemic or hypervolaemic and this classification system also guide the evaluation and management of hyponatremic patients. Classification of hyponatremia based on osmolality is important in diagnostic evaluation of hyponatremia and it is not much of therapeutic importance.

Conventional management strategies for hyponatremia range from saline infusion and fluid restriction to pharmacologic measures to adjust fluid balance. Consideration of treatment options should always include an evaluation of the benefits as well as the potential toxicities of any therapy, and therapies must be individualized for each patient. Briefly treatment of hyponatremia is narrated below.
(A) Hyponatraemia with severe symptoms:

(i) First-hour management, regard less of whether hyponatraemia is acute or chronic: Prompt iv infusion of 150ml 3% hypertonic over 20 min is recommended; the serum sodium concentration should be checked after 20 min while repeating an infusion of 150ml 3% hypertonic saline for the next 20 min. Repeating therapeutic recommendations should be suggested twice or until a target of 5 mmol/l increase in serum sodium concentration is achieved. Patients with severely symptomatic hyponatraemia should be managed in an environment where close biochemical and clinical monitoring can be provided.

(ii) Follow-up management in case of improvement of symptoms after a 5 mmol/l increase in serum sodium concentration in the first hour, regardless of whether hyponatraemia is acute or chronic: The infusion of hypertonic saline after first hours should be stopped. The i.v line should be kept open by infusing the smallest feasible volume of 0.9% saline until cause-specific treatment is started. It is recommended to start a diagnosis-specific treatment if available, aiming at least to stabilize sodium concentration and limiting the increase in serum sodium concentration to a total of 10 mmol/l during the 1st 24 hours and an additional of 8 mmol/l during every 24 hours thereafter until the serum sodium concentration reaches 130 mmol/l. Checking the serum sodium concentration after 6-12 hours & daily afterwards is suggested until the serum sodium concentration has stabilized under stable treatment.

(iii) Follow-up management in case of no improvement of symptoms after a 5 mmol/l increase in serum sodium concentration in the first hour, regardless of whether hyponatraemia is acute or chronic: Continuing an i.v. infusion of 3% hypertonic saline or equivalent aiming for an additional 1 mmol/l per hour increase in serum sodium concentration. Then stopping the infusion of 3% hypertonic saline or equivalent when the symptoms improve, the serum sodium concentration increases 10 mmol/l in total or the serum sodium concentration reaches 130 mmol/l, whichever occurs first. Additional diagnostic exploration for other causes of the symptoms than hyponatraemia should be carried out. Checking the serum sodium concentration every 4 hours is also suggested as long as an i.v infusion of 3% hypertonic saline or equivalent is continued.

(B) Hyponatraemia with moderately severe symptoms:

A prompt diagnostic assessment is started first and if possible, medications and other factors that can contribute to or provoke hyponatraemia should be stopped. Cause specific treatment should be initiated as early as possible. Immediate recommended treatment is suggested with a single i.v. infusion of 150 ml 3% hypertonic saline or equivalent over 20 min, aiming for a 5 mmol/l per 24 hour increase in serum sodium concentration. The increase in serum sodium concentration should be limited to 10 mmol/l in the 1st 24 hours and 8 mmol/l during every 24 hours thereafter, until a serum sodium concentration of 130 mmol/l is reached. The serum concentration after 1, 6 and 12 hours should be checked. Additional diagnostic exploration for other causes of the symptoms if the symptoms do not improve with an increase in serum sodium concentration should also be looked for. The patient should be managed as in severely symptomatic hyponatraemic if the serum sodium concentration further decreases despite treating the underlying diagnosis.

(C) Acute hyponatraemia without severe or moderately severe symptoms:

It should be made sure that the serum sodium concentration has been measured using the same technique used for the previous measurement and that no administrative errors in sample handling have occurred. If possible, fluids, medications and other factors that can contribute to or provoke hyponatraemia should be stopped. Prompt diagnostic assessment and cause-specific treatment should be started. If the acute decrease in serum sodium concentration exceeds 10 mmol/l, then a single i.v. infusion of 150 ml 3% hypertonic saline or equivalent over 20 min can be afforded to patients. Checking of the serum sodium concentration after 4 hours, using the same technique as used for the previous measurement should be applied.

(D) Chronic hyponatraemia without severe or moderately severe symptoms:

(i) General measurement: Non-essential fluids, medications and other factors that can contribute to or provoke hyponatraemia should be stopped and cause-specific treatment should be initiated. In mild hyponatraemia, treatment with the sole aim of increasing the serum sodium
concentration should not be done. In moderate or profound hyponatraemia, avoiding an increase in serum sodium concentration of >10 mmol/l during the first 24 hours and >8 mmol/l during every 24 hours thereafter. In moderate or profound hyponatraemia, checking the serum sodium concentration every 6 hours until the serum sodium concentration has stabilized under stable treatment.

(ii) Patients with expanded extracellular fluid: Treatment with the sole aim of increasing the serum sodium concentration in mild or moderate hyponatraemia should be avoided. Fluid restriction should be the main aim and use of vasopressin antagonist and demeclocyclin is not useful.

(iii) Patients with SIAD: In moderate or profound hyponatraemia, restricting fluid intake is the first-line treatment. In moderate or profound hyponatraemia, the following can be considered equal second-line treatments: increasing solute intake with 0.25–0.50 g/kg per day of urea or a combination of low-dose loop diuretics and oral sodium chloride. Lithium or demeclocycline and vasopressin antagonist should be avoided.

(iv) Patients with reduced circulating volume: Restoring extracellular volume with i.v. infusion of 0.9% saline or a balanced crystalloid solution at 0.5–1.0 ml/kg per hour is the aim. Patients with haemodynamic instability should be managed in an environment where close biochemical and clinical monitoring can be provided preferably ICU setting. In case of haemodynamic instability, the need for rapid fluid resuscitation overrides the risk of an overly rapid increase in serum sodium concentration.

(E) **What to do if hyponatraemia is corrected too rapidly?** Prompt intervention for re-lowering the serum sodium concentration if it increases >10 mmol/l during the first 24 hours or >8 mmol/l in any 24 hours thereafter and discontinuing the ongoing active treatment. It is appropriate to start an infusion of 10 ml/kg body weight of electrolyte-free water (e.g. glucose solutions) over 1 h under strict monitoring of urine output and fluid balance. It is appropriate to add i.v. desmopressin 2 µg, with the understanding that this should not be repeated more frequently than every 8 hours.

**REFERENCES:**

Type 1 Hereditary Methemoglobinemia...
Relatively Rare But Treatable Condition

D Das*

Abstract
Methemoglobinemia is a disorder characterized by the presence of a higher than normal level of methemoglobin in the blood. Acquired methemoglobinemia is relatively more common than that of hereditary one. Type 1 hereditary methemoglobinemia is relatively benign condition but very uncommon and ascorbic acid supplementation is sufficient to treat it. In view of this the following case of type 1 hereditary methemoglobinemia has been presented.

Keywords : Methemoglobin, Ascorbic acid.

INTRODUCTION :
Methemoglobinemia (or methaemoglobinaemia) is a disorder characterized by the presence of a higher than normal level of methemoglobin (metHb, i.e., ferric [Fe³⁺] rather than ferrous [Fe²⁺] haemoglobin) in the blood. Methemoglobin is a form of hemoglobin that contains ferric [Fe³⁺] iron and has a decreased ability to bind oxygen. However, the ferrous iron has an increased affinity for bound oxygen.¹

With methemoglobinemia, the hemoglobin can carry oxygen but is unable to release it effectively to body tissues.

Alternative Names
Hemoglobin M disease; Erythrocyte reductase deficiency; Generalized reductase deficiency

Causes² :
This condition can be passed down through families (inherited or congenital) or it is caused by exposure to certain drugs, chemicals or foods (acquired). There are two forms of inherited methemoglobinemia. The first form is passed on by both parents. The parents usually do not have the condition themselves, but they carry the gene that causes the condition. It occurs when there is a problem with an enzyme called cytochrome b5 reductase.

There are two types of this form of methemoglobinemia:
• Type 1 (also called erythrocyte reductase deficiency) occurs when red blood cells lack the enzyme.
• Type 2 (also called generalized reductase deficiency) occurs when the enzyme doesn’t work anywhere in the body.

The second form of inherited methemoglobinemia is called hemoglobin M disease. It is caused by defects in the hemoglobin protein itself. Only one parent needs to pass on the abnormal gene for the child to inherit the disease.

Acquired methemoglobinemia is more common than the inherited forms. It occurs in some people after they are exposed to certain chemicals and drugs, including:
• Anesthetics such as benzocaine
• Benzene
• Certain antibiotics (including dapsone and chloroquine)
• Nitrites (used as additives to prevent meat from spoiling)

The condition may also occur in infants who are very ill or who are fed too many vegetables containing nitrates (such as beets).

As the incidence of congenital methemoglobinemia is very less the following case has been reported who
presented with features of congenital type 1 methemoglobinemia. Informed written consent has been taken from the parent of the patient for its publication.

CASE HISTORY:
Md HA Borbhuiya, a 18 year boy presented with H/O bluish coloration of whole body including lips and tongue for last 5 years. It was gradual in onset and progressive in nature without associated difficulty in breathing, exertional dyspnea, nocturnal cough, history suggestive of PND, cough, fever, swelling feet with uneventful birth history with near normal childhood history without any H/O squatting, repeated respiratory tract infection in his childhood with normal playing habits in his early childhood. His school activities and daily life activities are average. His bowel and micturition habit is normal. He takes normal non-veg diet as other family members. No significant drug history like anti asthmatics, nitrate etc could be elicited.

He lives with his parents and 2 brothers and all are enjoying good health without similar history in other family members. He is from poor socio-economic strata, takes water from well with normal vaccination history.

On examination only finding was central cyanosis which was unresponsive to oxygen inhalation therapy.

Other examination findings like pulse, blood pressure, pallor, JVP, neck glands and other lymph nodes were normal without edema, clubbing.

His systemic examination findings were also normal including CVS, Respiratory system, Nervous system including higher motor functions like speech, memory, intelligence.

Based on the history and findings of examination a provisional diagnosis of Methemoglobinemia/ Sulphhemoglobinemia was made with a very rare possibility of congenital heart disease with right to left shunt. On examination his Hb- 18gm%, TC- 8000/mm³, PLT count-1.5 Lac/mm³, ESR-4 mm AEFH, DLC- normal, O₂ saturation – 85%, CXR PA view, ECG, Echocardiography, X Ray PNS, USG Abdomen were found to be normal.

The colour of the blood was chocolate red and was sent for Hb Photospectrometry to look for presence of Methemoglobin level and it was found to be very high—12.3 gm%.

Ultimately his diagnosis was made as Methemoglobinemia. As the patient was not much symptomatic other than the presence of cyanosis even in the presence of 68.3% of methemoglobin, he was diagnosed to be a case of congenital type 1 methemoglobinemia and he was treated with Ascorbic acid supplementation. His cyanosis disappeared within 2 days and he is presently doing well without use of Methylene blue.

DISCUSSION:
Methemoglobinemia is a disorder in which the hemoglobin molecule is functionally altered, hampering the dissociation of oxygen from Hb to the tissues. A variety of etiologies including genetic, dietary, idiopathic and toxicological sources may cause methemoglobinemia. Symptoms vary from mild headache to coma or death, and may not correlate with measured methemoglobin concentrations. Patients with methemoglobinemia appear deeply cyanotic, but are unresponsive to standard oxygen therapy. It is essential for the clinician to recognize the problem rapidly in patients without hypoxia by analysing their arterial blood gas. Methemoglobin interferes with the accuracy of pulse oximetry. The antidote is methylene blue.

When an infant presents severe cyanosis which is not associated with respiratory distress, methemoglobinemia should always be suspected. In children its main inducers are contaminated water or vegetable broths with high nitrate levels (especially spinach and carrots) used to prepare powdered formula or soups.

Methemoglobinemia is a condition that occurs infrequently but is potentially life threatening. The etiology may be congenital or acquired. Methemoglobin is haemoglobin in which the iron molecule is oxidized. It loses the ability to bind O₂, and the O₂ affinity for each other heme is raised, making the O₂ dissociation curve shifts to the left which results in tissue hypoxia.

Small amounts of methemoglobin are produced physiologically, but the relative proportion of the total haemoglobin is kept constant to 1% of the total haemoglobin by physiological reduction (NADH-dependent methemoglobin reductase)
Symptoms of type 1 methemoglobinemia (erythrocyte reductase deficiency) include:

- Bluish coloring of the skin

Symptoms of type 2 methemoglobinemia (generalized reductase deficiency) include:

- Developmental delay
- Failure to thrive
- Intellectual disability
- Seizures

Symptoms of hemoglobin M disease include:

- Bluish coloring of the skin

Symptoms of acquired methemoglobinemia include:

- Bluish coloring of the skin
- Headache
- Fatigue
- Shortness of breath
- Lack of energy
- Signs and symptoms of methemoglobinemia (methemoglobin level above 1%) include shortness of breath, cyanosis, mental status changes (~50%), headache, fatigue, exercise intolerance, dizziness and loss of hairlines.
- Patients with severe methemoglobinemia (methemoglobin level above 50%) may exhibit seizures, coma and death (>70%).³ Healthy people may not have many symptoms with methemoglobin levels below 15%. However, patients with co-morbidities such as anemia, cardiovascular disease, lung disease, sepsis, or presence of other abnormal hemoglobin species (e.g. carboxyhemoglobin, sulfhemoglobin or sickle hemoglobin) may experience moderate to severe symptoms at much lower levels (as low as 5–8%).

TREATMENT:

Methylene blue is used to treat severe methemoglobinemia. Methylene blue may be dangerous in patients who have or may be at risk for a blood disease called G6PD deficiency, and should not be used. If you or your child has G6PD deficiency, always tell your health care provider before receiving treatment. Ascorbic acid may also be used to reduce the level of methemoglobin.

Alternative treatments include

- hyperbaric oxygen therapy
- exchange transfusions

In most cases of mild acquired methemoglobinemia, no treatment is needed. But we should avoid the medicine or chemical that caused the problem. Severe cases may need treatment, which may include a blood transfusion.

Outlook (Prognosis):

People with type 1 methemoglobinemia and hemoglobin M disease usually do well. Type 2 methemoglobinemia is much more serious, and usually causes death within the first few years of life. People with acquired methemoglobinemia usually do very well once the drug, food, or chemical that caused the problem is identified and avoided.

REFERENCES:

Wernicke’s Encephalopathy: A Rare Complication of Hyperemesis Gravidarum

M Das*, P Bhattacharjee**, B K Nath***, A Bharadwaj****

Abstract
Wernicke’s encephalopathy which occurs due to thiamine deficiency is common in alcoholics and is classically characterized by the symptoms of acute mental confusion, ataxia and ophthalmoplegia. Diagnosis is usually difficult at the initial stage and runs the risk of progression to korsakoff syndrome and carry a mortality rate of approximately 20% without thiamine replacement.

A case is hereby presented wherein a 20 yr old primigravida at 24 weeks of gestation who presented with acute history of mental confusion, irrelevant talking, convergent gaze, diplopia blurred vision, vomiting, bilateral weakness of lower limbs, moderate anaemia and hyponatremia. MRI scan of brain showed T2 hyperintensity in the bilateral caudate nucleus, lentiform nucleus, mamillary body and adjoining areas such as periaqueductal areas, bilateral medial thalami, vermis, tectal plates, bilateral paravermian area, showing diffusion restriction; suggestive of cytotoxic edema. A diagnosis of Wernicke's encephalopathy based on clinical and MRI findings was made and she was placed on intravenous thiamine with simultaneous correction of electrolytes. The clinical improvement was observed from 3rd day onwards and was discharged on 10th day.

Wernicke's encephalopathy due to hyperemesis gravidarum is a rare manifestation and calls for an early diagnosis, appropriate management including urgent thiamine replacement to prevent catastrophe.

Keywords: ophthalmoplegia, korsakoff, hyperintensity, Wernicke’s encephalopathy, hyperemesis gravidarum

INTRODUCTION:
Wernicke’s encephalopathy is classically characterized by a triad of symptoms: acute mental confusion, ataxia and ophthalmoplegia. It occurs due to deficiency of thiamine, which, if untreated may progress to a state known as ‘Wernicke-Korsakoff’ psychosis. Etiological factors are chronic alcoholism, prolonged starvation, hyperemesis gravidarum, bariatric surgery and HIV infection. Of these, chronic alcoholism is the commonest cause reported. Iatrogenic exacerbation of WE can occur with prolonged glucose or carbohydrate loading in setting of thiamine deficiency.

CASE REPORT:
A 20 year old lady presented to the emergency with mental confusion, irrelevant talking, convergent gaze, diplopia and blurred vision for 3 days. She was a primigravida at 6 months of pregnancy. Patient was apparently well 15 days back when she started vomiting for several episodes daily. She was treated by a local physician with some antiemetic and dextrose infusion. She recovered of her symptoms temporarily but after 2 to 3 days, she started developing weakness of bilateral lower limbs, progressively increasing with time and difficulty in walking. Then she was admitted in a private nursing home for 4 to 5 days and was discharged home after improvement of symptoms. She was well for few days after which she developed mental confusion, irrelevant talk, convergent gaze, diplopia and blurred vision and was brought to SMCH and was admitted here.

On general examination she was pale, edematous. Her BP 130/80, pulse rate 100 beats per minute and respiratory rate 18 per minute. Her GCS was 9/15 (E4V3M2), muscle tone reduced, bulk normal, DTR absent, muscle power and sensory system could not be evaluated as her GCS score was low, plantar response absent bilaterally. There was nystagmus on lateral gaze, anisocoria and neck holding was absent. Other systemic examination was within normal limit.
Her laboratory values were Hb 7.8 gm%, total WBC count 7.26×10³, total RBC count 2.99×10⁶, total platelet count 185×10⁶, Sr Na level was low 122 mg/dl, K 3.45; total protein low 4.63 g/dl with albumin 1.90 and globulin 2.73 g/dl. USG whole abdomen showed single live intrauterine gestation at 24(+-) 3 weeks of pregnancy. Rest of her routine tests were within normal limit including ECG and X-ray chest.

Electrolytes were corrected within 48 hours of admission. Her symptoms were suggesting towards Wernicke’s encephalopathy and MRI brain was done on day 3 after hospitalization. It showed T2 FLAIR hyperintensity of bilateral caudate nucleus, part of bilateral lentiform nucleus, bilateral mamillary body, periaqueductal area, bilateral medial thalami, vermis, tectal plates, bilateral paravermian area, showing diffusion restriction; suggestive of cytotoxic edema.

The findings were also consistent with diagnosis of Wernicke’s encephalopathy. Thiamine level could not be estimated as it is not done in the hospital and also too costly outside. She was started on intravenous thiamine, 100 mg/day in 500 ml 5% plain dextrose as infusion over 5 hours for 3 days then continued at a dose of 100mg weekly IM for 1 month and 100mg IM monthly thereafter.

Her symptoms improved gradually over next 3 to 4 days. Neurological examination after 3 day showed GCS 15/15, power 2/5 bilateral lower limbs and 3/5 bilateral upper limbs, sensory intact, planter response absent bilaterally and rest of the findings were normal. Lateral gaze nystagmus persisted and neck holding was negative.

She was followed up in next week and showed persistent improvement of symptoms. Power improved gradually over next month and neck holding was also positive on subsequent check up and the nystagmus disappeared.

DISCUSSION:

Wernicke’s encephalopathy is a metabolic disorder due to Thiamine deficiency, first described by Carl Wernicke’s in 1881. He first reported a trio of symptoms consisting of drowsiness, ophtalmoplegia and ataxia. On autopsy, he detected punctuate haemorrhages affecting the grey matter around the third and fourth ventricles and aqueduct of Sylvius, and designated the term “polioencephalitis hemorrhagica superioris”.1

In 1997, Caine et al. proposed an operational criterion for the recognition and diagnosis of Wernicke’s encephalopathy accordingly; Wernicke’s encephalopathy is recognized if there are two of the following four signs; (i) dietary deficiencies, (ii) oculomotor abnormalities, (iii) cerebellar dysfunction, and (iv) either an altered mental state or mild memory impairment.2

Wernicke’s encephalopathy commonly develops in alcoholics as a result of thiamine deficiency, although it remains largely underdiagnosed in this group. Typical brain lesions are observed in 0.8-2% of unselected autopsies of alcoholics, but only 1-20% of these lesions are diagnosed clinically.3 Diagnosis of the disease is sometimes difficult because of non-specific initial symptoms such as headache, abdominal discomfort and fatigue; furthermore, the classic triad of symptoms are observed only in about 16% of patients.4 Without thiamine treatment, the disease incurs 17-20% mortality and progresses to Korsakoff’s syndrome with memory impairment in 80% of cases.5

Successful treatment or prophylaxis of Wernicke’s encephalopathy depends on a number of related issues.
and is not simply a matter of supplementing thiamine. While thiamine replacement is important for the treatment and prophylaxis of Wernicke’s encephalopathy, an effective dosing template has not yet been established.7

Although most cases of Wernicke’s encephalopathy today are related to chronic alcoholism, it is vital to recognise other rare causes of this condition, such as systemic diseases (malignancy, disseminated tuberculosis, AIDS); starvation (anorexia nervosa, prisoners of war, schizophrenia, terminally ill cancer patients); iatrogenic (refeeding after starvation, chronic haemodialysis) and persistent emesis such as hyperemesis gravidarum. The prevalence of Wernicke’s encephalopathy in a non-alcoholic patient varies from 0.04% to 0.13%.8 Wernicke’s encephalopathy in a patient with hyperemesis gravidarum was first described by Sheehan in 1939.9 To our knowledge, only 49 cases of Wernicke’s encephalopathy during pregnancy have so far been reported in the literature.10

The mechanism by which thiamine deficiency causes the focal neuropathology lesions found in Wernicke’s encephalopathy might be multiple.11 Thiamine is an important co-enzyme for three critical enzymes in the Kreb’s and pentose phosphate cycle: transketolase, ketoglutarate dehydrogenase, and pyruvate dehydrogenase complex. Deficiency of thiamine and hence deficiency of these enzymes result in focal lactic acidosis, cerebral energy impairment, depolarization of neurons due to n-methyl-D-aspartate receptor mediated excitotoxicity. Ultimately, it results in alteration of blood brain barrier, generation of free radical, prompting cell death by necrosis and apoptosis.11

The body has approximately 18 days of thiamine storage. It is well understood that thiamine requirements are increased during pregnancy, and even more by the impaired absorption due to hyperemesis gravidarum.12 Thiamine dependence is also increased in conditions with high metabolic rates and high glucose intake, and therefore its depletion due to reduced intake as well as IV dextrose administration results in thiamine deficiency and Wernicke’s Encephalopathy.13,14

Wernicke’s encephalopathy is a potentially treatable condition if diagnosed early. If untreated it may lead to even irreversible and persistent neurological sequelae or death. Therefore a high index of clinical suspicion must be maintained for thiamine deficiency in high risk patients.

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An Uncommon Presentation in Sjogren’s Syndrome

U Islam*, N Goswami**, S Bharadwaj***

KEYWORDS: Sjogren’s Syndrome, Vasculitis, Gangrene.

INTRODUCTION:
Sjögren’s syndrome is a systemic autoimmune disease with a predominant involvement of exocrine glands leading to sicca symptoms. Extraglandular involvement occurs in about 40% of patients with skin, musculoskeletal, neurological and organ manifestations.1 Systemic vasculitic manifestations of Sjögren’s syndrome can be assumed in approximately 5%-10% of patients. Leukocytoclastic or cryoglobulinic vasculitis represent classic vasculitic manifestations of Sjögren’s syndrome. Necrotizing vasculitis of medium-sized vessels resembling polyarteritis nodosa can occur in Sjögren’s syndrome patients.2 In the pathogenesis of vasculitis, B-cell-driven autoimmune processes play a major role by producing autoantibodies against the Ro/SS-A and La/SS-B antigens and cryoglobulins. We report here a case with Sjögren’s syndrome and gangrene of right distal lower limb and review the relevant literature.

CASE REPORT:
A 20 year lady was referred to Gauhati Medical College & Hospital casualty due to severe pain over both distal lower limbs with high grade fever for last one week. On admission, she had mild pallor, was tachypnoeic with a blood pressure of 116/86 mm Hg and temperature of 102°F. On local examination of both lower limbs tenderness with discolouration of digits were noted in right lower limb. Distal pulses were not felt in both lower limbs, however, upper limb pulses were normally felt. She also gave history of dryness of mouth and eyes. Rest of the examination was normal. Colour Duplex Doppler study of both lower limbs revealed absent flow in the right dorsalis pedis artery with monophasic flow in the left anterior tibial artery. Serum ANA was positive along with a weak positive SS-A.

DISCUSSION:
Primary Sjogren’s syndrome (pSS) is an autoimmune chronic inflammatory disorder affecting 0.2% to 3% of the population, with a 9:1 female to male ratio. Features are oral and ocular dryness, local and systemic autoantibody production, and progressive focal mononuclear cell infiltration in the affected salivary and lacrimal glands. Lymphoma is the most severe complication of pSS, occurring in 4% to 5% of patients. Genetic studies have identified an association with HLA and susceptibility genes in cytokine genes and genes involved in B cell differentiation. Genetic variations may help explain why...
Disease manifestations differ among patients and supports the hypothesis of certain distinct disease phenotypes.

Among the extra glandular manifestations reported in Sjogren’s syndrome, one of the more significant in terms of outcome is vasculitis. The prevalence of vasculitis in pSS has been reported to be between 5% to 10%. The precise cause of vasculitis in Sjogren’s syndrome is not entirely known; however, it is hypothesised that a B-cell driven autoimmune process produces antibody against SS-A and SS-B antigens that form circulating immune complexes that are not properly cleared. In addition there seems to be an immunogenetic basis to SS-A and SS-B production and immune complex clearance efficiency.

In the early 1980s, Alexander and Provost and colleagues reported a study of 22 patients with pSS with a documented skin rash. After a skin biopsy 19 were found to have cutaneous vasculitis with 14 of them being classified as leucocytoclastic vasculitis. In a larger study looking at 558 patients with pSS, 52 had a form of cutaneous vasculitis. Patients with cutaneous vasculitis had more severe disease and more extra glandular manifestations than those without. The lower extremities were the most common areas affected by leucocytoclastic vasculitis in pSS.

Systemic vasculitis occurring in pSS has been described in several case reports and involves medium and small sized arteries. Acute necrotizing vasculitis in pSS is described as having a similar clinical presentation to polyarteritis nodosa but lacking the typical aneurismal formation. A more severe course of Sjogren’s was associated with acute necrotizing vasculitis compared with the course of Sjogren’s seen in other types of vasculitis. Endarteritis obliterans, which is characterized as a non-inflammatory obstructive vasculitis involving the medium sized vessels was also seen in a majority of cases and was believed to represent a healed pre-existing vasculitis.

Vasculitis does not seem to be as frequent as some of the other EGMs of pSS. However, vasculitis should be sought when evaluating a patient with pSS because its consequences can be very severe. In the study by Tsokos and colleagues, one patient died from gallbladder perforation secondary to necrotising vasculitis despite treatment.

CONCLUSION:

Vasculitis in Sjogren’s syndrome more commonly can result in neurological deficit, chronic cutaneous ulcerations, and seems to confer risk of Non-Hodgkin’s lymphoma. Complete evaluation should always be performed while evaluating patients with pSS because although rash is the most common presentation of vasculitis in Sjogren’s syndrome, it may not always be present when internal organ involvement occurs.

REFERENCES:
Case Report

Gitelman Syndrome

P Roy*, D Das**, M Sharma***, U Joshi****

Abstract

Gitelman syndrome is a rare autosomal recessive renal tubular disorder characterized by hypokalemic metabolic alkalosis with hypocalciuria and hypomagnesemia. We report a case of 55 yr old male patient presented with generalized weakness, fatigue. Clinical and laboratory evaluation helped in making a diagnosis of Gitelman syndrome.

KEY WORDS : Hypokalemia, Hypocalciuria, Metabolic alkalosis, Gitelman syndrome.

INTRODUCTION:

Gitelman syndrome is an autosomal recessive salt losing renal tubulopathy that is characterized by hypokalemia and metabolic alkalosis due to secondary hyperaldosteronism; hypomagnesemia and hypocalciuria.1,3 It is caused by mutations in the solute carrier family 12, member 3, SLC12A3 gene, which encodes the renal thiazide sensitive sodium-chloride co-transporter (NCCT) that is expressed in apical membrane of cells in the first part of distal convoluted tubule.2

Gitelman syndrome patients usually present above six years of age and in many cases diagnosis is only made at adult age. Patients may present with muscle weakness, tiredness, fatigue, paraesthesia in face and sometimes even with tetany.3 Laboratory findings are characterized by hypokalemia, metabolic alkalosis, hypocalciuria, hypomagnesemia with normal renal function.

CASE REPORT:

A 55 yr old male patient was admitted in the medicine ward with complaint of generalized weakness and fatigue for a duration of one week. There was no history of fever, cough, diarrhea, vomiting or breathlessness. No history of diuretic or laxative abuse. No history of drug ingestion. There was no history of exacerbation of weakness by exertion or after heavy carbohydrate meal. No similar history in the past or in siblings.

On examination he was conscious, well oriented. Pulse rate was 82/min, regular. BP was 130/80, respiratory rate 16/min. and was well hydrated.

Neurological examination revealed normal higher function and normal cranial nerves. There was no neurological deficit. Other systemic examination was unremarkable.

Laboratory values were: TC – 6100/mm³(4000-11000/mm³), Hb – 12 gm%, platelet – 210000/mm³(150000-400000/mm³). S. sodium – 127mEq/L(135-145mEq/L), S. potassium – 2.0mEq/L(3.5-5.0mEq/L), S. calcium – 7.3mg/dl(8.4-10.2mg/dl), s. magnesium – 1.2mEq/L(1.5-2.0mml/L), s. chloride -97 mEq/L(95-105mEq/L). S. creatinine – 0.6 mg/dl(0.6-1.2mg/dl), s. uric acid – 3.5mg/dl, RBS 88mg/dl, s. TSH – 0.615 (0.5-5.0microU/ml). S.cortisol – 16.2 (5-25microg/ml)

Plasma aldosterone – 280 (42-200pmol/L), Plasma renin – 13.8 (0.2-2.8nmol/L/h), Arterial pH 7.59, pCO2-58.3mmHg, HCO3- 37.4mmol/L. Urine calcium – 1.4mmol/24hr(2.5-7.5), Urine chloride – 133mmol/24hr (110-250), Urine sodium – 18 mmol/L(40-120), Urine potassium – 24mmol/L (25-125), Urine creatinine – 612mg/day (500-2000).

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ECG showed PR prolongation, T wave inversion and presence of U wave. Chest X ray and abdominal ultrasound were normal. The biochemical picture of normal renal function, hypokalemia, hypomagnesemia and metabolic alkalosis was suggestive of Gitelman syndrome. Cytogenetical examination was not carried out due to technical reasons.

Patient was placed on oral and parenteral potassium and magnesium supplementation. Potassium level began to rise within 48 hours and patient’s weakness improved within 2 to 3 days of admission. Patient was discharged with spironolactone 50mg daily and oral potassium supplementation.

Unfortunately patient did not turn up for next visits, so, follow up could not be done.

DISCUSSION:

Once vomiting, diuretic and laxative abuse are excluded from the differential diagnosis of a non-hypertensive patient presenting with hypokalemia, rare conditions such as renal tubular acidosis, Bartter’s syndrome or Gitelman’s syndrome need to be considered.4

In Gitelman syndrome, mutations have been found in the thiazide sensitive NaCl transporter.2 The reduced sodium reabsorption in DCT lead to volume depletion and hypokalemia. Hypocalciuria occurs due to loss of activity of thiazide sensitive transporter which increases tubular reabsorption1. This disease is sometimes diagnosed in almost asymptomatic adults who have hypokalemia and unexplained transient periods of weakness, tetany, abdominal pain, vomiting and fever1. In our patient diagnosis of Gitelman syndrome was based on clinical findings and laboratory investigations like hypokalemia, hypocaliuria, hypomagnesemia and metabolic alkalosis. In some cases this syndrome is found by chance because of measurement of serum electrolytes for other reason.

The diagnosis of Gitelman syndrome is made on the basis of clinical, biochemical and molecular findings. Disease free intervals may be prolonged resulting in delay of diagnosis until adulthood.5 6 The tubular defect in Gitelman syndrome itself cannot be corrected so that adequate supplementation of magnesium and potassium remains the cornerstone of treatment in addition to potassium sparing diuretics.

CONCLUSION:

In general the long term prognosis of Gitelman syndrome is excellent and progression to end stage renal disease is however rare. Lifelong supplementation of potassium and magnesium is mandatory and high sodium diet is encouraged. Cardiac workup should be done to screen for risk factors of cardiac arrhythmias.

REFERENCES:

Purpura Fulminans

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**KEYWORDS:** Purpura fulminans, Sepsis, DIC.

**INTRODUCTION:**

Purpura fulminans is a rare syndrome of rapidly progressive hemorrhagic infarction of skin that is accompanied by vascular collapse and DIC. It usually occurs in children but has been noted in adults also. Purpura fulminans is seen in three clinical settings – (1) In the newborn period as a manifestation of homozygous protein C deficiency or rarely protein S deficiency or deficiency of antithrombin III. (2) Idiopathic purpura fulminans usually follows an initiating febrile illness that manifest with rapidly progressive purpura. (3) Acute infectious purpura fulminans most commonly follows a viral/bacterial illness involving the skin. It is commonly associated with meningococcemia/invasive streptococcal disease. Here, we are reporting a rare case where the offending organism resulting in purpura fulminans is Klebsiella pneumoniae. This syndrome is associated with >50% mortality secondary to multiorgan dysfunction syndrome (MODS) and is accompanied by long term morbidity. Early antibiotic administration and intensive care management of severe sepsis and shock is essential.

**CASE:**

A 40 year old female was admitted in AMCH on 04.11.14 with chief complaints of high grade intermittent fever with chills along with blackish discoloration of skin around the lower abdomen and upper parts of both thighs and buttocks for 3 days. There was associated colicky type of abdominal pain along with multiple episodes of vomiting. There was no history of sore throat, gum bleeding or vaginal bleeding.

Physical examination at admission revealed high fever with temperature 102°F and shock. Pallor was present, icterus absent, with no lymphadenopathy. Throat examination was normal. Palatal erythema was present. Hyperpigmented patches with erythematous margins with blister formation were seen over the lower abdomen, buttocks and upper parts of both thighs. Chest examination was normal, Cardiovascular system appeared normal except for sinus tachycardia, CNS – Normal. Per-abdominal examination revealed diffuse tenderness over...
lower abdomen but no organomegaly. Fundus examination was normal.

Laboratory findings were Hb-7.8 gm%, TLC-14,600, DLC – N$_{80}$, L$_{17}$, E$_{2}$, M$_{1}$, Platelet – 45000, BT-2 min 15 sec, CT–8 min, Urea – 67 mg%, Creatinine– 2 mg%, Albumin – 1.7 gm%, Globulin – 2.5 gm%, T- Bil-2.9 mg%, ALP – 281 mg%, Blood Culture – Sterile, Urine R/E- Pus Cells 5–8/hpf; Wound Swab C/S – *Klebsiella pneumoniae* sensitive to Imipenem, Piperacillin–Tazobactum, Ceftazidime, ASO < 200 U/ml. The coagulation profile showed prolonged PT with a PTT near normal range. FDP > 20 µg/ml (Normal value <5 µg/ml). Protein C was 72% (Normal range: 70-140%).

After admission, she was started treatment with intravenous fluids, inotrope and on day 3 of admission her vitals became stable. Initially she was started on Injection Ceftriaxone and Infusion Linezolid but when wound swab C/S report came it was changed to Injection Imipenem. She received 2 units of whole blood and 3 units of FFP along with low doses of corticosteroids. Gradually her skin lesions improved and she was discharged after 21 days. At present she is enjoying good health.

**DISCUSSION**:

Purpura fulminans is an acute often lethal syndrome characterized by DIC. It starts as well demarcated erythematous macules that progress rapidly with hemorrhagic necrosis resulting in dark raised lesion with vesicle or bulla formation. Most cases of acute infectious purpura fulminans are associated with meningococcal sepsis. The other organisms which have been reported to cause it are *Streptococcus pneumoniae*, *H.Influenzae* type B, *Gr B Streptococcus*, *Streptococcus pyogenes*, *Rickettsiae*, *Proteus* sp and *E. coli*. Besides this Purpura fulminans due to *Klebsiella pneumoniae* has been reported lately. Approximately 60-70% of Purpura fulminans have been reported among children below 2 yrs of age but our case was 40 years old.

Early recognition of Purpura fulminans and immediate initiation of therapy can decrease the fatality rate and possibly prevent necessity of surgical intervention. Administration of heparin together with large volumes of FFP is effective in halting the progression of the disease. The antibiotic should be administered early in the course of disease. Adjunctive therapies are activated protein C, anti-thrombin III, plasma exchange, tissue plasminogen activator, topical nitroglycerin, prostacyclin and hyperbaric oxygen.

**CONCLUSION**:

Purpura fulminans is a potentially life threatening and disabling disorder characterized by acute onset of progressive cutaneous hemorrhage and necrosis with DIC. It is important to recognize this uncommon cutaneous manifestation of severe sepsis early and institute aggressive management as it is associated with higher mortality.

**REFERENCES**:

Tracheobronchopathia Osteochondroplastica

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Abstract

Tracheobronchopathia Osteochondroplastica (TPO) is a rare disorder of airway lining cartilage. Reported 1 in 400 to 1 in 6000 from various studies. TPO is characterized by abnormal growth of cartilage from the tracheal and bronchial wall lining cartilage rings. Patient may remain asymptomatic or present with complains of cough, haemoptysis, chest pain etc. diagnosis is made by bronchoscopy where we can see abnormal over growth of cartilages into the airway lumen. We are presenting a case of TPO reported for the first time in Assam.

CASE REPORT:

A 55 year old male patient presented with history of chest pain from 27 years, recurrent cough for 15 years and haemoptysis for last 1 year. The history of haemoptysis was intermittent, every 3-4 months, small in amount, lasted for few days and there was no history of bleeding from any other site. The patient gives a history of cough for the last 15 years with minimal sputum production, no postural, seasonal and diurnal variation, no aggravating and relieving factors. The history of chest pain was intermittent, located on the left side of chest, with no aggravating and relieving factors, no radiation to any other site, with no history of palpitation or dizziness. There was no history of fever, shortness of breath and wheezing. Patient does not give history of smoking or taking alcohol. General physical examination was normal with pulse 100/min, BP 120/80, respiratory rate was 20/min, afebrile. Respiratory system examination was normal. Cardiovascular system examination showed a murmur in pulmonary area suggestive of pulmonary stenosis. Abdominal and central nervous system examination was normal. Investigation showed TC 7,000, Hb 13gm/dl, RBS 110 mg/ml, serum cholesterol 156mg/ml, TG 109 mg/ml. Chest X ray posterior-anterior view showed features within normal limits (figure1). Echocardiography showed mild pulmonary stenosis and mild mitral stenosis. On further investigation CT thorax was done which showed tracheal calcification (figure 2-5).

Fig 1: normal chest x-ray PA view
Fig 2: beaded calcification of trachea and both bronchus
Fig 3: virtual endoscopy showing irregular tracheal wall
Fig 4: CT thorax showing normal lung parenchyma
In view of radiological finding fiberoptic bronchoscopy was done which showed irregular tracheal cartilage and smooth calcified projection into the tracheal lumen with sparing of non cartilagenous part of trachea. Similar findings were noted in both main stem bronchus (figure 6-9). This makes obvious diagnosis of tracheobronchopathia Osteochondroplastica (TPO).

REVIEW OF LITERATURE:

Tracheobronchopathia Osteochondroplastica (TPO) is a benign disorder of the large airways. The exact prevalence of TPO is not known. There is wide variation in prevalence reported in autopsy and bronchoscopic studies. In autopsy studies TPO was reported from 1 in 400 cases to 3 in 1000\(^1\text{-}^2\). TPO was reported during bronchoscopic examination from 4 of 550 to 1 of 6000 bronchoscopic examinations\(^3\text{-}^5\). Most of the time patient remains asymptomatic. Till date 400 cases have been reported worldwide\(^6\text{-}^7\). We have found 1 case out of 500 bronchoscopies in last four years. The common clinical symptoms are non-specific and may include chronic cough, dyspnoea, hemoptysis, wheezing and recurrent respiratory infections. Symptoms are due to the narrowing of airways as a result of confluent submucosal nodules and loss of normal ciliated respiratory epithelium. It has been hypothesized that the cough results from combination of factors, including turbulent airflow, increased airway sensitivity, and impaired ciliary clearance. TPO is usually a benign disorder however Hussain et al reported significant disease progression in about 17% of cases\(^7\). In case of TPO, CT scan demonstrates a characteristic pattern of calcified nodules arising from the anterior and lateral aspect of the inner tracheal wall protruding into lumen, in severe form resulting in luminal narrowing with sparing of membranous part of trachea and large airways\(^9\text{-}^{11}\). Other causes of trachea calcification includes relapsing polychondritis, tracheobronchial amyloidosis, Wegner’s granulomatosis and normal age related calcification\(^10\text{-}^{11}\).

Although these lesions may extend anywhere from the larynx to the peripheral bronchi, they are more commonly seen in distal two third of trachea and proximal bronchi. Since these nodules arise from cartilage, therefore posterior membranous wall of trachea is typically spared. This distinguishes TPO from many other airway diseases such as tracheobronchial amyloidosis, Wegener’s granulomatosis etc where membranous part of trachea is
involved. Bronchoscopy is the most definitive diagnostic test for TPO and is characterized by the multiple, varied size smooth whitish nodules which are hard on touch and gives gritty sensation while passing the scope through the lumen\textsuperscript{11}. Biopsy can be done but is often not necessary due to definitive bronchoscopic finding\textsuperscript{7}. There is no definitive treatment for TPO available therefore symptomatic management is required\textsuperscript{6,7,8}. Symptomatic management includes maintaining airway humidity, reduction of airway irritation and treatment of respiratory infections. Those cases in which disease progresses and presents with severe airway stenosis, various bronchoscopic interventions have been used including removal of nodules by forceps, laser ablation, cryotherapy and external beam irradiation\textsuperscript{6,8}.

REFERENCES:
Short Case

Bilateral Thalamic Infarct – a Rare Stroke


Abstract
A rare presentation of stroke is bilateral thalamic infarcts. These were reported for the first time more than 100 years ago and only 11% of all vertebrobasilar infarcts are described as bilateral thalamic infarct. In 1973 Frenchman, G Percheron described artery of Percheron (AOP) and it is named after his name. It is a rare anatomic variation in the brain vascularisation and a single arterial trunk arising from the posterior cerebral artery (PCA). It supplies both sides of the thalamus and midbrain. AOP territory infarct is rare, on account of the relative rarity of the AOP and presents with a variety of signs and symptoms collectively termed the paramedian thalamic syndrome. The paramedian arteries usually arise from the first segment of PCAs (p1 segment) on both sides. The paramedian thalamic territories is the median part of the thalamus including the intralaminar nuclei and most of the dorsomedian nucleus. Midbrain infarcts may result after occlusion of the artery of Percheron and they are usually limited to periaqueductal gray matter and affect the oculomotor and reticular nuclei. To date, the diagnosis of AOP infarction has been uncommon and due to diverse etiology, it is important to distinguish this entity.

KEY WORDS: artery of Percheron, Stroke

CASE:
A 60 year right handed male patient, from Assam with history of smoking and ethanol intake took medical consultations one year back for upper gastrointestinal bleed and was subsequently diagnosed as adenocarcinoma of stomach and completed chemotherapy. Six months later, he presented in neurology clinic with sudden loss of consciousness, confusion and difficulty in speech. There was no clinical history suggestive of seizures, focal neurological deficit, diplopia, loss of vision, dysphagia, nasal regurgitation or nasal intonation of voice. There was no history of binge alcohol intake, decreased oral intake. General physical examination revealed bradycardia with pulse rate of 55/min, irregular with blood pressure of 90/60 mm Hg with anaemia. Neurological examination revealed patient confused with glass glow coma scale of E2V1M5, dysarthria, absent vertical eye movement with no motor deficit and both plantar up going. Clinical diagnosis of brain stem stroke was suspected and patient was admitted and investigated keeping in view the cardiac status with clinical evidence of bradycardia and low blood pressure. Routine blood parameters showed normal total leucocytes counts with high erythrocyte sedimentation rate of 78 mm after end of first hour and haemoglobin of 7.8 gm%, with normal iron profile. His biochemistry profile including renal function, liver function test, serum fasting blood sugar, fasting lipid profile, fasting thyroid profile were normal. Repeat upper Gastrointestinal Endoscopy revealed healed Ulcer. His cardiac evaluation including electrocardiogram showed bradycardia with irregular heart rate, echocardiography was normal and Holter monitoring was done suggestive of atrial fibrillation. Initial computerized tomography (CT) scan Brain showed hypodensities in left thalamus and subsequently his Magnetic resonance imaging (MRI) brain with Magnetic Resonance Angiography (MRA) revealed bilateral paramedian and midbrain infarct suggestive of Artery of Percheron Infarct and white matter ischemic changes and contrast was done to rule out metastasis. Colour Doppler neck vessel reveals normal study.
DISCUSSION:

The thalamus has integrated several important cortical functions as it contain strategic nuclei. In 60% of humans, the posterior communicating artery contributed. Percheron described possible variations by a well-characterised artery, the polar artery involving the paramedian thalamic-mesencephalic arterial supply. Our patient demonstrated infarcts in bilateral paramedian thalamus as well as parts of midbrain consistent with occlusion of the artery of Percheron. It may be due to cardiac embolism as a result of atrial fibrillation. In bilateral medial thalamic and rostral midbrain infarctions with a relative symmetrical distribution, occlusion of the artery of Percheron should be suspected. Because of this Infarction it may result in complex clinical syndromes, with patients manifesting varying symptoms and signs. It can range from motor deficits to behavioural and sensory alterations. The four main symptoms found in literature are vertical gaze palsy (65%), memory impairment (58%), confusion (53%), and coma (42%). Our patient presented with loss of consciousness, confusion and vertical gaze over his course of illness. The changes in mental status may be due to involvement of reticular activating system and the interruption of connections between the thalamus and parts of the prefrontal cortex involved in behavioural control. Vertical gaze palsy is due to disruption of the cortical input that traverses the thalamus to reach the rostral interstitial medial longitudinal fasciculus. Similar cases of bilateral paramedian thalamic infarction with clinical and MRI findings suggestive of artery of Percheron occlusion have been reported. Cassourret et al reported a case of occlusion of the artery of Percheron, comatose at presentation, with normal early imaging by CT Brain and MRI. A new head CT two days later revealed a bilateral paramedian thalamic infarct at the origin of the initial symptoms. Matheus and Castillo reported 3 cases with typical symmetric thalamic and mesencephalic lesions on MR imaging with distribution conforming to the occlusion of the artery of Percheron. Successful artery of Percheron in situ thrombolysis using tissue plasminogen activator in an angiographically diagnosed patient has been reported.

In the case reported here, conventional MR imaging and the diffusion-weighted imaging confirmed the presence of infarction in paramedian thalamic and midbrain region typically seen in occlusion of the artery of Percheron. These infarcts should be recognized as due to occlusion of a possible single rare artery that is a normal anatomic variant showing its peculiar supply and not to be blamed on occlusion of multiple vascular territories or other pathologic conditions such vasculitis or infectious disease. When bilateral paramedian thalamic infarcts with or without associated mesencephalic involvement are found, occlusion of the artery of Percheron should be considered as the foremost differential diagnosis. Because of the small size of the artery and its highly variable origin and course, lack of visualization of the artery does not exclude
its presence, however interventional explorations focused on potential treatment of occlusion of the artery of Percheron may be encouraged.\textsuperscript{12}

**CONCLUSION:**

In cases of bilateral paramedian thalamic infarction the possibility of artery of Percheron infarction should be considered. In artery of Percheron infarction, there can be additional involvement of periaqueductal grey matter of the midbrain. Signs and symptoms may vary from loss of consciousness, memory impairment, vertical gaze palsy and behavioural disturbances. Possibility of cardio embolism should always be kept in the etiological differentials of stroke.

**REFERENCES:**


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**The Review Process for Articles in ASSAM JOURNAL OF INTERNAL MEDICINE**

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