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Author's Instructions

The manuscript must have separate documents

1. **Cover letter.**
2. Main document should contain abstract and original Research Article/ Review Article/ Case report / Letter to editor.
3. Figure /Tables /Graph /Flow charts.

1. Cover Letter

A cover letter is a letter addressed to the Editor-in-Chief of the Journal of The Research Society of SKNMC stating why the article should be considered for publication. It should include source of funding and conflict of interest.

Main document should include Abstract & the research article

Abstract :

An abstract is a brief summary of a research article, A well written abstract is informative and completely self-explanatory. Abstract for original research article has to be structured and should be divided into the following section.(Objectives, Methods, Results and Conclusions)The abstract for Review article and case report may be unstructured and should not exceed 250 words.

2. Main document.

Its contents vary with the type of Article.

Original Research Articles

Original Research Articles should include Introduction Methods, results, statistical analysis, discussion it should not exceed 2500 words.

Introduction

Introduction should include Aims & Objectives & should consist of 75-100 word.

Methods

Methods should mention IEC approval, CTRI registry if any. Study design should be specified Selection of participants along with inclusion/ exclusion criteria and source of population must be mentioned.

Results

Results Maximum 6 tables/ graphs/ figures allowed . Tables should be labelled in Arabic (Not roman).

Discussion

Discussion should consist of summary of key findings, (primary and secondary outcomes, results, hypothesis), confounding factors, ROI, Strengths and limitations of study should be mentioned here. Do not repeat results in discussion.

Maximum authors allowed-6 (Others can be given acknowledgement).

Maximum 30 references.

Review article

Review article it is a scholarly analysis of the latest trends or current state of a particular topic . No new data or personal experiences should be presented . An analysis of the advances in this field is based on a literature review on the subject.

Abstract

Abstract – Upto 250 words (Unstructured)

Article (Main document should not exceed 2500 words.) 6 figures, 30 References.

Case Report

Interesting and rare cases can be presented. Cases with clinical significance & Implications will be given priority

Abstract-Should not exceed 150 words . Main document –upto 1000 words with maximum 2 tables/ figures allowed upto 10 references to be given .

Letter to editor

Letter to editor should contain maximum 250 words excluding references and tables.

Maximum 5 references and 2 tables can be incorporated.

Writing instruction -

While making presentation there should be single spacing. Font of 12 TNR, Page no. should be mentioned at bottom, references must be mentioned after punctuation as superscript without brackets, use UK English uniformly. Numerals at beginning of each sentence must be spelt out.

References

References should be written in Vancouver style. Name of Authors (Max 6 Followed by et al, if more). Name of the article. Name of the journal year of publication ; Issue : Page number. The citations should be in round brackets after fullstop.

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EDITORIAL

Challenges and Controversies : Covid-19 Disease

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INTRODUCTION

Occurrence of covid-19 disease added 6th corona virus pathogenic to human. First three are human corona virus producing mild URTI in seasonal type. Next one was SARS-COV which was short lived. Then came MERS(middle east respiratory syndrome) which too remained localized to middle east geography and did not spread to the world. The covid-19 virus spread all over the globe and created pandemic with 41.2 crore cases and 58.2 lacs deaths worldwide. This disease was associated with challenges and contaversies due to its variable presentation and treatment modalities.

Corona virus (Crown – Spike proteins)

Severe acute respiratory syndrome coronavirus (SARS Cov 2) is a strain of corona virus that causes COVID-19 (coronavirus disease 2019). The virus previously had a provisional name, 2019 novel coronavirus (2019-ncov), and has also been called human coronavirus 2019 (hcov-19 or hcov-19). First identified in the city of Wuhan, Hubei, China, the World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January 2020, and a pandemic on 11 March 2020

Various theories of origin-contraversies

Two explanations that have received considerable attention:

(1) "zoonotic origin ," virus was transmitted naturally from bats to humans, possibly from a food market in Wuhan.

(2) A conspiracy theory that it was human-engineered and leaked, deliberately or accidentally, from a research laboratory in Wuhan, China.

A separate committee of experts was appointed by WHO to investigate this theory of manmade virus. Large number of economic effects were mainstay for this theory. However committee did not have proofs for this theory.

To prevent spread-challenge.

When it started in December 2019, Human-to-human transmission of SARS-CoV-2 was confirmed in mid-December 2019. During that period, China had it's annual Lunar New Year, causing the epidemic to spread beyond Wuhan. The transmission of SARS-CoV-2 by travelers

continues to pose a serious public health threat.

Lockdown as a measure to prevent the spread was used by multiple countries. Effective lockdown and its effects on social system was a great challenge. This led to severe economic, social, educational impact. Also resulted in industrial closure. Worst hit was travel and tourism. Daily wagers were severely affected.

Lock down effect – in India

Considering the seriousness of the disease, initially, a 21-day nationwide lockdown (25 March 2020 to 14 April 2020: LD1.0) was announced to control the transmission of COVID-19 and due to which many industries, academic institutes, markets, as well as public gatherings were shut down.

After the first lockdown (LD 1.0), there have been three more lowdown phases in succession LD2.0: 15 April to 3 May 2020, LD3.0: 4 May to 17 May 2020, LD4.0: 18 May to 31 May 2020.

After that, to restart the Indian economy, two unlock phases (UL) have also been announced (UL1.0: 1 June 2020 to 30 June 2020, and UL2.0: 1 July 2020 to 31 July 2020).

In spite of series of lockdowns, number of cases in India went on increasing but with a gradual increase rather than a spike. This helped to rationalize medical facilities for patients and gave time for preparation new medical facilities. Controversy regarding need for lockdown and travel during it still alive and is on political agenda.

Migrants laborer and daily wagers with transport personals were severely affected.

In India 1st case

First case of COVID-19 infection reported in Kerala, India. On January 27, 2020, a 20 yr old female presented to the Emergency Department in General Hospital, Thrissur, Kerala, with a one-day history of dry cough and sore throat. She had returned to Kerala from Wuhan city, China, on January 23, 2020. An oropharyngeal swab was reported positive on on January 30, 2020 for covid-19.

There after cases were reported from all the state and panic was set in. various messages, videos on social media led to panic situation.

For prevention – three main objectives were planned

1) Mask

Use of N-95 mask is advised above surgical mask or cotton fabric mask. Mask should be properly worn such that it covers your nose, mouth and chin. Clean hands before putting mask on or take it off, and after touching it. Not to use masks with valves.

At start of epidemic, supply of mask became a major challange. N-95 mask was in scarcity and prices were increased by multiple times. Even surgical mask supply faced scarcity.

2) Sanitization and hand washing.

Alcohol based sanitizers are advised to be used as frequent as possible or when in contact with infected things. Alternatively soap water hand wash with WHO hand wash steps was used. Alcohol industries were compelled to make alcohol based hand-rub. Sanitizer bottles were also short supplied and attracted high price.

3) Social distancing

The term "physical distancing" (instead of social distancing) is being used to reinforce the need to stay at least 6 feet from others, as well as wearing face masks. Physical distancing was advised for the purpose of prevention of droplet infection.

However further research shows that aerosol generation can occur and wind spead can carry virus as long as 10 feet distance.

4) PPE kit

After numerous video of medical personal, security personal, front-line worker wearing PPE kit from Wuhan, china on social media, created panic and increased demand of PPE kit all over country. At start of epidemic challenge was to supply PPE kit. Till the epidemic began India was importing PPE kit from outside countries. Many startup started making PPE kit thereafter and now India is exporting PPE kit. Medical fraternity had to learn new clinical examination using PPE kit. Donning and doffing workshops were conducted by all the institute. Finally PPE kits use was restricted to ICU and aerosol generating procedures. Surgical gown was replaced for management of patients in wards. Face shields and innovation in face shield occurred for the first time.

Diagnostics Capacity

RTPCR test was not available throughout the country. To start with only national institute has capacity to perform same. With direction from NMC, ICMR test capacity were increased. Private labs, medical colleges were authorized to perform test.Turnaround time was almost 4-5 days to start with, it was reduced to 6 hours with increase capacity.

RT-PCR is currently the gold standard for SARS-Cov-2 detection due to its capacity to directly measure the viral genomic parts rather than the secondary biomarkers such as antigens or antibodies.Gene are ORF1,E gene, N gene, Rdrp

Controversy in RTPCR testing arose after second wave. Doubts were expressed regarding positivity of test in routine flu patient. Inability to differentiate between live virus and dead virus added to this. Now some countries like US, UK, Sweden are going away from RTPCR test.

Rapid antigen

The antigen tests, unlike PCR-based methods, detect viral components (i.e., S glycoprotein, M protein, or released N protein) or the virus directly without thermal amplification steps. Antigen tests can be operated on LFA strips for rapid detection purposes or in ELISA format for better sensitivity, and high throughput uses.

This test came as point of care test and was used for triaging patient. This test was useful for emergency procedure.

Self test became available using same principle. Home based testing relieved pressure on RTPCR capacity.

Algorithms were published by ICMR for rational use of RTPCR and rapid antigen test.Few videos of unconfirmed testing by tap water positivity added controversies to home based testing method. Reporting of this test to central agencies had multiple pitfalls.

CB NAAT

This is a costly test and reserved for pre-procedural test for emergency intervention. This is available only in research institutes

Antibody testing

An antibody test can measure the presence and concentration of IgG and IgM levels in the blood/serum/plasma samples to determine if the body is fighting with a pathogen. The most common antibody tests are based on lateral flow type assays (LFA) and enzyme-linked immunosorbent type assays (ELISA).

Antibody testing of general population to decide herd immunity had multiple setbacks. Even in presence of 80% herd immunity second and third wave occurred. Vaccine induced antibody failed to prevent infection. However severity of disease was limited. Now routine antibody testing for Covid-19 is not advised.

Others

Loop-mediated isothermal amplification (LAMP) is a cost-effective alternative to standard PCR since it does not require expensive thermocycler instruments that operate alternating temperatures for the amplification. The method can synthesize up to 10^9 copies of the target gene in less than an hour.

Clinical picture

1st Wave

1st case in India in late January 2020, and from march 2020 scenario changes and cases of covid - 19 positive started rising with peak in September 2020 around 90,000 cases per day and gradually decreased in February 2021. This wave was presented with typical picture of fever, URTI, followed by lung involvement after 5-7 days. Additional system involvement included kidney and heart predominantly. Loss of smell and taste was seen in most of the patients. To differentiate from influenza, bacterial URTI was really a challenge. Onset of cytokine storm manifestation was an additional feature

2nd wave

Begin in mid February of 2021,peaked in april 2021 and ended In june '21 In Pune around 2 lac cases out of which 4500 fatalities

Clinical feature in 2nd wave delta variants, had subacute presentation with low grade continuous fever, breathlessness, hypoxia, cough , loss of taste and smell , diarrhea with drop in SpO2.

Lab investigation of delta variants infected patients suggested leucocytosis with lymphopenia with high NL ratio. Inflammatory markers were raised with HYPERGLYCEMIA and radiological investigation suggestive of peripheral involvement.

Complication with delta includes thrombotic events, macrophage activation syndrome and secondary bacterial, fungal and viral infection with mucormycois being the dreaded one.This was seen in spite of no steroids, low dose steroids, high dose steroids. Defect in T cell mediated immunity was likely the cause.

3rd wave

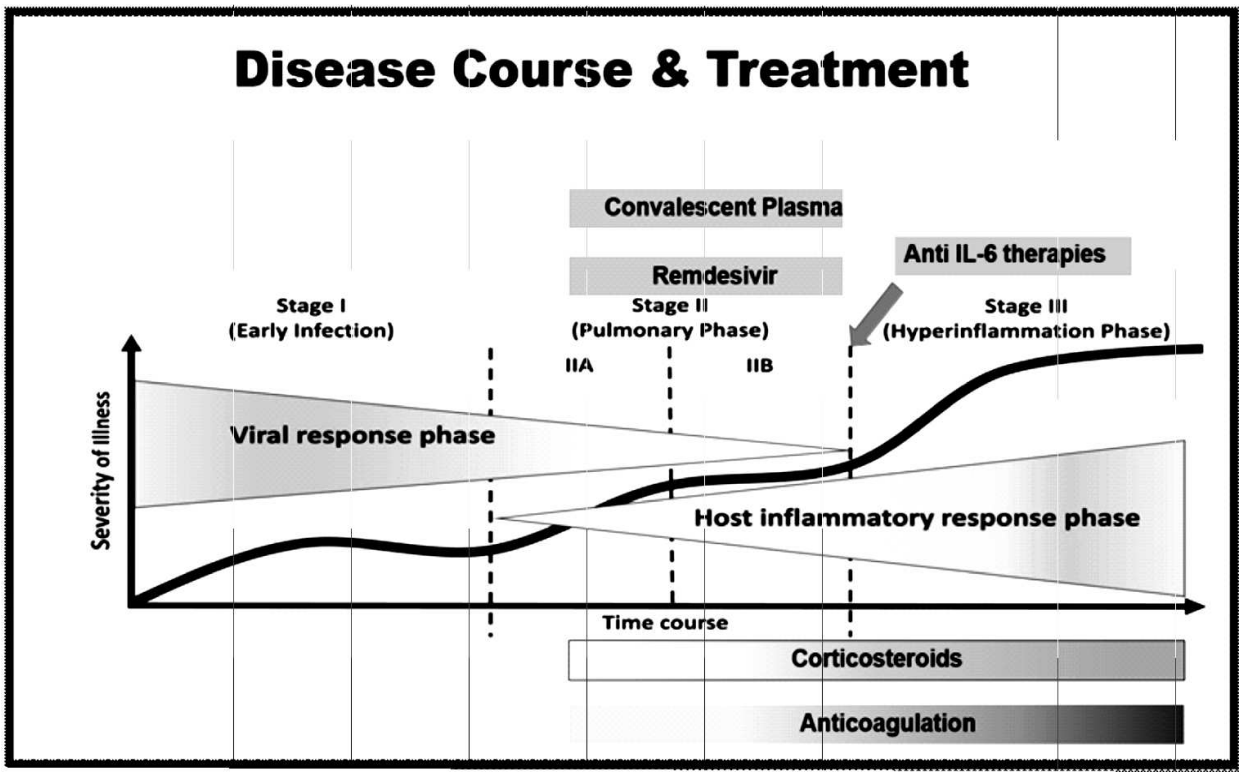
Begin in January 2022 and is still ongoing but receding.

Pune observed same number of cases as of 2nd wave in very small duration but mortality due to omicron per se is very less around 200 cases, likely due to greater coverage of vaccination. Omicron variant present with headache, severe body ache , fever – high grade or no fever at all , no loss of taste and smell unlike delta. And symptoms are self resolving in 99% cases and needs only symptomatic treatment.

Lab investigation in omicron – normal or reduced TLC with no lymphopenia and normal NL ratio. Marginally raised d-dimer and normal CXR

Complication with omicron that has been observed are Encephalopathy, nephropathy, bronchitis, co-infection with herpes.

Therapeutics



Repurposed drugs

- Hydroxychloroquine
- Lopinavir-ritonavir
- Doxycyclin
- Azithromycin
- Ivermectin
- Methylene blue

Physical agents

- Steam inhalation
- Hot saline gargles

Antibody therapy

- Convalescent plasma

All this repurposed drugs were used due to their ability to reduce or prevent viral multiplication in vitro. WHO conducted combined trial of this entire repurposed drug-solidarity clinical trial. All the above drugs failed to show any effect on disease progression. Hence were advised not to use.

Oxygen

As hypoxia was a major problem in covid-19 disease, oxygen therapy played a pivotal role. Training of medical personal to handle this therapy was a great challenge. With sudden spike in number of patients, adequate oxygen beds and ventilator beds were not available.

Oxygen was also in short supply. Oxygen needed to be imported from neighboring state as well as countries.

Prolong oxygen therapy leading to dung damage created controversy, hence oxygen audit and guidelines for oxygen management put into the place.

Cytokine Strom

Lot of discussion and effect of cytokine strom

on disease progression was available in literature. D-Dimer, ferritin, LDH, CRP, ESR, IL-6 were the predominant markers for cytokine strom. Its relation with disease manifestation and progression was hypothesized. This was the first time to use these markers to decide severity and outcome of patients.

Steroids

Corticosteroid therapy at this phase to reduce death rates has been proved in Britain. Low dose corticosteroid therapy ie methyl-prednisolone is given to patient in dose 20mg or 40mg or (in) dexamethasone 6mg to 8mg injection intravenously daily.

This helps to reduce inflammation in the lungs and other tissues and improves oxygenation. High dose steroids are to be avoided. Steroids to be given till oxygen level normalize at room level or maximum up to 10 days with close watch on side effects.

Heparin

COVID-19 disease leads thrombotic events of various organ. Pulmonary thomboembolism are more common and this leads to breathlessness and hypoxia. Cerebral thrombosis and coronary thrombosis are other complications. Hence to prevent this anti-coagulation drugs are used. Clotting tendency is reflected in increasing D-dimer level. Such patients should receive anticoagulation. Enoxaparin 30 to 40 mg

sub-cutaneous is given every 12 hourly. This cost 650/- rupees per dose. Those with deranged renal parameters receives plain heparin 5000 units sub cut every 12 hourly. Close monitoring is required.

Immunomodulator

Tocilizumab- This antibody is against il-6 receptors. It is given as 2 doses of 400mg each, 24 hours apart, intravenously. This drug produces immunosuppression. Other infection like bacterial and fungal can complicate patient's condition. This drug Cost 75,000/- rupees. Epidemic of post covid mucormycosis raised question about this drug. Instead of two doses single dose or half dose was advocated by many. Its availability was a challenge during first and second wave.

Itolizumab- If tocilizumab is not available this drug can be used as 0.75mg per kg single dose intravenously. This also has problems of superadded infection. Allergic reactions are more for this drug. This drug cost 40,000/- rupees. Fungal and tubercular infection restricted use of this drug

Baricitinib- this drug is used in dose of 4mg daily for period of 10 days. Close monitoring on hemogram is required. Daily cost is around 100 rupees. This was used at end of second wave and studies led to WHO recommendation for its use.

Anti – viral

Ramdesivir

Remdesivir, a drug originally developed for Ebola virus disease, is used as anti-viral drug when patient's oxygen level is low but doesn't require ventilator. Remdesivir is given as 200mg on day1 and then 100mg from day2 to day5 intravenously. This drug can lead to liver damage or kidney function problems as side effects. Each 100mg vial costs 2500/- rupees. Lot of side effects and long term effect describe on social media led to refusal by patients for its use. Clinical experience with this drug is encouraging. Now three days ramdesivir therapy, as prevention, in high risk patients is advocated.

Favipiravir

This anti viral was available towards end of first wave, however hepatic dysfunction and hyperuricemia restricted its use. Large number of pill burden was additional factor. Its effectivity is still questionable.

Molnupiravir

This drug was available at the start of third wave. It was used in mild symptomatic high risk patient. It has mild gastrointestinal toxicity. However teratogenicity and proposed long term effect led to restriction of its use. This drug was not included ICMR guidelines for Covid-19 management.

Paxlovid (nirmatrelvir + ritonavir) tablets have been described to have best anti viral effect. This is still to be available in Indian market.

Monoclonal antibodies

Antibody cocktail- combination of Casirivimab plus Imdevimab known as antibody cocktail, this prevent virus entry into the cells of various internal system and prevents disease progression, to be given as early as possible after COVID-19 RTPCR positive. This drug can be given up to 7-10 days of onset of illness. Cost of drugs for single dose therapy is 60,000/- rupees per patient. Allergic reaction occurs as side-effects. These antibodies were mainly directed against spike protein of delta variants of covid -19 virus. As third wave is by omicron variant of covid-19 virus having multiple mutation in spike protein, this is not used nowadays.

Sotrovimab – monoclonal antibiodies have been developed for omicron variant . This antibody are still to be available in Indian market.

Vaccines

Multiple types of vaccine were developed within 9 months of epidemic onset . All these vaccine were authorized for emergency use as proper clinical trials were not available.

mRNA vaccine had controversy regarding permanent genetic change while spike protein related protein had fear of thrombotic episode. Whole viral vaccine had doubts regarding its efficacy. Vaccine were introduced with claim of protection for at least one year how ever in practice protection started wearing off at end of 3 months and was undetectable by six month. Hence concept of booster dose came in. in country like Israel had used booster dose in multiples. All this vaccine failed to prevent new infection and spread of disease. Most important gain of mass vaccination was prevention of serious disease and deaths. Hence booster dose for mass vaccination was advocated. Still age group upto 15 are not included in vaccination process and in 15-18 recently been started. Mass vaccination of huge population in India was a great challenge and was tackeled efficiently.

Dead bodies

Dead body disposal protocols were prepared and with the help of social organizations, administration could overcome this challenge.

Post covid

Covid-19 disease was associated with distinct post covid manifestations. Simple malaise, fatigue, weight loss to thrombotic complication, neuropathy were seen. A separate post coivd OPD required to manage this. Some patient had post covid complaints right up to 3-6 months. As manifestations were varied, history of covid infection began norm in clinical history. Post covid

orthostatic tachycardia syndrome (POTS) was described.

FUTURE

There is always a threat of new mutation leading to more infectious, more dangerous virus. Covid-19 virus is of highly mutating type. Even after more than 80% herd immunity due to infection or vaccine, this threat persist. Hence covid appropriate behavior is going to stay with us longer. This new normal behavioral pattern will help us to avoid another wave. Research is going on for new drugs to tackle variants, new vaccine to protects us from variants.

Silver lining

This covid-19 pandemic taught us new methods and ways to manage public health emergency. Lots of addition to infrastructure has led to increase number of beds oxygen beds, ventilators. Oxygen generating and storing capacity has increased many folds. Trained manpower which includes intensivist, doctors, nurses, class four employees are available now. This epidemic has given boost to health, infrastructure and manpower . this definitely will be useful to tackle any upcoming public health emergency in far better way.

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Original Article

Mucormycosis - A serious threat in the COVID-19 pandemic? Our Experience in SKNMC&GH, Pune

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Abstract

Background

Mucormycosis is a life-threatening invasive fungal infection that occurs in immunocompromised patients and is associated with a mortality of 25-62%. There has been a staggering increase in the number of rhino-orbital-cerebral mucormycosis cases during the ensuing COVID-19 pandemic and also as post COVID sequelae. Our study aimed at scrutinizing a possible /infection of invasive mycoses and COVID -19, and also its management.

Methods

We did a retrospective observational study of 50 patients presenting with invasive fungal rhinosinusitis from April' 21 to June' 21 in SKNMC & GH, Pune.

Observation

Majority of our patients were immunocompromised. Since they presented during the pandemic, all patients were subjected to rapid antigen and RT-PCR testing for COVID. On retrospective analysis of the patient's records, we found that 90% patients

had received steroids for treatment of COVID-19 and majority had co-morbidities like diabetes mellitus. All the patients in our study received treatment with intravenous (IV) Amphotericin B and surgical debridement. The mortality rate was 16%.

Conclusion

We conclude that patients with COVID-19 infection are susceptible to mucormycosis because of impairment of barrier defence, dysfunction phagocytes and lymphocytes and the use of immunosuppressive medications such as steroids, remedesivir and tocilizumab.

Keywords

COVID-19, Invasive mucormycosis, Amphotericin B, Steroids, Post COVID sequelae

INTRODUCTION

Zygomycetes comprises of mucorales and entomothorales. The former order causes life threatening fungal infections, like mucormycosis, primarily in immuno-compromised hosts while the latter order causes superficial and mucocutaneous infections in immunocompetent hosts. Among *Mucoraceae*, *Rhizopus oryzae* is the most common cause of infection. The prevalence of mucormycosis in India is approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries.[1] Phagocytes are the major host defence mechanism against mucormycosis [2,3] while corticosteroid treatment affects the ability of macrophages to prevent the germination of the spores of these fungi. A hallmark of mucormycosis infection is the presence of extensive angioinvasion with resultant vessel thrombosis and tissue necrosis.[4]

In the current times there is a pandemic due to SARS-CoV-2. It is a non segmented negative sense RNA virus which causes profound lymphopenia. In later stages of the infection when viral replication accelerates, epithelial-endothelial barrier integrity is compromised. The inflammatory response is triggered, accentuating an influx of monocytes and neutrophils. Collectively, endothelial barrier disruption, dysfunctional alveolar-capillary oxygen transmission and impaired oxygen diffusion capacity are characteristic features of COVID-19.[5]

Recently, we have noticed that there is an increase in the incidence of invasive mucormycosis infections in COVID-19 disease. We have come across 50 such cases and all the cases were found to have some similarities.

The Indian Council of Medical Research released guidelines for the screening, diagnosis, and management of mucormycosis in patients with COVID-19.[3] The most common causes attributed to the rise of mucormycosis in COVID-19 patients are uncontrolled diabetes, excessive use of corticosteroids for immunosuppression, and long-term stays in the intensive care unit. No official figures about mucormycosis in COVID-19 cases were released by the Union Health Ministry during the first wave of COVID-19. However, based on recently published literature, India contributed to approximately 71% of the global cases of mucormycosis in patients with COVID-19 between December 2019 to the start of April 2021.[4]

OBSERVATION

We retrospectively reviewed patients with rhino-orbito-cerebral mucormycosis and COVID-

19 infection admitted at our SKNMC and GH, Pune, between April and June 2021. The patients were jointly managed by the departments of General Medicine, Ophthalmology, Oral & Maxillofacial Surgery and Otorhinolaryngology. The medical records were retrieved and the demographic findings along with clinical, histopathological and radiological data were reviewed.

Out of 50 patients, 13 (26%) were females and 37 (74%) were males. The age range of patients was 24 - 81 years, with majority of patients between 40 and 60 years of age. Eye pain, proptosis, facial pain and swelling, headache, blurring of vision, nasal block and palatal perforations were some common presenting complaints (Fig. 1 & 2). Few patients presented with concomitant ptosis and unilateral facial paralysis. Orbital involvement was seen in 16 (32%) cases. Most of the patients presented within two weeks to two months of recovery from COVID-19 infection. 17 out of 50 patients (34%) were still RT-PCR positive for COVID -19 at the time of presentation. All the 50 patients (100%) had received steroids and 40% had received inhalational oxygen during management of COVID disease. Only 3 (6%) patients had received Remdesivir.

Majority of the patients were diabetic and hypertensive, with underlying IHD and CKD. Most of the post COVID mucormycosis patients in our study had a glycated haemoglobin (HbA1c) ranging from 7-15 with majority having HbA1c of above 10.

KOH mount of nasal discharge/scrapings from 10 (20%) patients revealed broad aseptate fungus while remaining patients had a negative KOH report but they later tested positive for zygomycetes on histopathological examination. All the patients had imaging evidence in the form of CT PNS and MRI (brain + PNS + orbit) revealing mucosal thickening of ethmoid and maxillary sinuses and adjacent bony erosions (Fig 3 & 4).

Of the total 50 patients, 40 (80%) patients underwent sinonasal debridement, 3 (6%) patients underwent orbital exenteration and medial orbital wall decompression was done in 5 (10%) cases (Fig 5 & 6). In 5 (10%) patients total maxillectomy was done, subtotal maxillectomy was performed in 8 (16%) patients and Caldwell Luc operation was done in 9 (18%) patients and palatal debridement was done in 4 (8%) patients. Transorbital retrobulbar amphotericin B (TRAMB) injection was given to 13 (26%) patients. Rest 10 (20%) patients had to be managed medically only as they were not fit for general anaesthesia due to severity of COVID-19 infection and other uncontrolled comorbidities. Out of our 50 patients, majority presented with rhino-orbital mucormycosis. Intracranial involvement was seen in 3 (6%) patients. On histopathological examination, mucormycosis was seen in 34 (68%) cases, aspergillosis was present in 3 (6%) cases and in rest 3 (6%) cases mixed type (mucormycosis and aspergillosis) of fungal infection was seen (Fig 7 & 8).

All the patients were given IV Amphotericin B with cumulative dose of 5 gms over 21-42 days. Patients were given oral Posaconazole (300mg per day) as maintenance for a duration of 3 months. At the time of discharge, patients with aspergillosis were given oral Itraconazole (100mg two times a day for 3 months) as maintenance therapy. Post operatively all patients were advised local diluted Amphotericin douching. In those patients who had severe COVID -19 disease with concomitant uncontrolled diabetes and requiring O_2 support, IV Amphotericin B was started empirically based on clinical suspicion of mucormycosis. These patients were taken up for debridement once stable. In the post-operative period, out of 40 patients there were 3 mortalities due to complications arising out of pre-existing comorbidities. Out of 10 patients who were not fit for surgery 5 died. Overall mortality was 16% (8 of 50 patients).

DISCUSSION

Mucormycosis is a very rapidly progressive disease and may prove fatal if timely diagnosis and treatment are not given. Several genera are associated with this disease, the most common forms are Rhizopus, Rhizomucor and Absidia. Rhizopus is the predominant pathogen accounting for 90% of the cases of rhinocerebral mucormycosis.[5]

While our country battles with COVID-19, the issue of post COVID-19 sepsis has emerged as a significant problem. India bears the dubious distinction of being both the diabetes as well as the mucormycosis 'capital' of the world. COVID-19 and its treatment, against this backdrop, amounts to a recipe for disaster.

With an estimated 77 million cases in the adult population, diabetes is India's fastest growing epidemic. A recent cross-sectional study from all states of India, revealed that 47% of Indians are unaware of their diabetic status and only a quarter of all patients achieved adequate glycemic control on treatment.[1] The unholy association between diabetes and the severity of SARS-CoV-2 infection has been repeatedly established in various studies from across the world.[2]

Mucormycosis sometimes appears as the diabetes-defining illness, and remains one of the most devastating complications in uncontrolled diabetics with mortality rates ranging between 40-80%. India contributes to 40% of the global burden of this "rare mould" infection as it is called in western literature, with an estimated prevalence of 140 cases per million population.[3]

Post COVID-19 sepsis is what occurs after SARS- CoV-2 has had a rampage in the human body and we are literally left picking up the pieces. It leads to a dysregulated innate immune response, ciliary dysfunction, cytokine storm, thrombo-inflammation, microvascular coagulation and eventual immune exhaustion. This cascade of events facilitates secondary bacterial and fungal infections especially in critically ill patients subjected to emergency invasive procedures, mechanical ventilation, CRRT, ECMO, poor nursing ratios, prolonged hospital stays and breaches in asepsis. Further, the use of corticosteroid treatment and anti-IL-6-directed strategies in these highly susceptible hosts along with high fungal spore counts in the environment creates the perfect setting for mould infections.

Mucorales are ubiquitous moulds, abundantly found in the environment on decaying organic matter. Various studies from hospitals across the country have revealed heavy mould spore counts even in hospital air due to predominantly hot, humid conditions in our tropical climate.[5]

While COVID-19-associated pulmonary aspergillosis (CAPA) has received much international attention, the Indian epidemiology of invasive mould infections in the ICU reveals a significant burden of invasive mucormycosis.[4] This has recently emerged as a life threatening complication of COVID-19 in our country. Although the predisposing factors and pathogenesis are somewhat similar to that of other mould infections, certain unique characteristics and key distinguishing factors must be kept in mind in order to promptly suspect the infection, confirm the diagnosis and offer timely therapeutic intervention.

Unlike CAPA, invasive mucormycosis has been observed even in patients with mild to moderate SARS- CoV-2 infections. The strongest predisposing factor appears to be hyperglycemia in undiagnosed or uncontrolled diabetics. Hyperglycemia leads to increased expression of the endothelial receptor GRP78, resulting in polymorphonuclear dysfunction, impaired chemotaxis and defective intracellular killing. An important virulence trait of Mucorales is the ability to acquire iron from the host which is an essential

element for its growth. In conditions of ketoacidosis, free iron becomes readily available in the serum. This excess endogenous iron is efficiently taken up by the Mucorales through siderophores or iron permeases, further enhancing their virulence. These effects are greatly amplified by the use of corticosteroids and immunosuppressants in susceptible hosts. Corticosteroids themselves cause impairment in the neutrophil migration, ingestion, and phagolysosome fusion. Coupled with the potential implications of steroid-induced hyperglycemia, the diabetic COVID 19 patient receiving corticosteroids or other immunosuppressants is exceptionally vulnerable to the development of mucormycosis.[6,7]

The landmark RECOVERY trial published in June 2020 has served as a 'license' to use steroids in patients with COVID-19. However, the fine print clearly revealed some important messages that we seem to have overlooked. Benefit was specifically shown with low dose, short duration dexamethasone in moderate to severe illness. Although, higher doses and longer durations may be used in exceptional cases due to compelling reasons, such patients should be evaluated for undiagnosed diabetes, checked for strict glycemic control and closely monitored for secondary infections. A cavalier attitude to the use of steroids should be discouraged at all costs.

The two most important manifestations of Mucormycosis in this setting are rhino-orbital-cerebral and pulmonary. Suspicion is based on subtle clinical and imaging clues, risk factors and disease development or progression while on any antibacterial or antifungal therapy that does not cover Mucor. Physicians need to have seen a 'critical' number of cases to recognize the signature of Mucor.

The clinical hallmark is tissue necrosis manifested as a necrotic lesion, eschar or black discharge in the nasal or oral cavity. Orbital, ocular and cranial nerve involvement are ominous signs that must be taken seriously. Alternative erroneous diagnoses lead to antibacterial and further steroid use which add fuel to the fire. Pulmonary Mucormycosis has certain radiologic findings which help to distinguish it from Aspergillosis. There is no biomarker for mucormycosis and hence a negative galactomannan and beta-d-glucan are useful pointers to rule out other mould infections. A false positive galactomannan due to generic piperacillin tazobactam use etc. can lead to the erroneous diagnosis of invasive aspergillosis. Although challenging, the need to distinguish Mucor from bacterial infections and from aspergillosis in a timely fashion is of essence. Treatment with voriconazole for suspected invasive aspergillosis increases the pathogenicity of Mucor with obvious dire consequences.

Rapid diagnostic methods include biopsy, KOH mount and Calcofluor stain. Mucor is difficult to routinely culture. Biopsy remains the mainstay of diagnosis and the benefits of the procedure outweigh the risk, even in a 'difficult to access' location or in the presence of coagulopathy.

Treatment principles include antifungal agents, surgical debridement, reversal of underlying predisposing factors and adjuvant therapy. Amphotericin B has been the standard of treatment for invasive mucormycosis. COVID-19 patients may have developed acute on chronic renal failure which may be mitigated by switching to a less- or non-nephrotoxic alternative. Therefore Posaconazole or Isavuconazole may have to be used. The latter has the added advantage of shortening the QT interval which may have been affected by HCQ, Azithromycin which many patients still continue to receive. Surgical debridement, the earlier the better, is pivotal in the management of mucormycosis. The optimal time of surgery to reduce the operative risk to the patient with COVID-19 and the risk of transmission to the

operating team is a contentious issue. Replication competent virus has not been recovered from patients with mild to moderate illness after ten days, from patients with severe illness after fifteen days or from any critically ill patient after twenty days.[8]

Adjuvant therapy with caspofungin, deferasirox, statins, aspirin, and hyperbaric oxygen may have to be considered. Mucormycosis needs to be actively managed by a team which includes members from almost all departments in the hospital. Therapy is toxic and very resource intensive. In a recent Indian study, 24.3% patients left the hospital against medical advice due to the anticipated cost, morbidity of surgery and prognosis.[9]

Mucormycosis developing in the post COVID-19 setting 'breaks the back' of a patient's family that is barely recovering from a treacherous viral infection. This scenario is nothing short of 'recovery from the frying pan and into the fire.'

Our case series highlights the possibility of a correlation between COVID-19 and mucormycosis infections. We know from the pathogenesis of mucormycosis that mononuclear and polymorphonuclear phagocytes of normal hosts kill mucorales by generation of oxidative metabolites and defensins, hence neutropenic patients and those with dysfunctional phagocytes are susceptible to develop invasive mucormycosis.[2,3] In COVID-19 there is profound lymphopenia and in advanced infections viral replication accentuates the inflammatory response and neutrophil and monocyte influx in the blood stream.[5] This leads to an imbalance between neutrophil and lymphocyte action making the patient more susceptible to systemic fungal infections.

CONCLUSION

We propose that, patients with COVID-19 infection are susceptible to mucormycosis because of impairment of barrier defence, dysfunction of phagocytes and lymphocytes and the use of immunosuppressive medications such as steroids. So, clinicians must be aware of possibility of invasive fungal infection in such COVID patients with history of diabetes and other co-morbidities. Unless diagnosed and treated early, this type of mucormycosis is often fatal due to cerebral involvement. Early diagnosis with surgical excision, appropriate debridement, proper antifungal treatment and management of risk factors lead to subsequent reduction in mortality and morbidity.

Thus, successful treatment of mucormycosis requires four steps –

1) early diagnosis;
2) reversal of underlying predisposing risk factors, if possible;
3) surgical debridement where ever applicable; and
4) prompt antifungal therapy.

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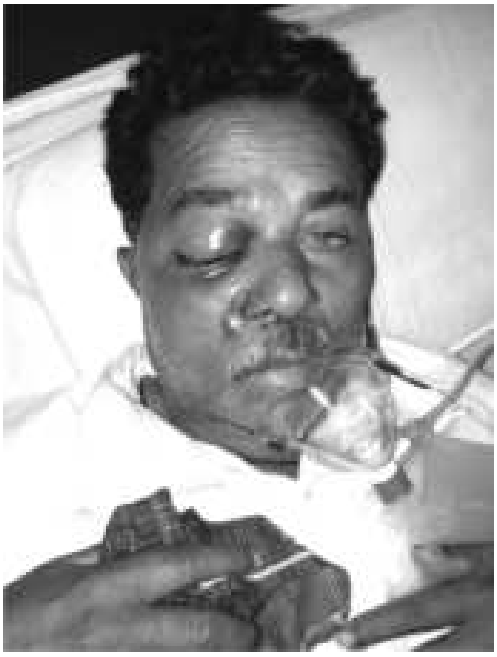

Fig 1 : Pre-operative photo with facial swelling, blackish discolouration of skin & ptosis

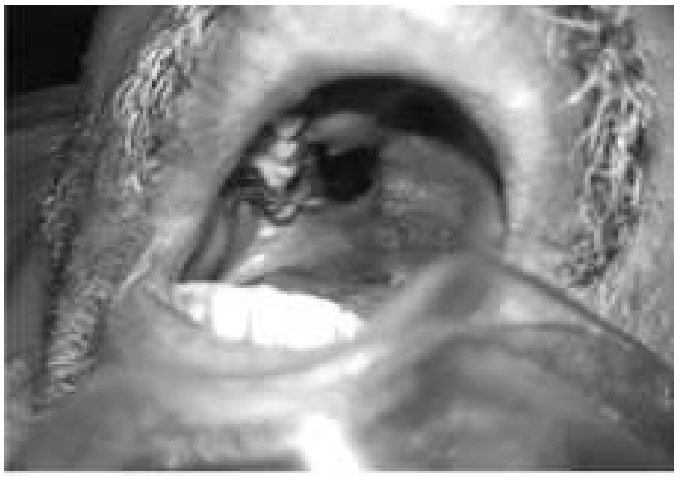

Fig 2 : Pre-operative photo with palatal perforation

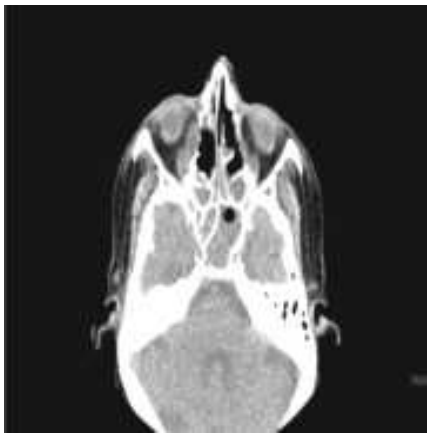

Fig 3: CT scan showing bilateral involvement of paranasal sinuses

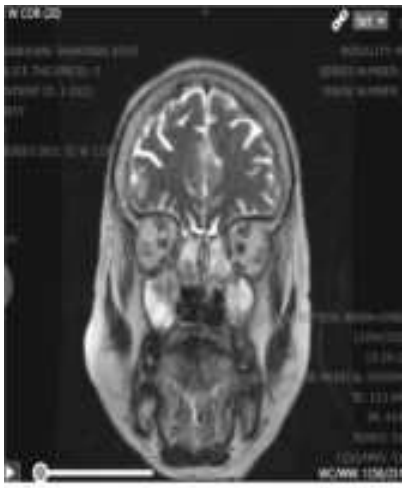

Fig 4: MRI showing bilateral involvement of paranasal sinuses

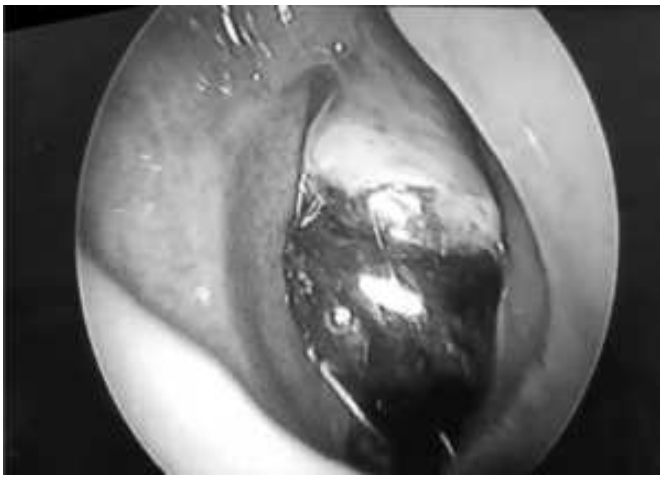

Fig 5: Intra-operative photo showing blackish discolouration of middle turbinate

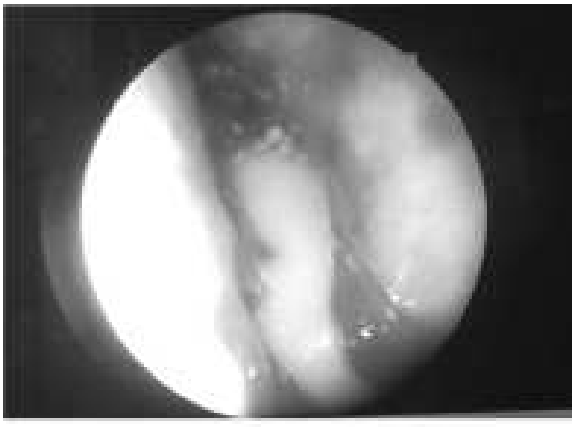

Fig 6: Intra-operative photo showing frank pus from sinuses

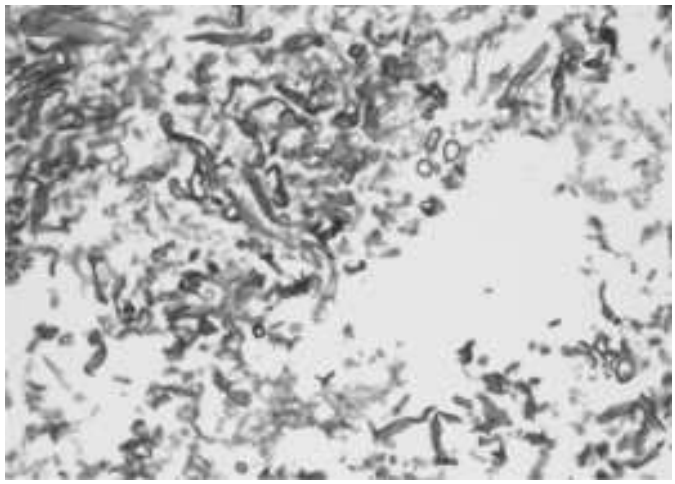

Fig 7: H & E stain suggestive of mucormycosis

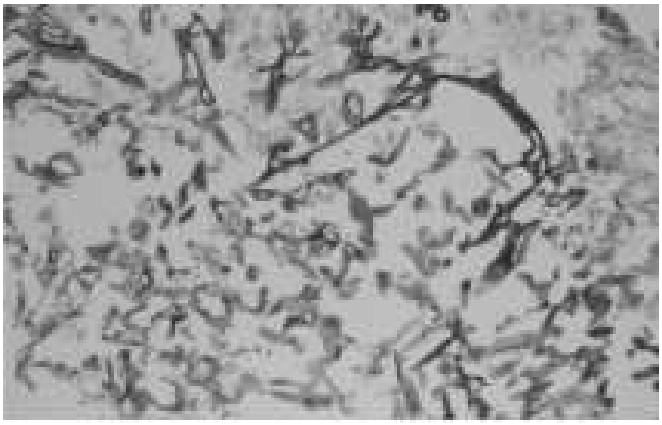

Fig 8: Special PAS stain suggestive of mucormycosis

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Original Article

Psychiatric illnesses & Covid 19 infection during the second wave of pandemic

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Abstract

Background

COVID-19 infection has rapidly escalated into a global pandemic and the incidence of mental health issues with it is likely to have increased during the pandemic, due to a variety of factors discussed in this study . Here, we study impact of COVID-19 infection on known cases of psychiatric illnesses.

Method

This is a descriptive cross- sectional study of psychiatric outpatients over a period of one month , who had developed Covid infection. We have studied consecutive 20 such patients. 50% of the patients. had a diagnosis of a psychiatric disorder in the past one year and prior to that , while 50% of them were new comers to psychiatry OPD. We conducted clinical interview & used DASS-21 scale for evaluation.

Results

Sample included 10 males and females each. 40% patients had drug drop out due to a variety of factors such as lockdown , difficulty in availability of transport , financial problems. On the DASS 21 scale we found that the 60% had anxiety score, 15% depression score and 5% stress score above threshold . Among our patients, 7 patients were using one or more substances. Increase in the substance use has been observed during the pandemic particularly tobacco smoking and alcohol. Sleep was disturbed in

80 % of the patients, even those on regular treatment.None of the patients had significant complications of covid infections.

Conclusion

History of Covid infection should be asked to every patient coming to psychiatry OPD and psychosocial impact should be assessed for effective treatment of mental illnesses during Covid pandemic.

Background

Mental disorders are estimated to affect 20-25% that is 450 million globally.[1] Covid infection is known to be commoner in patients with history of psychiatric illness, as mentioned in recent research by Wang and Volkow 2021[1,2]. Difficulty in following Covid appropriate behaviours could be due to various reasons like poor immunity, poor self care, inattentiveness, less motivation etc. On the other hand, this infection can cause lot of anxiety in the patients[2,3,4]. Apart from its physical complications, the patients who are already suffering from a psychiatric disorder are further prone to mental health effects due to Covid infection.They are more prone to get anxious due to the infection& anticipate outcome in a negative way[5,6].Effect of the immune system is also known in cases of mood disorders[7] . Increase in the substance use has been observed during the pandemic particularly tobacco smoking and alcohol. Drug discontinuation may be common after acquiring Covid infection in old cases of psychiatric illness. This may precipitate exacerbation occurrence ofa new episode of illness. There are many Community-based studies who have screened for mental health effects during Covid pandemic. Also studies on children and older adults where variations according to age gender and social background were undertaken.

Method

We studied the psychiatric outpatients that had developed COVID infection during second wave of this pandemic coming to us for treatment of their mental illness and assessed them for their current symptoms , psychosocial impact of COVID and documented various challenges faced by them . We had screened about 116 patients coming to psychiatric OPD to obtain this data. This is a descriptive cross- sectional study of psychiatric outpatients over a period of one month who had developed Covid infection we have studied consecutive 20 such patients coming to psychiatry OPD. The patients were assessed by a semi-structured pro-forma to record socio-demographic details, noted their social stresses and diagnosed according to ICD 10 and their psychological problems and also were given a structured questionnaire DASS 21 (21 item scale Depression Anxiety stress scale by Lovibond)for assessment of depression anxiety and stress. Valid Marathi translation of this tool is freely available and could be used for the study.[8,9]

Results

Sociodemographic's - The demographic characteristics of the study sample which was 20 patients coming to the psychiatry OPD 5 out of 20 people were of age above 50, while the other 75% were between the age group of 20 to 50 years. Equal number of male and females were present in the study sample.(n=10)

Most of the of the population nearly 90% (18 out of 20) were living in urban settings while 20% were of the rural background.

Out of which 17 were employed while 3 were homemakers before the Covid pandemic. After the pandemic 7 people among them faced job losses and financial issues as a result of the pandemic. Maximum number of patients presented to the OPD within one month of being Covid positive

50% of the patients had a diagnosis of a psychiatric disorder in the past one year and prior to that , while 50% of them were diagnosed for the first time .

20% of the total study population had a medical comorbidity in the form of Hypertension (15%), Diabetes mellitus (10%) and hypothyroidism (5%).

Current psychiatric symptoms - On the DASS 21 scale we found that the most common symptoms faced by patients coming to psychiatry OPD were that-

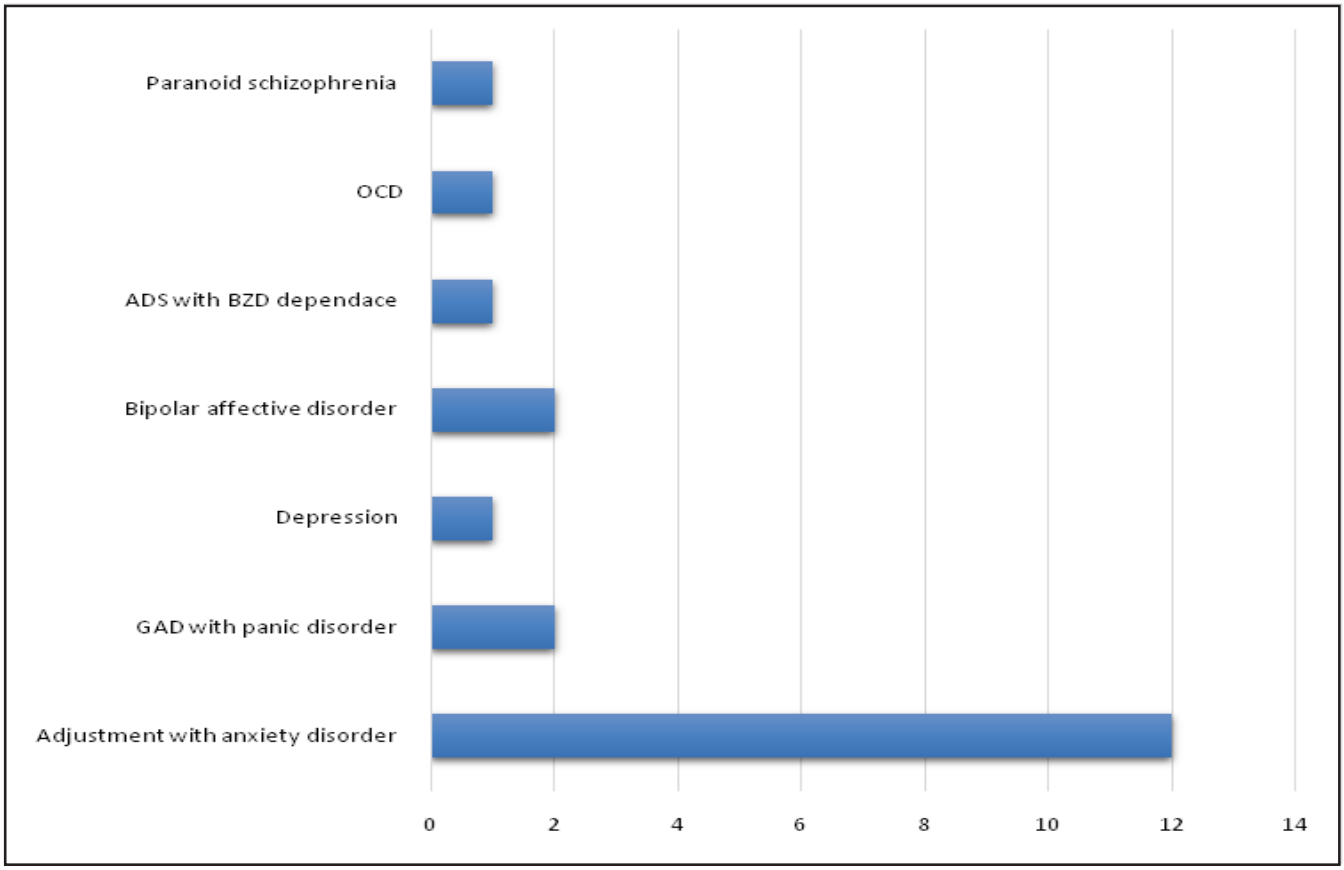
They found it difficult to relax had tremulousness and were aware of the action of their heart in the absence of physical exertion

Difficulty to experience any positive feelings at all. So in anxiety symptoms were reported most commonly more than the cut-off mentioned in the guidelines of assessment of DASS21.

Worrisome thoughts about the future due to the uncertainty and family's well-being were among the key symptoms in many patients.

16 out of 20 (80%) patient had sleep disturbances which were significant enough to cause impairment in functioning.

Psychiatric diagnosis - 60% had anxiety score above threshold, 15% depression score and 5% stress score . Common stresses reported include loss of job, financial problems, increased interpersonal problems and loneliness due to lockdown.Clinical diagnosis of the 20 patients coming to Psychiatry OPD are given in the figure



Course - Condition of 7 out of 10 (70%) who had history of psychiatric illness in the past had worsened while 3 out of 20 (30%) were stable, asymptomatic and on regular treatment.

4 out of 10 (40%) patients had drug drop out due to a variety of factors such as lockdown , difficulty in availability of transport , financial problems .

4 out of 10 who had a history of past psychiatric illness were on SSRIs did not need hospitalisation and had no complications due to Covid 19.

Impact - The patients who required hospitalisation reported of the most stressful factors being isolated and from their family members and worry about their well-being.

During the hospitalisation the most helpful factor reported by the patients were that the doctors and the staff was very empathetic towards the patients , also communication over the phone with the family members and relatives helped them to overcome the situation.

Also many people who previously did not exercise or practise yoga /meditation started practising it during this pandemic and found it very helpful in coping with the uncertainties due to the pandemic.

Discussion

Burden of mental illnesses continues to grow with significant impact on health leading to disability[10] and their incidence is likely to have increased during the pandemic, due to a variety of factors[11,12,13]

20% Covid-19 patients develop mental health issues by a study from UK , by Julian et all in 2020

Common mental health problems were anxiety, depression, PTSD there are also higher chances of triggering dementia in older patients[20]

However, in the patients already having mental health problems impact of Covid is less studied. The patients who are already having a psychiatric disorder may get further affected and morbid condition can worsen or there can be other effects which need to be studied. There are also community-based studies who have screened for mental health effects during Covid pandemic.

Also studies on children and older adults where variations according to age gender and social background like for example children with various problems like ADHD and mental sub-normality are also affected .Impact on teenagers is also significant.[18,19]

There are various ways in which mental illness can affect Covid related behaviour their motivation for taking precautions may be lowered and there may be more vulnerable for developing the infection also it may be harder for them to cope with the uncertainties isolation and various socio-economic challenges.[20]

In an Indian article by Rajkumar et all 2020 symptoms of anxiety and depression were seen in 16 to 28% patients at sub syndrome levels and mental health problems was a common response to COVID-19 pandemic.

Higher sensitivity to stress is more common in patients with mental disorders which makes it difficult for them to cope with uncertainties isolation and economic challenges linked with COVID-19 pandemic and increases the risk for relapse and disease exacerbation. This was also reported by our patients.

Among our patients, 7 patients were using one or more substances. Increase in the substance use has been observed during the pandemic particularly tobacco smoking and alcohol.[18]But all of our patients were using the substance since a long time, before the onset of pandemic.

Some studies also reveal that the younger population that is the age group of 20 to 50 years of age was more stressed than the other age group as this was the active working group which was more affected by the economic crisis due to the

Covid outbreak.

In a similar study conducted in Iran using DASS 21 also had higher and positive significant relationship with the DASS 21 scores and significantly associated with anxiety depression and stress.

Many studies have quoted the possible immune-regulatory and anti-inflammatory effects of SSRIs as Covid results in weakening of the patients in news response and hence more severe respiratory symptoms or even death[14,15,16]

As the severity of COVID-19 depends largely on the immunity and release of inflammatory mediators most infected with COVID-19 have showed mild to moderate breathing problems and recover without any vigorous hospitalisation or interventions while on SSRIs [17]

The upper respiratory tract being the entry of the SARS COV 2 virus infection the health of the respiratory system is very important in preventing the fatality therefore several clinical trials have suggested an overall effect of yoga training towards improved pulmonary function in patients[16]

Limitations of the study

* Small sample size and less duration of study.
* Also elaborate assessment using diagnostic tools was not done as it was not safe to conduct prolonged interviews.

Conclusion

In this study we observed the various mental health consequences in psychiatric patients who had developed Covid infection.It was observed that psychiatric drugs were often stopped following acquiring Covid infection (40% patients)which could be avoided.Thus more awareness and interaction with psychiatrist by physicians while treating Covid is deemed necessary . These need detailed assessment and appropriate management for better outcome in these patients. Sleep was significantly affected in 80% patients, even those on regular treatment.

The inflammation immune response and cytokine levels have been associated with both depression and stress in a large body of literature.

Hence history of Covid 19 and it's impact should be asked to every psychiatric patient coming to OPD by treating psychiatrist.

None of the patients had significant complications of covid infections, more research on protective effect of SSRI group of antidepressants is required.

Hence a detailed assessment and appropriate management for better outcome in these patients is needed.

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Review Article

Continuous Glucose Monitoring (CGM) Sensor for Better Glycemic Management

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ABSTRACT

Glucose monitoring is a necessary component and cornerstone of glycemic control for patient sand health care provider stoassess progression in a chieving glycemic targets, adjusting medications, detecting hypogly cemicandhy perglycemic excursions of Blood Glucose.(1) Continuous glucosemonitoring (CGM) allows for continuous measurement of glucose concentrations frominterstitial fluid (ISF), and there fore produce sadetailedseries of successive observation sofinterstitial glucose (IG) concentration.(2)

INTRODUCTION

Diabetes Mellitus is metabolic disorder in which the body's blood glucose (sugar) levels rise higher than normal, known as hyperglycemia. In many cases, it can be effectively managed through diet, exercise, medication, and blood glucose monitoring. As a supplement to the traditional finger-prick technology that people with diabetes have relied upon for many years to check their blood glucose levels, continuous glucose monitors (CGMs) offer a more convenient and less painful way for people to track their blood sugar and make positive lifestyle choices.

For many years, in patients with Diabetes Mellitus, Blood sugars has been monitored with conventional glucometer and accordingly diabetic management was advised. Blood glucose measured by glucometer gives point source information of body's blood glucose level and it isn't be reliable

every time, significant barrier to the use of blood glucose measurement by glucometer exist, such as inconvenience and lack of timely and regular feedback. Furthermore, important information regarding glucose trends may be missed.[3]

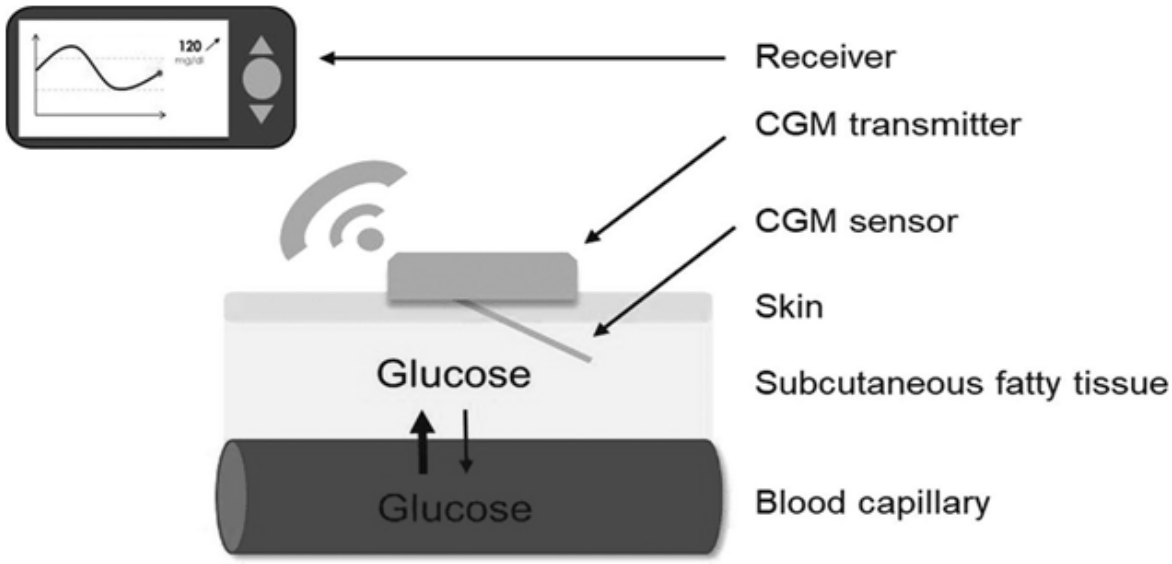
Multiple hourly glucose measurements are required to accurately characterize glucose waveform of hospitalized patient. In reality, the concentration of Blood Glucose is measured only 4-5times / day in the majority of hospitalized patients with diabetes. Only few hospitalized patients are treated aggressively with hourly glucose monitoring.Due to low frequency of monitoring, the risk of severe and prolonged hypoglycemia and hyperglycemia has beenincreased greatly in hospitalized patients.[4]

Another Method like HbA1c also misses to tell day to day changes in glycemic trends of body. It gives idea about average blood glucose for last 3 months based on glycalyted hemoglobin value. This may get altered in conditions such as hemoglobinopathies, hemolytic anemia, recent blood transfusion etc.[5]

WHAT IS CONTINUOUS GLUCOSE MONITORING (CGM)?

Continuous Glucose monitoring system monitors interstitial glucose levels continuously and updates glucose levels on display every 5-10 minutes. Advancements in chemistry, outer membrane biocompatibility, electronics, optics, miniaturization, signal processing, and manufacturing have improved CGM accuracy, stability, sensitivity, specificity, and robustness.[6]

Most of CGM systems consists of monitor which displays information in graphical format, a sensor which is usually inserted subcutaneously & transmitter which transmits data from sensor to monitor. (Figure 1)

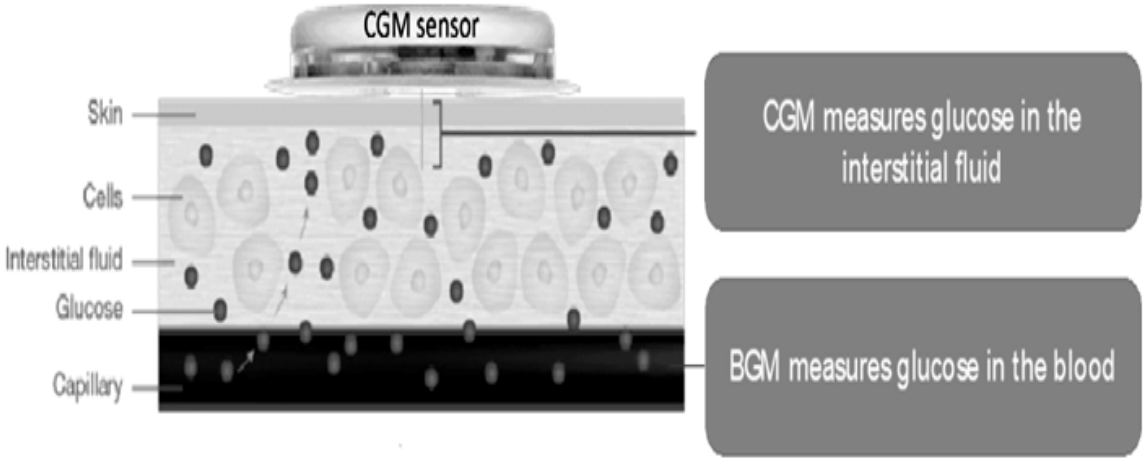


(Figure 1)

All CGM systems alarm when the glucose level exceeds a high or low threshold. Several systems have alarm algorithms that predict the onset of hyperglycemia and hypoglycemia 10 to 30 minutes into the future.Sensitivity and specificity for hypoglycemia detection are improved when the algorithm considers rate of change and threshold. False alarms, missed hypoglycemia events, and data loss can be decreased by averaging multiple CGM sensors.[4]

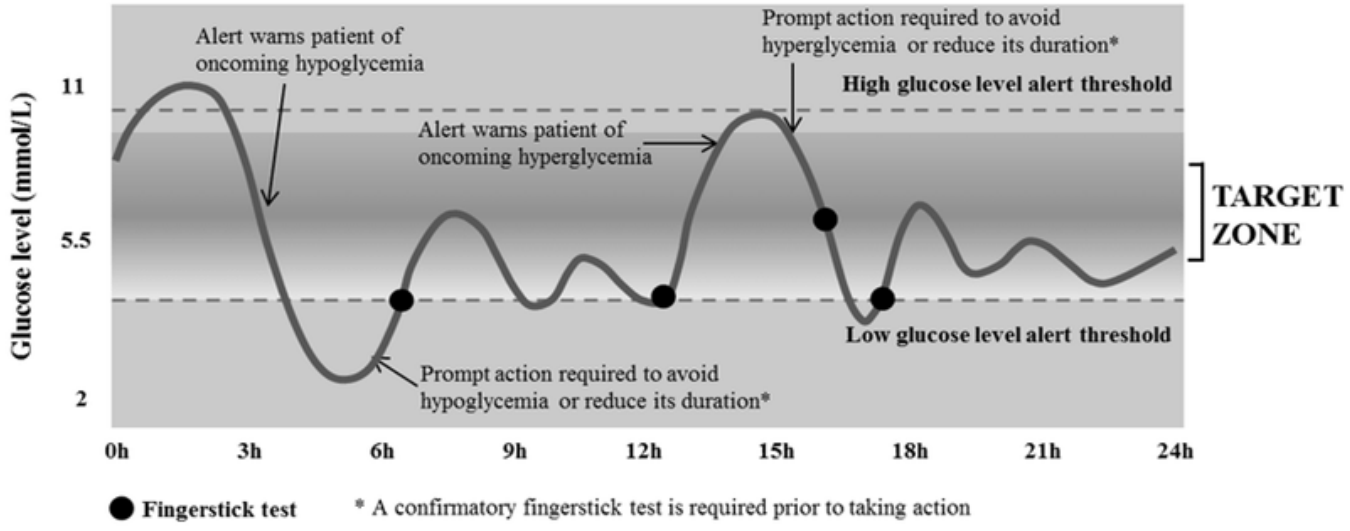
CGM helps in assessing

(1) Glucose concentration (mg/dl or mmol/liter) are detected from interstitial glucose. Interstitial glucose levels may vary from blood glucose likely after eating , after taking medication and after strenuous exercise.[7]However glucose over time diffuses into interstitial fluid from capillaries hence can be measured with CGM sensor. (Figure 2)



(Figure 2)

(2) Glucometrics is analysis of glucose variability in body with time. It helps in better judgment of glycemic variability due to diet& lifestyle of patient.It helps both patient and medical provider to make fine tune adjustments to medication therapy and provide insight to the patient on behavioral changes to achieve glycemic control.[5](Figure 3)



(Figure 3)

(3) Rate of change in glucometrics can help in detecting impending events of hypoglycemia or excursion of hyperglycemic event. So adjustment can be made accordingly with medication and diet depending upon condition of patient.

(4) Real-time CGM measurements can be used during hospitalization of patients with uncontrolled glucose levels such as in Diabetic ketoacidosis, hyperosmolar coma, in patients with drug induced hypoglycemia, in patients requiring regular glucose monitoring like stroke or prolonged NBM status for surgery or patients in postoperative care.

(5) Real time CGM and Retrospective Analysis of Glucometrics can help in adjusting insulin and fixing in diabetic patients. It can also help while shifting patients from insulin to oral anti diabetic agents to maintain optimized dosage.

Considering Cost and number of pricks required for every 5 minutes measurement of Blood glucose levels , CGM is very cost effective and better method for monitoring glucose levels as well as real time & retrospective glucometrics helps in better management.

Real Time CGM as a Part of Artificial Pancreas

Artificial Pancreas consists of three parts which are a CGM sensor which wirelessly updates real time glucometrics to program stored on a smartphone or on an insulin infusion pump. This program calculates how much insulin is needed and signals the insulin infusion pump when insulin needs to be delivered & third is Insulin Pump will delivers required amount of insulin in small doses throughout the day when blood glucose levels are not in target range.[8]

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Review Article

Thiamine Deficiency – Neglected, Underdiagnosed Yet Widely Prevalent

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ABSTRACT

Thiamine deficiency is considered as a widely neglected, misdiagnosed and under treated disorder yet it is highly prevalent around the globe.Clinical manifestations of thiamine deficiency are variable. Also, there is a lack of a readily accessible standardized biomarker of thiamine status which has diminished efforts to diagnose thiamine deficiency and assess its prevalence. Strategies to identify regions at risk of thiamine deficiency through proxy measures, such as analysis of food balance sheet data and month-specific infant mortality rates, may be helpful for understanding the scope of thiamine deficiency. Biofortification, maternal supplementation and parboiling of rice are a few ways that have proven effective in raising

the thiamine status. This article provides an overview of thiamine deficiency disorders, challenges faced in investigating these as well as treatment and prophylaxis of these disorders.

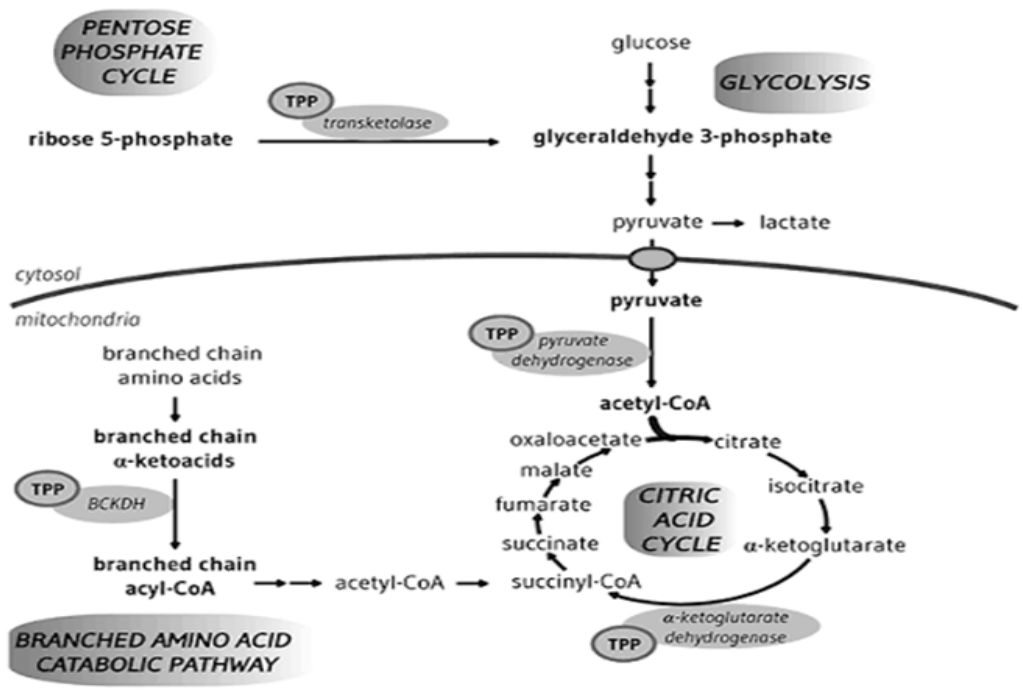
Thiamine :

Thiamine, or vitamin B1, was the first vitamin to be identified. It functions as a catalyst in the generation of energy through decarboxylation of branched-chain amino acids and alpha-ketoacids. It acts as a coenzyme for transketolase reactions. Thiamine is present in the body as free thiamine,

as well as in several phosphorylated forms: thiamine monophosphate (ThMP), thiamine diphosphate (ThDP), and thiamine triphosphate (ThTP). Thiamine pyrophosphate, is the metabolically active form, constituting some 80% of total body thiamine. It is an essential cofactor involved in the metabolism of carbohydrates and amino acids in enzyme complexes such as pyruvate dehydrogenase complex, the -ketoglutarate dehydrogenase complex, and the branched chain -keto acid dehydrogenase complex.

The recommended nutrient intake (RNI) of thiamine is 1.2 mg/day for men and 1.1 mg/day for women, and increases to 1.4 mg/day for pregnant and 1.5 mg/day for lactating women. In infancy, the adequate intake is set at 0.2 mg/day (0"6 months) and 0.3 mg/day(7"12months)[1].

Figure 1. Metabolic Pathways Requiring Thiamin Pyrophosphate



BCKDH, branched chain α-ketoacid dehydrogenase complex; CoA, coenzyme A; TPP, thiamin pyrophosphate.

DEFICIENCY DISORDERS

Overt thiamine deficiency syndromes represent a spectrum of clinical presentations that have been historically divided into two categories based on symptomatology: (1) Wet beriberi, predominantly affects the cardiovascular system or Dry beriberi if it predominantly affects the peripheral nervous system; and (2) Wernicke's encephalopathy (WE) or Wernicke-Korsakoff syndrome which primarily presents with neurological signs (e.g., encephalopathy and peripheral neuropathy forms). The symptoms of thiamine deficiency disorders are given in the table below.

	MAJOR MANIFESTATIONS	MINOR MANIFESTATIONS
INFANT	Sudden heart failure between 1-6 months Incessant crying Cynosis Liver enlargement Bulging fontanelles Nystagmus Muscle twitch Loss of consciousness	Refusal to feed for 48 hrs Repetitive vomiting Constipation Tachycardia without fever
ADULT OR CHILD	Ataxia Nystagmus Confusion, behavior change Impaired consciousness Coma	Bilateral tingling and numbness in limbs Lethargy, apathy Tachycardia without fever Angular stomatitis

WE is classically considered a disease of alcohol dependent patients. However, there are many other conditions that increase the likelihood of developing thiamine deficiency in patients with no history of alcohol misuse. These conditions are associated with decreased access, absorption, storage capability or cellular utilization of thiamine, or increased metabolism or loss of thiamine.

INVESTIGATIONS

Analytical methods.

ThDP assessment

ThDP can be measured directly using HPLC (High-Performance Liquid Chromatography) with either pre-or post-column derivatization coupled with fluorescence detection. It has been available for several decades and is the most common method in current use. In this method, samples are prepared by removal of proteins and derivatization to produce fluorescent thiochrome compounds that are separated on a reverse phase analytical column, then detected and quantified.

Limitations of ThDP assessment.

Specimens should be protected from light as thiamine compounds being photosensitive, must be stored in the dark. To Avoid spontaneous hydrolysis, they require careful procedures for sample collection, transport, and storage at least -20^{o} Celsius as they are labile. Specimens of whole blood must be frozen to ensure lysis of erythrocytes.[2]

Erythrocyte transketolase activity assessment .Erythrocyte transketolase (ETK) activity is suboptimal when thiamine intake is low. Therefore, on the addition of saturating amounts of ThDP there is a change in ETK activity which indicates thiamine functional status.

Limitations of ETKAC assessment.[3][4]

Preanalytical:

As freezing causes erythrocyte lysis, erythrocyte washing must be completed before freezing. Fresh-frozen specimens must be used; freeze thaw cycles can diminish the transketolase activity.

Analytical :

1. There is a requirement for identical temperature for each enzyme assay procedure.
2. There is no gold-standard assay against which to standardize the ETKAC assay.
3. This assay is difficult to standardize.

Interpretational :

ETK activity is influenced by factors other than ThDP concentration, such as age, genetics, and variability in binding of the apoenzyme.

PROBLEMS IN INVESTIGATION

It is generally agreed that discrepancies in data produced by different laboratories and assay methods complicate assessment of the global prevalence of thiamine deficiency; and there is no universally accepted biomarker data thus undermining efforts to determine the burden of disease. Current laboratory reference ranges for thiamine diphosphate (ThDP) are based on the range of thiamine status in populations without thiamine deficiency, and there are no commonly accepted clinically relevant cut-points for thiamine deficiency based on ThDP. A more appropriate cutoff for deficiency should consider clinical manifestations of thiamine deficiency in at-risk populations to better assess and define thiamine deficiency. Also,

owing to the highly variable clinical presentations of TDD and the lack of consensus on clinical case definitions or biomarkers,these conditions are often misdiagnosed, possibly leading to gross underestimation of the prevalence of TDDs in many parts of the world.[3][4]

MRI scans When WE is suspected in the absence (or even presence) of clinical signs, an MRI scan can be useful to assess if there are neurological abnormalities. 'Typical' lesions are seen in only 58% of patients,where there is an increased T2 signal (signifying oedema) in the paraventricular regions of the thalamus and hypothalamus and the periaqueductal region, and the cerebellum and mamillary bodies may be reduced in size. To detect WE, MRI has a sensitivity of 53% but a specificity of 93%.[9][10]

Diagnosis at postmortem examinationAs clinical signs are variable, the diagnosis of WE is often made postmortem. Shrunken and discolored mamillary bodies are the most common abnormality, seen in around 80% of patients affected by WE. Atrophy of the cerebellum and dilation of ventricles are also common.

TREATMENT

Because of uncertainties regarding the diagnostic criteria of TDDs, it may only be possible to diagnosis beriberi after a patient demonstrates significant improvement following treatment with thiamine.

The main approaches to preventing thiamine deficiency affecting large populations are as follows:

- Providing food rations containing adequate amounts of thiamine by regularly including sufficient legumes and vegetables.
- Providing parboiled rice or undermilled rice or other undermilled cereals instead of polished rice or other highly milled cereals.[5]
- Fortifying commodities with thiamine, e.g. cereals and legumes

Treatment of Acute Thiamine Deficiency with Cardiovascular or Neurologic Signs/ Symptoms

200mg intravenous (IV) or orally (PO) thiamine three times daily until symptoms resolve or plateaus, at which time the patient should transition to 10 mg/day oral thiamine until expected recovery is complete.[11]

SUPPLEMENTATION

In circumstances where a population is at high risk of thiamine deficiency or where cases of

thiamine deficiency have already prevailed and all the different alternatives for treatment are not possible the following is useful: Supplementation with thiamine (vitamin B-complex) tablets.

Routine daily supplementation is only a means to treat outbreaks of the deficiency disorder.

Parboiled rice. While rice naturally contains thiamine in its outer husk and bran (aleurone layers), the practice of milling away those layers, or "polishing," to produce shelf-stable white rice renders it very low in thiamine. Parboiling rice before milling reduces this loss, allowing some migration of thiamine from the aleurone layer to the endosperm.[8]

Education of healthcare providers. TDDs are often under-recognized by clinicians, leading to missed or delayed diagnosis. Additionally, it is not uncommon for infants to present with beriberi while their mothers remain asymptomatic. Countries with known cases of TDD should develop culturally significant education tools to assist identify, treat, and prevent suboptimal thiamine status.

PRACTICAL IMPLICATIONS:

- In Alcoholics with suspected WE 250-300 mg parenteral thiamine three times a day (cumulative dose of upto 1 gm/day thiamine) for 5 days should be supplemented whereas if there is low risk of WE then 250-300 mg oral thiamine is given for the same duration followed by 100 mg daily later on.
- Subclinical Thiamine deficiency if detected by the analytical methods mentioned above then 100 mg daily supplement should be given for longer duration.
- Prophylactically vitamin B-complex tablets should be given to pregnant and lactating women to meet the increasing demand during Pregnancy and Lactation.[6][7][8]
- Along with Thiamine Deficiency, concurrent other Vitamin B complex and other Vitamin (A,C,D) deficiency may coexist, which should be rectified and corrected accordingly.
- During Thiamine correction special attention should be paid towards monitoring of serum Electrolytes as potassium dissociates from Extracellular to Intracellular compartment causing Hypokalemia and other electrolytes disturbances. These needs to be corrected accordingly.
- Every patient getting admitted in hospital must be assessed for Vitamins and Micronutrients deficiency and adequate supplementation must be provided to boost immunity and help speedy recovery of such patients. Special attention should be paid for proper nutrition of such patients.

CONCLUSION

It is of utmost importance that thiamine deficiency be diagnosed at an early stage. It is a reversible disorder if diagnosed on time. Around 80% of patients with the condition do not receive a diagnosis, and many cases are only diagnosed postmortem. The delay in identifying and treating the condition can be clinically disastrous, hence assessing the thiamine status of a population should be a priority. New research suggests that even subclinical deficiency may impair neurocognitive development, which brings reason for concern.Increasing the number of countries that conduct thiamine status surveys using a biomarker such as ThDP or ETKAC would substantially improve global prevalence estimates. The reported cases of TDD is a strong indication of thiamine deficiency among the population, and an intervention is likely required. In such cases of known or suspected thiamine deficiency, there are a number of possible interventions, including food fortification and supplementation of pregnant and lactating women and of young children.

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Case Report

A Rare Case of Migrated ERCP Stent in Gall Bladder

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Abstract :

A rare case of stent migration into the gall bladder was encountered in a patient of obstructive jaundice secondary to choledocholithiasis. A 35 year old female patient, was diagnosed with cholelithiasis with choledocholithiasis with obstructive jaundice.The patient underwent Endoscopic Retrograde Cholangio-Pancreaticography with biliary stenting for biliary decompression. The patient was scheduled for interval cholecystectomy 6 weeks later. Intraoperatively it was found that the stent had migrated into the gall bladder.

Laparoscopic cholecystectomy was performed with stent removal.

Endoscopic Retrograde Cholangiopancreatography Stenting is a well-established treatment for benign as well as malignant biliary obstruction. The most frequently encountered complication is stent clogging. Stent migration (proximal or distal), on the other hand, is not very common in literature.

Introduction:

Although the migration of plastic biliary stents has been reported a few times, proximal migration into the gallbladder has been reported only once. This report presents a rare case of migrated biliary stent into the gallbladder where it was identified while cutting the cystic duct.

Case report:

A 35-year-old female was admitted with right upper abdominal pain, nausea and yellowish discoloration of the eyes and urine for 3 days. She reported no significant history of alteration in stool colour, anorexia or weight loss. Laboratory investigations were consistent with the diagnosis of obstructive jaundice, with a serum bilirubin level of 5.5 mg/dL and a serum alkaline phosphatase level of 712 U/L. Ultrasonography (USG) of the abdomen revealed a dilated common bile duct (CBD) with multiple stones and multiple gallbladder stones. The patient was referred for endoscopic retrograde cholangiopancreatography (ERCP) to a gastroenterologist. The cholangiogram showed mild dilatation of the CBD with multiple small filling defects at the lower end [Figure 1]. After confirmation of the guidewire in the CBD, sphincterotomy, papillotomy with balloon sweep was performed to remove the stones. A 7F 10-cm double pigtail plastic biliary stent was inserted in the CBD. Stent deployment was routinely smooth with no hurdles encountered. The post-ERCP course was uneventful. The patient was scheduled for interval laparoscopic cholecystectomy 6 weeks later. Minor symptoms were managed conservatively. Preoperative Abdominal USG revealed multiple gallstones; the biliary stent was noted in situ within the CBD which was otherwise normal. Blood investigations were normal. While performing laparoscopic cholecystectomy, it was noticed that the stent waspresent in the cystic duct and gall bladder and was inadvertently divided while cutting the cystic duct [Figure 2]. An intraoperative cholangiogram was performed to check the CBD and hepatobiliary anatomy; both right and left hepatic ducts were seen clearly along with free passage of contrast through the CBD into the duodenum. The stent was seen in the gallbladder and was removed along with the cholecystectomy specimen. The post-operative course was unremarkable, and the patient was discharged on the 3rd post-operative day.

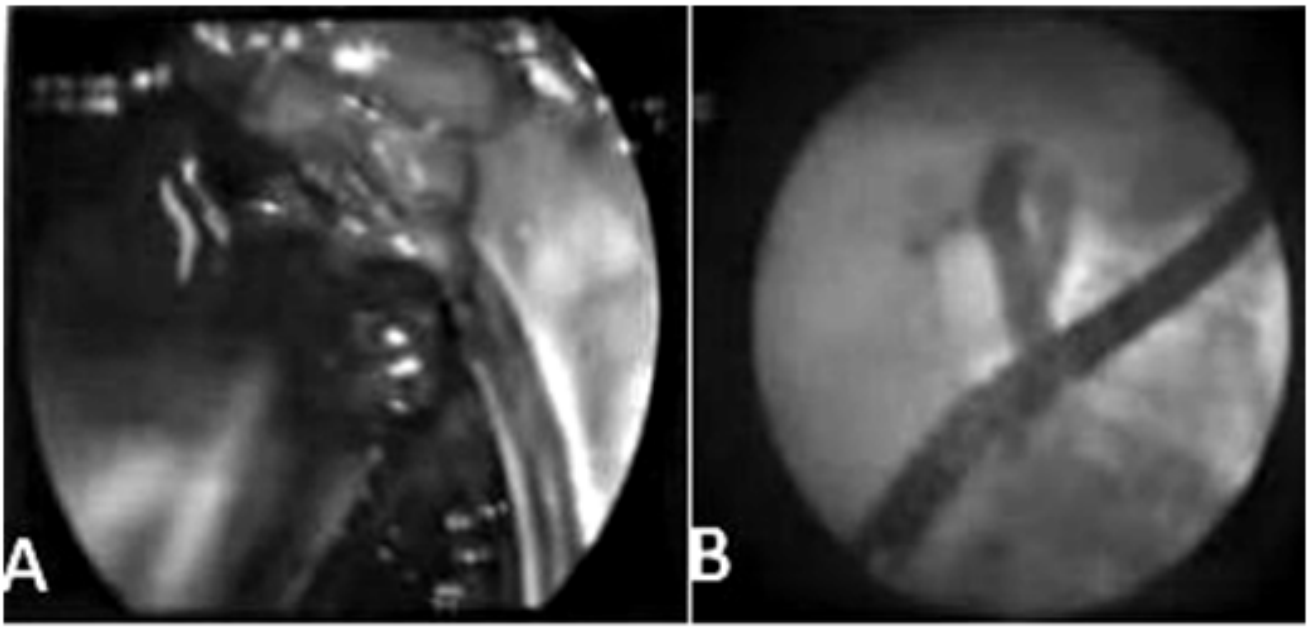

Figure 1 : A) ERCP showing multiple CBD calculi,
B) ERCP stenting and biliary clearance.

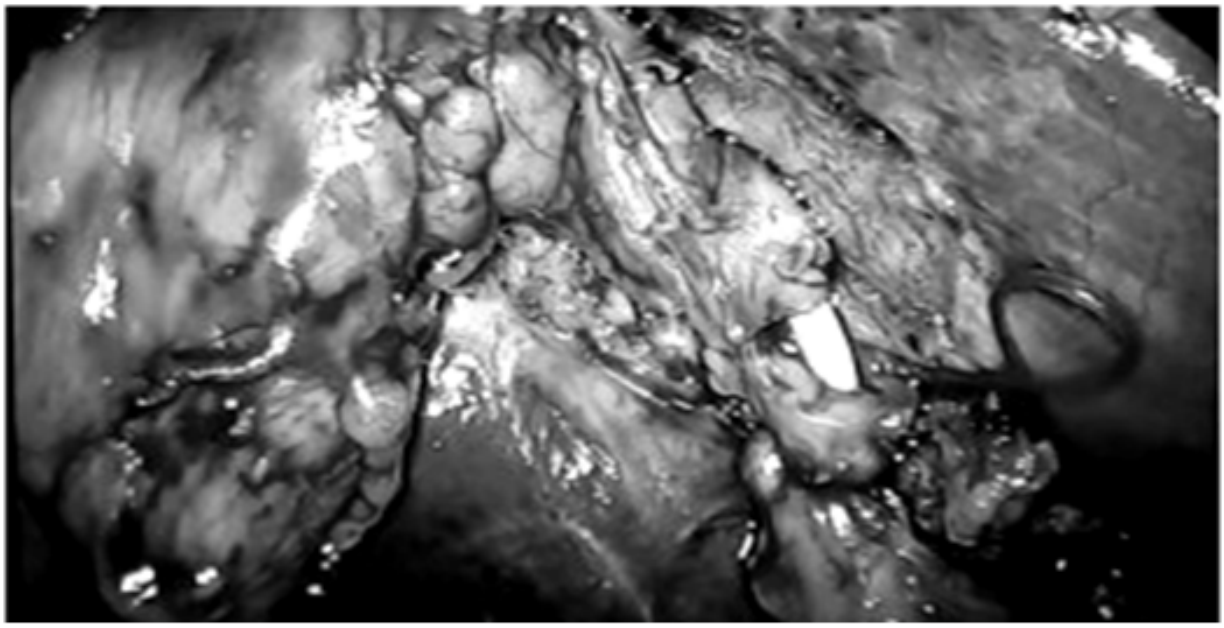

Figure 2 : Migrated ERCP stent in gall bladder encountered during laparoscopic cholecystectomy.

Discussion:

Soehendra and Reynders-Frederix in 1980, were the first to report Endoscopic Retrograde Cholangiopancreaticography (ERCP) with stenting as a treatment modality for obstructive jaundice. Since then ERCP and stenting have become well established as the treatment for benign as well as malignant biliary obstruction.[1] Stent-related complications are primarily due to stent occlusion or stent migration. The most frequently encountered complication is cholangitis; this is frequently the consequence of stent clogging due to microbial biofilm growth and biliary sludge accumulation.[2] Stent migration (proximal or distal), on the other hand, is not very common. Arhan et al. have observed that the overall migration rate for plastic stents in patients with benign and malignant diseases is 8.58% (proximal 4.58% and distal 4.00%). Stent migration can occur both proximally (hepatic ducts) and distally (intestinal lumen).[4,5] Proximal stent migration, although a rare entity, it is comparatively more common than distal migration. This can be attributed to dilated proximal hepato-biliary segment and a narrow distal segment. Proximal migration into hepatic ducts have been previously reported in a few studies, but proximal migration into gall bladder is reported in only one other instance by Yagnik et al.[6]As diameter of cystic duct is comparatively less than common hepatic duct and the slightly angulated anatomy, may be the reasons behind the rarity of stent migration into the gallbladder.

Factors related to stent migration can be divided into two categories: (1) stent-related factors and (2) nature of the disease.

Stent-related factors: These include length and diameter, material, design (straight or double pigtail) and the number of stents (single or multiple)

Nature of the disease: according to the literature, benign biliary disorders have a higher rate of migration.[3] However, proximal stent migration was more commonly associated with malignant strictures, larger diameter stents and shorter stents.[7]Not all stents that migrate cause symptoms, unless there is concurrent stent clogging

and features of cholangitis. Proximal migration of the stents often causes obstructive jaundice and cholangitis, while most distally migrated stents are eliminated spontaneously. Straight stents are more commonly associated with complications, including perforation of the intestine.[8]Yagnik and Joshipura recommend the use of double-pigtail stents to avoid perforation.[8] In this case, proximally displaced segment of the stent was most probably obscured by the acoustic shadowing from the calculi and therefore missed on the pre-operative ultrasound of the abdomen. To the best of our knowledge, proximal migration of a choledochal stent into the gallbladder has been reported only on one other instance in the literature. This is probably the only other report documenting this rare but noteworthy CBD stent migration, and we stress upon the need for awareness in a patient with a relevant history of endoscopic biliary intervention.

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Case Report

A Case of Invasive Mucormycosis in Uncontrolled Diabetes Mellitus

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Abstract

Mucormycosis is a rare but fulminant opportunistic fungal infection, which occurs most often in diabetic and immunocompromised patients.

Dental extractions may create a portal of entry for the fungal infection. In some of The mucormycosis may be the original cause of the pain and can be misdiagnosed as dental pain.

In this case report mucormycosis is reported after dental extraction.

The case we describe exemplify the fulminant mucormycosis of maxillary sinuses after dental extraction.

Patients with uncontrolled diabetic support the findings that this predisposing condition created a suitable environment for the Mucorales growth. These case report emphasise that early recognition and urgent treatment of mucormycosis is necessary to prevent the spread of infection . Therefore, dental surgeons and physicians should become familiar with early diagnosis and should understand importance of early initiation of treatment of mucormycosis.

CASE REPORT :

A 65 year old male with no known history of diabetes or hypertension came to dental opd with history of dental pain on the left side since 5 days it was associated with bleeding from gums.

On examination the left upper molar was showing signs of decay with gingivitis hence tooth was extracted by dentist.

3 day after tooth extraction patient came with

complaints of sever pain at the site of tooth extraction with swelling of left side of face with decreased vision in the left eye, patient also had breathlessness and nausea and vomiting.

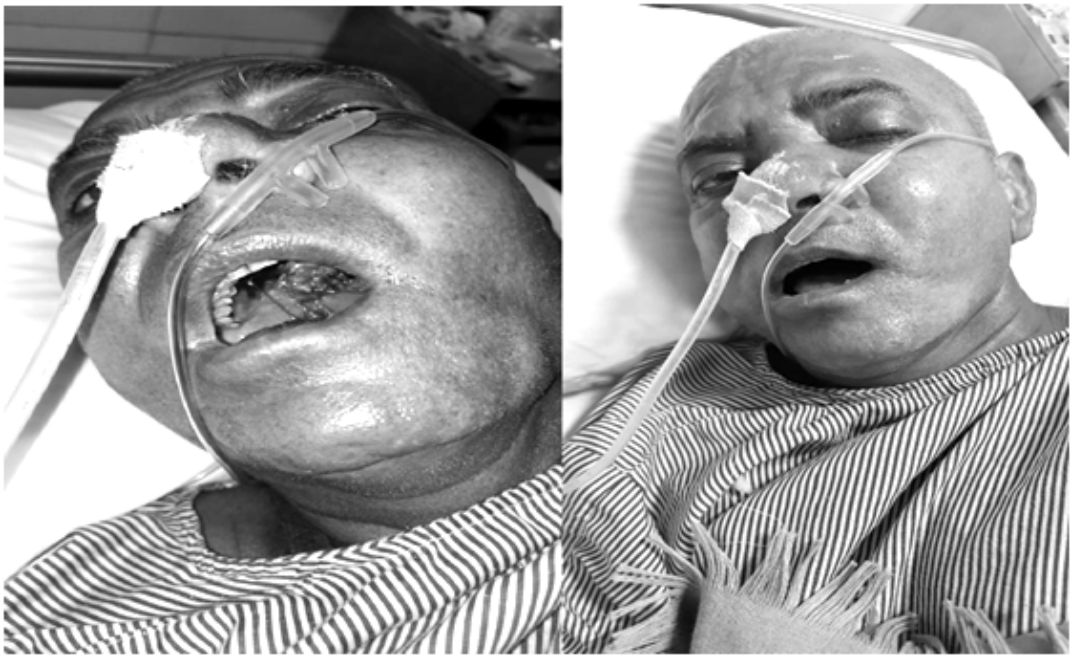
ON EXAMINATION:

Left sided facial swelling was present,
Patient was afebrile.
Pulse-102/min RR-26/min
BP-126/90 mm of hg SPO2-96%
with Room air

On oral examination – crustings were seen on hard palate with a oroantral fistula on postero lateral side of hard palate was seen.

Tongue was dry

On Ophthalmic examination- left pupil was not reacting to light with no perception of light.



seen.

Patient was admitted for further evaluation. Random Blood Sugar Level on admission was 488mg/dl. HbA1c was 13(elevated). With urine ketone positived

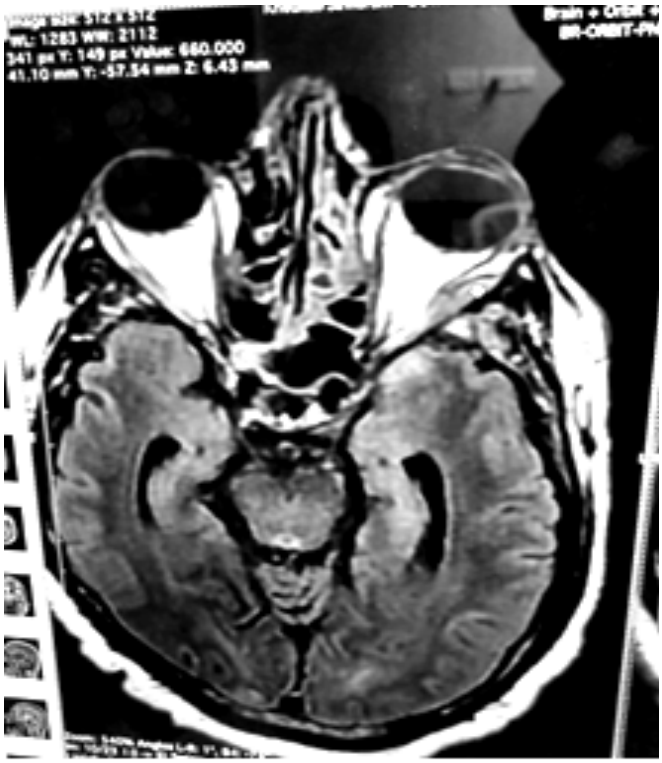
Patient had an episode of general tonic clonic seizure on ûrst day of admission following it the patient was disoriented for 4 hrs patient also had dysarthria . There was no other neuro deûcit

0N INVESTIGATION:

CT Brain+orbit+PNS was done which was suggestive of Pan sinusitis with inûammatory changes and extensions in le‘ lateral extra conal compartment of orbit and premaxillary space and bony erosion in infra temporal fossa with extension in le‘ temporal lobe of brain.

On Functional endoscopic sinus surgery was done which revealed Black crusting seen of posterolateral wall of maxillary sinus.

Histo- Pathological Examination of maxillary palatal bone was suggestive ofFungal infection



Mucormycosis.

TREATMENT

Patient was started on Inj Amphoterecin B ,inj levitracitam & inj mannitol with other supportive treatment.

On day 4 of admission patient had episode of desaturation followed by asystole & died

DISCUSSION

Mucormycosis is a rare and life threatening fungal infection with rapid progression. Death rates greatly depend on the site of infection and the condition of the host.

However, it is estimated to be 40–70 %, even with antifungal therapy [1].

The causative agents of mucormycosis are of the order Mucorales and family of mucoraceae in fungi kingdom. These fungi are often saprophytic organisms and mostly terrestrial in habitat, living in soil or on decaying plant or animal material [2]. These organisms are frequently found to colonize the oral mucosa, nasal mucosa, paranasal sinuses and pharyngeal mucosa of asymptomatic patients [3].

A few species such as Rhizopus, Mucor and Lichtheimia (formerly Absidia) cause almost 70–80 % of mucormycosis in human and animals.

Host factors are important in establishing the infection and the progression of mucormycosis .It generally occurs in immunocompromised hosts as an opportunistic infection [4].

The common risk factors for mucormycosis are poorly controlled diabetes with or without ketoacidosis, prolonged neutropenia, broad-spectrum antibiotic use, severe malnutrition, extensive skin lesions (due to injury or burn) .

The causative agents enter the host tissues after decrease in host defenses or through an invasive portal, such as a dental extraction . The most common presentation in the head and neck region is maxillary and orbital cellulitis

Mucor infections of lungs gastrointestinal tract and maxillary sinuses are reversible but intracranial involvement has a poor prognosis

Hence early diagnosis and aggressive treatment by physicians is crucial.

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Case Report

Airway Management in Paediatric Patient with Huge Antrochoanal Polyp with Subtotal Airway Obstruction.

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ABSTRACT

Anaesthetic management of patients with large antrochoanal polyps needs anticipation and adequate preparation for the associated problems especially in paediatric age group. Presenting as nasal polyp, these may mislead and cause unexpected problems in ventilation as well as intubation. We present a case of 12-year-old female having large antrochoanal polyp undergoing polypectomy under AIRTRAQ guided intubation.

INTRODUCTION

Antrochoanal polyp or Kilian's polyp is a benign solitary polypoid lesion that affects children and young adults mainly. It originates from a hypertrophy of the mucous membrane of the maxillary antrum, grows through maxillary sinus towards nasal cavity and posterior portion of pharynx.

It may be cause unexpected problems for the anaesthesiologist during intubation and ventilation. Therefore, preoperative assessment and appropriate anaesthetic management is very important. This has to be followed by a careful planning, for safe anaesthesia.

CASE REPORT

A 12-report year old,40 kg weight presented in the ENT outpatient department with complaints of right nasal obstruction, difficulty in swallowing andbreathing. (Fig 1) On examination, patient was predominantly a mouth breather. Oropharynx examination was done which revealed right side nostril was totally occluded and the mass was protruding into oral cavity obstructing posterior choana bilaterally. Mouth opening was inadequate and Mallam Patti grade could not be assessed due to mass protruding through oral cavity. Neck extension was normal. Computerized tomography scan of paranasal sinuses reported large non enhancing hypodense lesion occupying entire right maxillary sinus extending into right nasal cavity and oropharynx compromising airway. Systemic examination did not elicit any abnormality. Patient was planned for awake tracheal intubation (ATI) in view of anticipated difficult airway and CT findings.

Preoperative evaluation was done, NBM status confirmed. Written consent was taken. Nebulization with 4% lignocaine and gargles with 2% lignocaine given. Monitoring included ECG, pulse oximetry, blood pressure and capnography.

Patient was given airway block with preservative free lignocaine. She was counselled for ATI; Patient was given conscious sedation with dexmetomidine IV 0.2mcg/kg. Mask ventilation was checked. Airtraq was gently inserted to confirm whether cords could be visualized.(Fig 2) Once visualization of cords was confirmed, inhalational induction was carried out with oxygen and sevoflurane. Patient was intubated with Airtraq with ETT no.5, placement was confirmed with ETCO2.Polyp was removed in total. After haemostasis was achieved, orotracheal suction was done under vision. Patient was reversed and extubated uneventfully and shifted to ward.

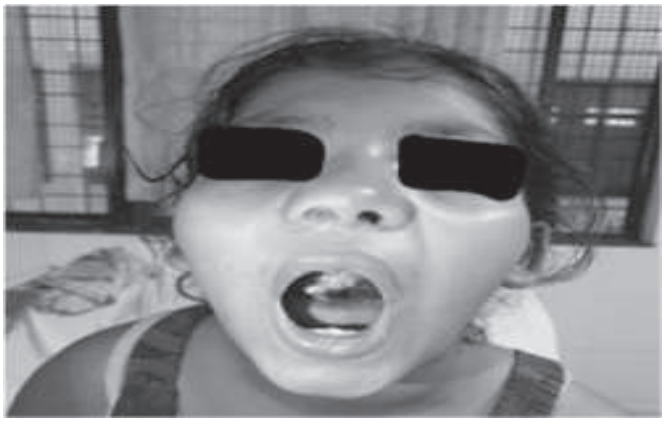

Figure 1 :

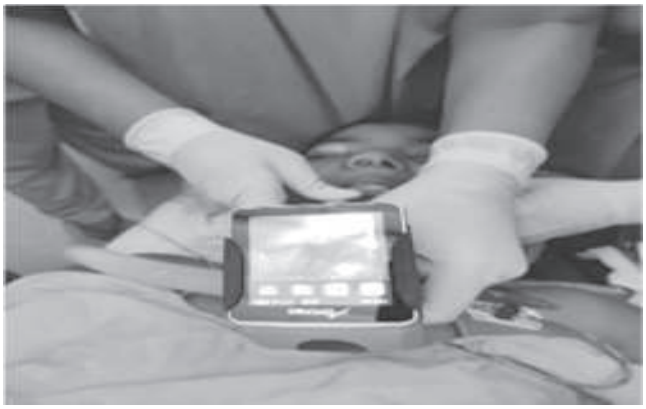

Figure 2 :

DISCUSSION

The antrochoanal polyp is benign solitary polypoidal lesion arising within the maxillary sinus but passing through and enlarging the sinus ostium or more commonly an accessory ostium into the choana and posterior nasopharynx.[1]Antrochoanal polyps in children are uncommon but occur at a higher rate than in the adult population. Antrochoanal polyp are reported to represent one third of all nasal polyps in children.[2]

These patients are usually young ASA I/II patients who are posted for trans nasal endoscopic Sino nasal polypectomy or functional endoscopic sinus surgery (FESS). Large choanal polyps obstructing the oropharyngeal airway have been reported in scientific literature.[3] A similar case of unilateral antrochoanal polyp with bilateral nasal obstruction has also been reported.[4] A history of change in voice should be suggestive of pharyngeal

extension of the polyp. Thorough preoperative evaluation of the airway including indirect laryngoscopy to see the post nasal space and larynx for any growth and CT paranasal sinuses to see the extent of the mass is a necessary prerequisite. CT scans are helpful in attempts to quantify the extent of polyp disease and are essential before any surgical intervention.[5] The polyps are expansible and, in some cases, may expand and erode the skull base[6] CT scan is essential for gathering data on the state of the skull base in these patients. A contrast x-ray neck lateral view may also prove useful in these cases.[7] Although larger masses may prolapse posteriorly and be visible through the mouth as they hang down from the nasopharynx, in our case no mass was visible on oral examination. A similar finding has also been reported by other authors7 which may sometimes lead to judgemental errors. In our case the mass extended from the maxillary sinus ostium into the nasopharynx, and so was not visible on oral examination. Polypoidal masses arising from posterior ethmoidal sinus hang down in the oropharynx and are better visible.

In our case there was oropharyngeal obstruction, due to which ventilation and intubation was difficult. We were prepared with airway aids like, fibreoptic intubation, Airtraq. Awake intubation was preferred choice and FOI was recommended for securing airway in this case. As the patient had bilateral choanal obstruction with oropharyngeal extension, securing airway with FOI would have been difficult. Therefore, we chose Airtraq guided intubation under spontaneous ventilation.

CONCLUSION

We would like to emphasize through this case report that the anticipated airway difficulties could overcome with adequate preparation. In paediatric difficult airway, maintaining oxygenation and appropriate use of technique and available gadgets can aid in successful intubation.

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Case Report

A Rare Case Report of Hemophagocytic Lymphohistocytosis Secondary to Chikungunya Fever

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ABSTRACT

Hemophagocytic Lymphohistocytosis[HLH] is an uncommon hematologic disorder seen more often in children than in adults. It is a life-threatening disease of severe hyperinflammation caused by uncontrolled proliferation of activated lymphocytes and macrophages, characterised by proliferation of morphologically benign lymphocytes and macrophages that secrete high amounts of inflammatory cytokines. It is classified as one of the cytokine storm syndromes. Herein, we report a young male who presented with persistant fever , associated with rash,multiple joint pain , myalgia ,and bilateral pedal oedema was diagnosed with hemophagocytic lymphohistocytosis sencodary to chikungunya fever.

CASE REPORT

Young male presented with persistant fever ,non responding to antibiotics associated with rash ,arthralgia,myalgia with bilateral pedal oedema.On examination,hepatospleenomegaly was present along with bicytopenia and evidence of non palbable rash.With these clinical and laboratory findings,we suspected viral

fever with abnormal functioning of imune system which was later confirmed as HEMOPHAGOCYTIC LYMHOHISTOCYTOSIS by hlh diagnostic criteria with H-scoring system.

CONCLUSION :

In this case report, a young male who presented to us with persistant ,non responding high grade fever with thrombocytopenia wth edema ,myositis with derranged serum Triglyceride and serum FERRITIN with CHIKUNGUNYA ig M positive and no history of similar episodes in the past was found to HLH SECONDARY TO CHIKUNGUNYA VIRAL FEVER with hepatic dysfunction and severe thrombocytopenia

KEY WORDS

Hemophagocytic lymphohistocytosis , chikungunya fever, steroids

INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening condition caused by an overactive, abnormal response of the immune system..

The immune system is a complex network of cells, tissues, organs, and proteins that work together to keep the body healthy. In hemophagocytic lymphohistiocytosis, the immune system responds to a stimulus or 'trigger', often an infection, but the response is ineffective and abnormal.

This ineffective, abnormal response, causes a variety of signs and symptoms, which, if not treated, can potentially become life-threatening.

Some affected individuals may have a genetic predisposition to developing hemophagocytic lymphohistiocytosis. This is known as the primary or familial form. In other individuals, the disorder occurs sporadically usually when there is an underlying predisposing condition or disorder. This is known as the secondary form.Early diagnosis and prompt treatment is essential.

CASE REPORT

A 27-year-old male presented with complaints of persistant fever ,multiple joint pain, severe bodyache and bilateral pedal oedema, generalised weakness for 4 to 5 days.Patient was referred from an general practitioner with blood investigations suggestive of thrombocytopenia with deranged liver function tests and negative dengue profile . patient's wife haad dengue around same time . As they were unable to pin point the crux of the problem, patient was referred to our institution in view of persistent fever, edema and severe thrombocytopenia. On examination he was febrile, pulse rate 124/ min,RR was 22/min with blood pressure 106/70 mmHg, rash [Figure 1] with pedal edema [fig 2] was present. On per abdomen examination, soft ,non tender with Grade 1 hepatomegaly and grade 2 spleenomegaly was present.Initial laboratory tests (Table 1) revealed thrombocytopenia, elevated liver enzymes, negative direct and indirect coombs test and normal serum creatinine.Peripheral blood smear was suggestive of severe thrombocytopenia with mild reduction in rbcs count with normal MCV. PBS

did not show any parasites. Laboratory findings also shown elevated total and MB fraction of CPK ,raised ldh.At this point of time,we came to a conclusion that our patient had acute febrile illness with myosits with myocarditis with thrombocytopenia.patient was given broad spectrum antibiotics with antimalarial treatment.labs for tropical illness sent and Patient now diagnosed with CHIKUNGUNYA fever on third day of admission, But patient continued to be febrile even after medications, Myalgia and arthrlgia was persistant .These features made us to suspect some other/additionaldiagnosis. Ultrasonography (USG) of abdomen and pelvis was suggestive of hepatosplenomegaly.we suspected abnormal immune response to infection. Serum triglyceride and serum ferritin was sent and found to be markedly elevated. According HLH diagnostic criteria and H- scoring system [patient had 189 score which was significant for diagnosis of HLH],we diagnosed the patient to have CHIKUNGUNYA FEVER WITH HEMO-PHAGOCYTIC LYMPHOHISTOCYTOSIS. patient was started on steroids [inj methyl prednisolone 500mg stat dose followed by ,Tab.wysolone 40 mg once a day in tapering doses] along with vit.B12 and Folic acid supplements. Patient's complete blood count improved by then and fever subsided with much more symptomatic improvement was observed 7days after starting the treatment.Serum triglyceride and serum ferritin was reduced after day 5 of starting steroids. He was discharged with the treatment to be continued as advised with tapering steroids. On subsequent follow-up patient was asymtomatic and hemogram showed well preserved hemoglobin, leukocyte and platelet count along with improvement in serum Triglyceride

and serum FERRITIN. When patient has been followed up for almost 1months, we found that he had recovered from symptoms with lab recovery.

Table 1 : Laboratory Investigation Reports

Hemoglobin	15.5 g/dL%
Total leucocyte count	6600
Platelets	67000/mm3
Total protein	6.2
Albumin	3.2
Globulin	3.0
Total bilirubin	1.3
Direct	0.7
SGOT	224
SGPT	112
ALP	72
Urine analysis	NAD
Dengue	NEGATIVE
crp>90	
Hemoglobin	13.64g/dl
Total leukocyte count	7300
Platelets	**66000**
Coomb's test(direct/indirect)	Negative
Total bilirubin	1.5mg%
Direct bilirubin	0.7mg%
SGOT	300 IU/L
SGPT	160 IU/L
Alkaline phosphatase	86IU/L

Table 2 : Laboratory investigations during admission

Cardiac enzyme	
Cpk mb	84
Cpk total	3868
Sr.ldh	1549
Pbs for mp	negative
Rmt	negative
CHIKUNGUNYA ig m	**POSITIVE**
SERUM TG	662
SERUM FERRITIN	7258
SERUM FIBRINOGEN	380
USG [A+P]	SPENOMEGALY with grade 1 hepatomegaly

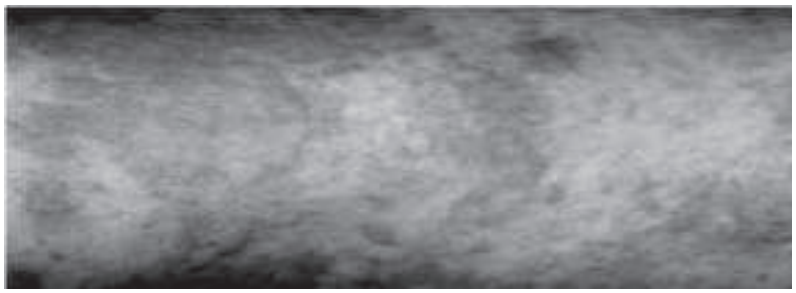

Figure 1 :
Demonstration of Rash

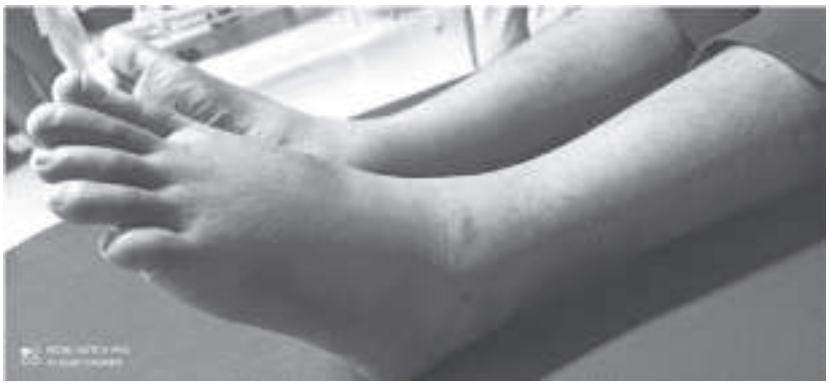

Figure 2 :
Demonstratio of Edema

DISCUSSION

We report a young male who presented with persistant fever ,with myalgia ,oedema,with hepatosplenomegaly with raised serum TG,FERRITIN with CHIKUNGUNYA ig M positive.. Diagnosis as SECONDARY HLH was suspected by clinical features, laboratory investigations and confirmed by HLH diagnostic criteria and H-SCORING system.

Haemophagocytic disorders arise from defects in critical regulatory pathways responsible for the natural termination of immune and inflammatory responses with a subsequent failure of a homeostatic removal of cells that are superfluous or dangerous to the host organism. The role of granule (perforin/granzymes)-mediated cytotoxicity is important in both the killing of infected cells and the termination of the immune response [3]. Genetic HLH can be attributed to a defect in the mechanism of granule (perforin/ granzymes)- mediated cytotoxicity.

The pathophysiology of acquired HLH is not fully understood. It certainly involves the interaction between T cells and macrophages but this does not exclude a genetic predisposition in affected cases.

The persistent activation of lymphocytes is the result of an uncontrolled immune response causing a hypersecretion of pro-inflammatory cytokines such as IFN [6], TNF [7], IL-6 [8], IL8, IL-10 [8], IL-16 [9], IL-18 [10] and macrophage-colony-stimulating factor (M-CSF). IL-18 appears to play a crucial role particularly in autoimmune related HLH. In addition, higher levels of IFN and IL-10 are associated with a worse prognosis in childhood HLH [11]. The activation of T lymphocytes also results in an elevation of soluble IL-2 receptor [12] which is one of the diagnostic criteria of HLH and correlates with prognosis [13]. Furthermore, the presence of a specific TNF polymorphism has been associated with an increased susceptibility to reactive HLH in certain asian population[14].

The proloferation of histocytes is characterised by an up-regulation of adhesion and MHC class 1 and 2 molecues [15] on monocytes / macrophages and expansion of inflammatory monocytes[increase in CD14/CD16 expression[16].The persistent activation of lymphocytes [17] and proliferation of histocytes leades to organ infiltration and hemophagocytosis of various blood cells by macrophages present in bone marrow , lymph node and spleen.

CLASSIFICATION:

1. Molecular Diagnosis consistent with HLH
2. At least 3 of 4
   Fever
   Splenomegaly
   Hepatitis
   Cytopenias
3. At least 1 of 4
   Hemophagocytosis
   Heperferritinemia
   Increased soluble IL 2R alpha
   Absent or very decreased NK cell function
4. Supportive HLH
   Hypertriglyceridemia
   Hypofibrinogenemia
   Hyponatremia

1 - PRIMARY [genetic] HLH :-

a) Familial HLH [4 subtypes]
b) Immune Deficiency Syndromes.

2 - SECONDARY [acquired] HLH :-

a) Infections,
b) Autoimmune Disease,
c) Malignancies
d) Transplantation.

HLH DIAGNOSTIC CRITERIA 2009

Criteria for diagnosis of HLH18,19 ,proposed by the Histocyte Society,include clinical ,laboratory and histopathological feature.fever and splenomegaly are most common signs,but hepatomegaly, lymphadenopathy and rash also seen.

TREATMENT

For patient with reactive HLH associted with pathogen other than EBV, supportive care and treatment of underlying infection is associated with recovery in60-70%. The pooe prognosis suggest that ,patient should be treated initially with combination chemotheropy and immunotheropy,regardless of wheather they are thought to have familial HLH. Chemotheropy with etoposide, anti-thymocyte globuline, dexamethasone cyclosporine A is recommended, with the use of intrathecal methotrexate in patient with neurologic symptoms or persistent csf abnormilities. Allogenic bone marrow transplantation is theropy of choice in patient with familial HLH , who attain remission.20

CONCLUSION

Haemophagocytic syndrome is a rare, often fatal disease frequently triggered by viral infections, most notably EBV. The treatment of the underlying infectious trigger alone tends to lead to suboptimal results. Early recognition and prompt treatment have been shown to improve prognosis with severe cases often requiring chemotherapy with or without BMT. Clinicians, therefore, need to be alert and suspect this entity in patients with high fever not responding to broad-spectrum antibiotics, organomegaly and characteristic laboratory and histologic findings.

Our case report suggests that when a young patient presents with persisistant fever, rash, hepatosplenomegaly and lab findings with bicytopenia, raised serum triglyceride, ferritin, hepatitis, one must suspect HLH. HLH is a uniformly fatal disease if left untreated. Short course of androgenic synthetic steroids is helpful in the treatment when the patient is not affordable for the definitive treatment.

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Case Report

Obesity Hypoventilation Syndrome – A Silent Pandemic

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ABSTRACT

In a setting of a pandemic like COVID we often tend to misdiagnose other causes of breathlessness one of the many being obesity hypoventilation syndrome. This is a case of a morbidly obese woman presenting with breathlessness, anasarca and who was being treated as COPD. Thorough workup revealed patient had obesity hypoventilation syndrome. Patient was treated for the same and discharged.

INTRODUCTION

Obesity hypoventilation syndrome (OHS) is defined as a combination of obesity (body mass index ~*30 kg·m2,daytime hypercapnia (arterial carbon dioxide tension ~*45 mmHg) and sleep disordered breathing, after ruling out other disorders that may cause alveolar hypoventilation. OHS prevalence has been estimated to be <"0.4% of the adult population. OHS is typically diagnosed during an episode of acute-on-chronic hypercapnic respiratory failure or when symptoms lead to pulmonary or sleep consultation in stable conditions. The diagnosis is firmly established after arterial blood gases and a sleep study. The presence of daytime hypercapnia is explained by several co-existing mechanisms such as obesity-related changes in the respiratory system, alterations in respiratory drive and breathing abnormalities during sleep. The most frequent comorbidities are metabolic and cardiovascular, mainly heart failure, coronary disease and pulmonary hypertension. Both continuous positive airway pressure (CPAP) and non-invasive

ventilation (NIV) improve clinical symptoms, quality of life, gas exchange, and sleep disordered breathing. CPAP is considered the first-line treatment modality for OHS phenotype with concomitant severe obstructive sleep apnoea, whereas NIV is preferred in the minority of OHS patients with hypoventilation during sleep with no or milder forms of obstructive sleep apnoea.

HISTORY :

53-year-old morbidly obese female was brought by son to casualty with chief complains of Shortness of breath for 6 months associated with generalised swelling of body for one week. Patient was apparently alright 6 months back when she started feeling shortness of breath which was gradual in onset, intermittent in nature, and was aggravated while she slept on the bed.After a few months patient preferred sleeping with multiple pillows under her head in order to avoid breathlessness. This was also associated with swelling of bilateral lower limb which started at ankle joint 1 month back and progressively increased up to knee joint 2 weeks back. It then increased up to the face causing facial puffiness for last three days.She also has complaints of generalized weakness and lethargy in activities of daily living. On enquiry, patients relative gave a history of day time sleepiness and excessive snoring at night. She was alsotaking ayurvedic treatment for the same. The relative noticed that she was falling asleep even while cooking food and having a bath. She was broughtto emergency medicine department in view of breathlessness and generalized swelling all over the body.COVID Rapid antigen test was done which was negative and hence patient was shifted to MICU for further management. Patient had history of hospitalization in view of similar complaints 3 years back. She has been intermittently having breathlessness in these two years and also hasgained weight. She is a known case of Hypertension since 2 years non - compliant to medication. She is a habitual tobacco chewer and drinks alcohol daily however last drink was 2 years back.H/O Biomass fuel exposure present. She had excessive day time sleepiness especially after having meals over the past 4 – 5 year which was associated with snoring present and had constipation and irregular bowel habits.

EXAMINATION :

Patient is drowsy, prefers to sleep, easily arousable obeys verbal commands once alert.BMI – Obese 34 kg/m2 Waist Hip Ratio – 0.9, madarosis, macroglossia{Mallampatti Grading 2}and shortneckpresent,pedal oedema – Present up to knee pitting in nature, Facial puffiness present. VITALS - Temp: 99 F,Pulse: 88 / min regular, RR – 26 /min {shallow; use of accessory muscles of respiration present}, BP – 128/70 mm of Hg {Right arm supine position}, SPO2 86 % on Room Air, JVP – Raised 7cm. On RS examination chest expansion was decreased breath sounds were alsodecreased. On CVS examination patient had loud P2 and right parasternal heave.Other systems were normal.

INVESTIGATIONS :

Electrocardiogramhad Low voltage complexes, Right bundle branch block andRoentgenogram -Suggestive of widened mediastinum.Patients' routine labs hemogram, renal function tests, liver function tests were normal.She had subclinical Hypothyroidism {TSH-5.4}. Arterial blood gas analysis revealed type 2 respiratory failure with a pCO2 of 84. Echocardiography revealed RA RV Dilated, good LV systolic Function EF 60 %, paradoxical septal motion, moderate to severe PAH.

MANAGEMENT :

Patient was taken intermittent Positive

pressure non-invasive ventilation. CO2 washout was promoted up to 60 as more decrease would decrease the respiratory drive of the patient. Sequential Arterial blood gas analysis were done to monitor the same. Suitable antibiotics were added to treat underlying lower respiratory tract infection like Inj. Ceftriaxone 1g iv 1—0—1,Tab. Clarithromycin 500 po 1—0—1 X 6 days.Inj. Furosemide 40 iv 1—1—0 as the patient was in Cor 1, Aspirin + Atorvastatin 75/10 po 0—0—1Tab. Acetazolamide 250 mg po 1—0 –1 to prevent raised Intracranial tension was given. Tab. Modafinil 100 mg po 1—0—1. Tab. Thyroxine 50 mcg before breakfast for subclinical hypothyroidism. Syp Milk of Magnesia for constipation.

After stabilization patient was subjected to Polysomnography to establish a diagnosis of Obesity Hypoventilation syndrome which revealed Alveolar hypoventilation index of 12.1per hour {Mild}. Respiratory parameters showed 97 events which included 40 Obstructive apneas and 57 hypoapneas with nadir oxygen of 42%. Patient was discharged with home bipap to prevent apneas at night thereby improving quality of life

DISCUSSION :

Our patient presented with a complex of signs/symptoms consistent with previous descriptions of malignant obesity hypoventilation syndrome (MOHS), with a BMI greater than 40 kg/m^2 and a PaCO2 greater than 45. With increased prevalence of morbid and super obesity, we are treating an increasing number of individuals with BMI > 40 in our tertiary care ICU. These complex patients present many diagnostic, treatment, and ethical challenges.

The morbidly obese with respiratory issues are often erroneously diagnosed with asthma and COPD. Notably, our patient was also previously diagnosed with asthma and treated for COPD exacerbation, although a diagnosis of obstructive sleep apnoea and OHS is better supported by the clinical picture. Physicians should be more vigilant for the diagnosis of OHS in this setting.

Pulmonary hypertension is the condition likely to be directly linked to chronic hypoventilation; it is highly prevalent with about half of patients with OHS exhibiting pulmonary hypertension. NIV may be more effective in improving pulmonary hypertension than CPAP. CORRAL et al. hypothesised that NIV may allow for a better control of nocturnal hypoventilation than CPAP, consequently leading to a more significant reduction in pulmonary hypertension. They observed significant improvement in pulmonary hypertension with NIV only and these improvements were accompanied by a concomitant reduction in left ventricular hypertrophy and improvement in exercise performance. However, daytime blood pressure did not improve. Although few short-term studies have specifically assessed the impact of NIV on blood pressure and other cardiometabolic or inflammatory markers, none have reported any significant improvement with NIV alone. Therefore, to further reduce the high cardiovascular and metabolic burden in OHS, there is a need for a multimodal therapeutic approach combining home NIV/CPAP with lifestyle interventions and rehabilitation programmes

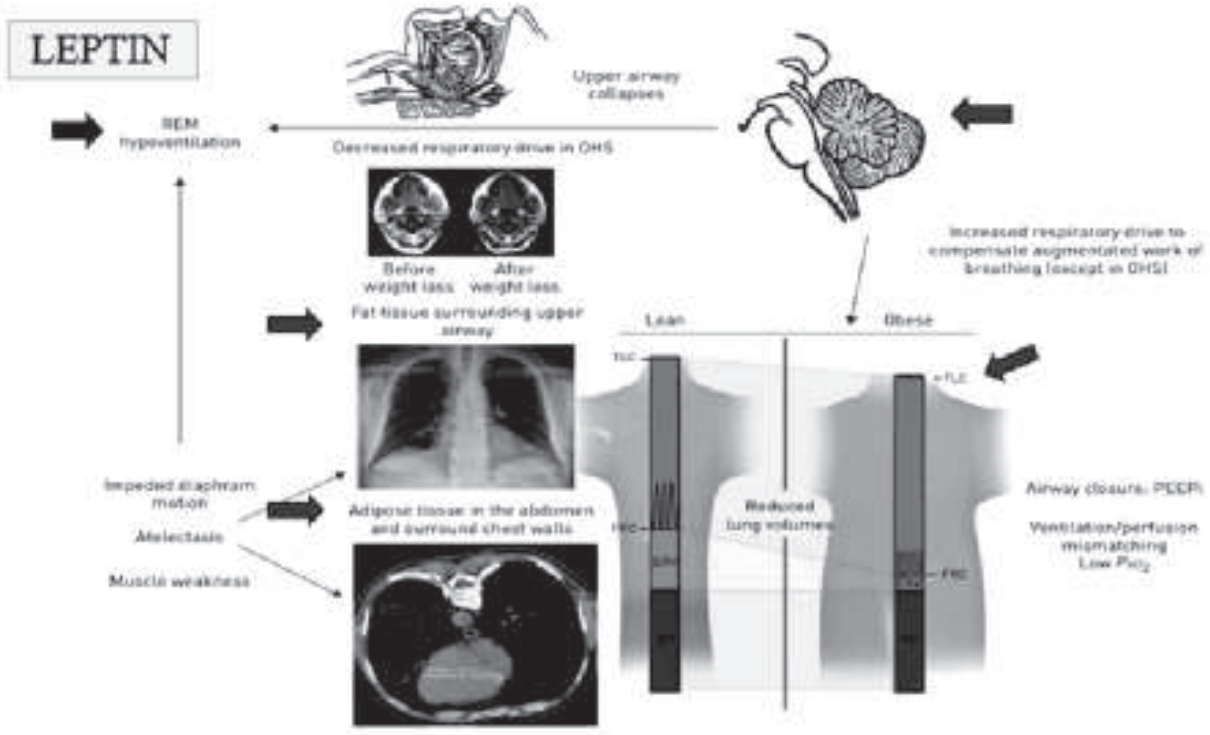

Figure 1- MECHANISM OF OBESITY HYPOVENTILATION SYNDROME

MECHANISM OF OHS - Pathophysiology of obesity hypoventilation syndrome (OHS). The implicated mechanisms leading to daytime hypercapnia are, potentially, the obesity-related changes in the respiratory system, central hypoventilation, obstructive sleep apnoea's and hypoventilation during sleep, mainly during rapid eye movement (REM). PEEPi: intrinsic positive end-expiratory pressure; PaO2: arterial oxygen tension; FRC: functional residual capacity; ERV: expiratory reserve volume; RV: residual volume; TLC: total lung capacity.

OBESITY RELATED CHANGES excess of adipose tissue in the abdomen and surrounding chest wall reduces lung volume, namely functional residual capacity with a significant decrease in the expiratory reserve volume impeding diaphragm motion, reducing lung compliance and augmenting lower airway resistance.

CENTRAL CONTROL: the majority of obese patients develop increased respiratory drive to compensate and thus remain eucapnia.

During REM sleep there is generalized postural muscle atonia and the persistence of ventilation is primarily dependent on diaphragm activity and central drive.

ROLE OF LEPTIN ; The repetitive occurrence of hypoventilation, initially limited to REM sleep, induces a secondary depression of respiratory centers leading to daytime hypercapnia and obesity hypoventilation syndrome The high prevalence of central hypoventilation during REM sleep in OHS is hypothesized to be due to dysfunction of the leptin axis.

Leptin acts as a powerful stimulant of ventilation and in OHS the central resistance to leptin may lead to a deterioration of respiratory control and also favors cardiometabolic consequences.

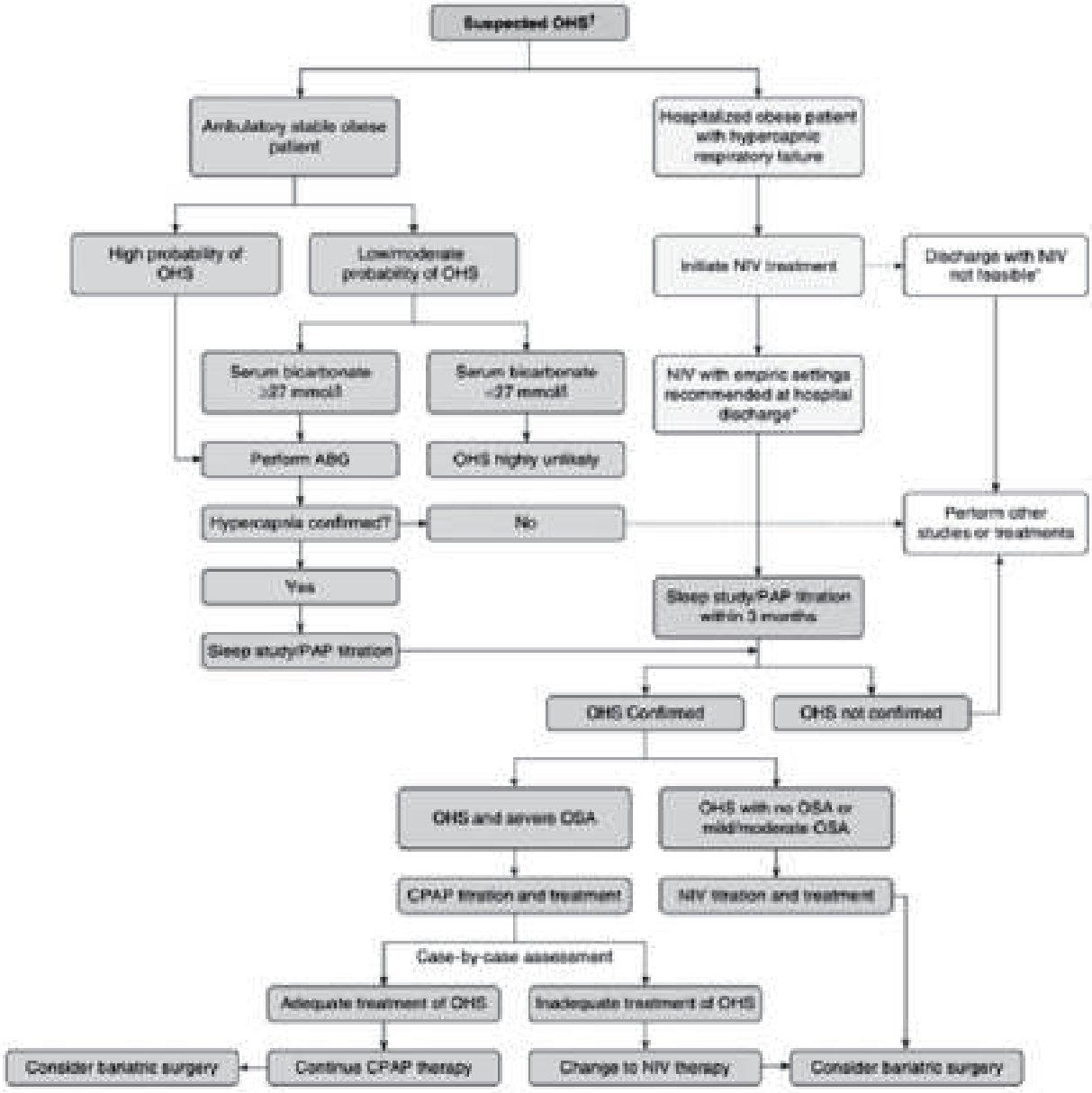

Figure 2- MULTIDISCIPLINARY APPROACH IN MANAGEMENT OF OHS

CONCLUSION

We present a case of a patient with an unusually high BMI, who presented to our medical ICU with a clinical picture consistent with malignant obesity hypoventilation syndrome (MOHS). As obesity rates continue to increase nationwide, more morbidly obese patients will require intensive care, and MOHS will be encountered with increasing frequency. Physicians should be aware of this relatively common syndrome with high morbidity and mortality, so that correct diagnosis and prognosis can be established. This report adds to the understanding of illness in extremely obese critical care patients.

Further study is needed to characterize the optimal treatment of this condition, including medical and surgical therapies. Given the complexity of these patients, a multidisciplinary care approach is necessary forbest outcomes.

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Case Report

Evaluation of a Young Female with Abdominal Pain & Hematuria

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INTRODUCTION

Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare acquired clonal hematopoietic stem cell disorder that leads to abnormal red cell membrane lysis due to activation of membrane attack complex(MAC)[1].

Its characterized by complement mediated intra-vascular hemolysis, pancytopenia & thrombosis.

Its prevalence in population world-wide is 0.5-1.5 per million people[2].

Intervention is warranted in severe cases of PNH, MDS, aplastic anemia & severe hemolysis.

Danazol is used in cases of bone marrow failure along with cyclosporine or steroids. Treatment itself can lead to fatal complication like acute pancreatitis.

CASE:

A 32 years old female patient resident of Gultekadi, Pune had come to SKNGH on 5/12/2020 with c/o passage of red colored urine since 4 days. She passed red colored urine in the morning on waking up which decreased as the day progressed & was not associated with abdominal pain [FIGURE. 1.4]. She had multiple similar episodes in the past 1 year & had past history of multiple blood transfusions & jaundice.

She was vitally stable; Pallor with mild icterus was present. She has no signs of heart failure & there was no organomegaly.

Laboratory reports were suggestive of pancytopenia & Indirect hyper-bilirubinemia; Antinuclear Antibodies were positive,Hemoglobin electrophoresis pattern was normal& Bone marrow studies were suggestive of compensatory response to anemia. Ham's serum test was negative but PNH clones were identified on flow cytometry.

She was started on Cap.Danazol 200 mg BD, Tab.Deflazacort 30 mg OD tapered to 6mg ODgradually over 1 year. After 6 months she landed up in renal failure due to pigment nephropathy but creatinine resolved with adequate hydration.

On 20/09/21 she got readmitted to SKNGH with complaints of severe abdominal pain, multiple episodes of vomiting & hematuria.

History of amenorrhea was present since 1 year & hirsutismwas also present. [FIGURE. 1.3]. Abdominal pain which she had was initially attributed to uremic gastritis.

She was dialyzed on urgent basis in view of oliguria & Acute Kidney Injury (Sr. Creatinine 17.7). Abdominal pain didn't relieve post hemodialysis & she started having green colored vomiting which was bilious.

She was kept NBM & Ryle's tube was inserted. Serum amylase &serum lipase were sent. Urgent USG abdomen was suggestive of acute pancreatitis.

INVESTIGATIONS

	3/12/2020	20/9/2021	23/9/2021
HEMOGLOBIN(gm/dL)	8.0	5.4	
TLC(cells/mm^3)	2400	4180	
PLATELET COUNT(lacs/mm^3)	0.93	1.2	
Serum urea(mg/dL)	31	139	196
Serum creatinine (mg/dL)	1.1	15.9	17.7
Total Bilirubin(mg/dL)	3.8	4.6	
Direct Bilirubin(mg/dL)	1.0	1.1	
SGOT (IU/L)	45	428	
SGPT(IU/L)	42	256	
Alkaline Phosphatase(IU/L)	100	70	
HAMS SERA TEST	Negative		
Sr. AMYLASE(IU/L)			3370
Sr. LIPASE(IU/L)			12478
URINE ROUTINE	RBCs abundant Proteins trace		

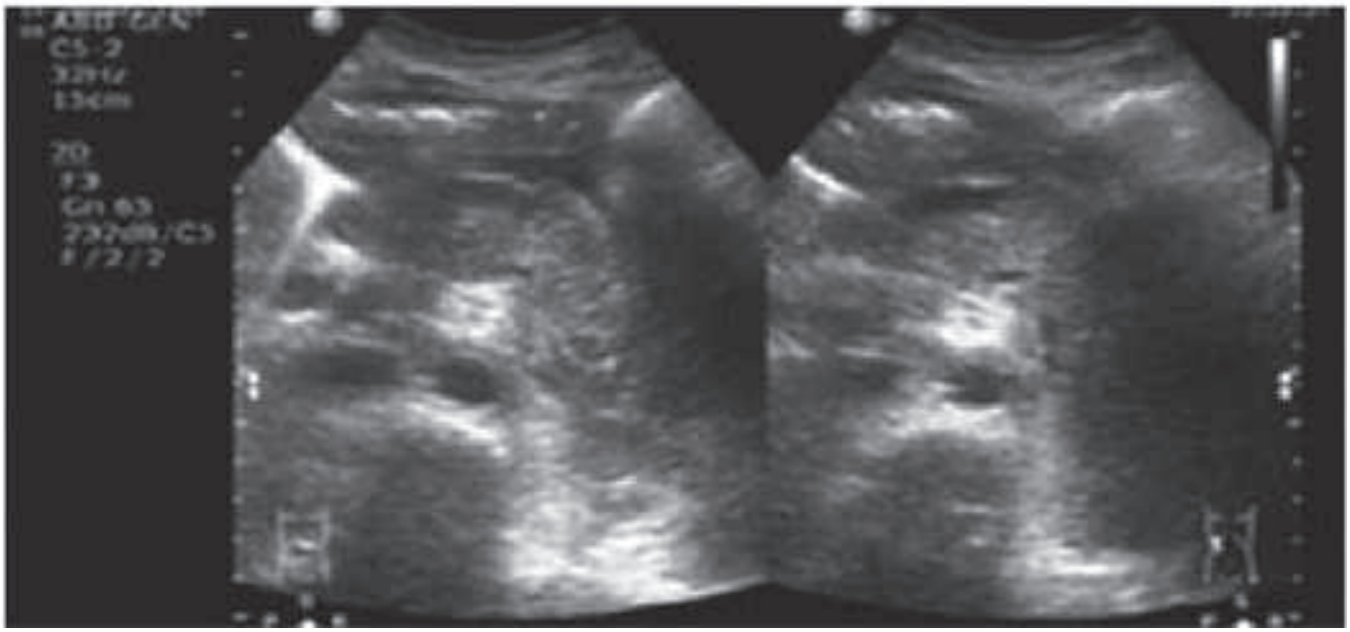

Figure : 1.1

USG(A+P) s/o Bulky head of pancreas with heterogeneous echotexture.
Bilateral raised cortical echogenicity s/o medical renal disease

::PNH- FLOWCYTOMETRY REPORT ::

SPECIMEN: Peripheral blood.

ANTIBODIES:

Immunophenotypic analysis was performed using gating antibodies CD45, CD33, CD235a and GPI - linked antibodies CD59, CD157 as well as fluorescent aerolysin (FLAER).

FLOW RESULTS:

Cells Type	Deficiency	Result
Red blood cells	Type I (Normal CD59 expression)	87.6%
Red blood cells	Type II (Partial CD59 deficiency)	2.7%
Red blood cells	Type III (Complete CD59 deficiency)	10.5%
Monocytes	FLAER/CD157 deficiency	84.1%
Granulocytes	FLAER/CD157 deficiency	92.1%

DIAGNOSIS: WBCs: PNH CLONE IDENTIFIED (84.1% in monocytes and 92.1% in granulocytes). RBCs: PNH CLONE IDENTIFIED (Type III - 10.5%, Type II -2.7%)

IMPRESSION:

Flow cytometric analysis shows a PNH clone within 10.5% of the RBCs, 92.1% of granulocytes and 84.1% monocytes. These findings are consistent with a diagnosis of paroxysmal Nocturnal Hemoglobinuria (PNH).
A potential difference in the clone size between the white blood cells and the red blood cells may be due to hemolysis and/or recent transfusion.

Figure : 1.2

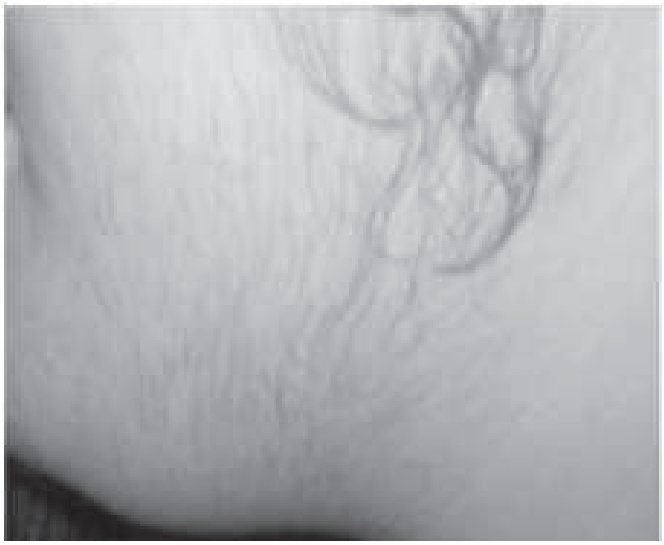

Figure : 1.3

Figure : 1.4

TREATMENT GIVEN

Considering cause of pancreatitis Danazol was stopped and started on injectable antibiotics (Inj. Meropenem) in renal dose and continued on oral steroids along with other supportive care.

DISCUSSION

Danazol is associated with multiple side effects including hepatitis & pancreatitis. [3]

Few case reports suggest pancreatitis can be caused by Danazol when used for treating endometriosis, SLE, Bone marrow failure. [4]

Danazol is included in the list of medications definitely associated with pancreatitis. [5]

Hypo-estrogenic& androgenic effect was seen in form of hirsutism & amenorrhea in this patient.

Deflazacort is oral steroid & corticosteroids can also cause pancreatic injury aggravating acute pancreatitis. Hence steroid pulse therapy as treatment for persistent hematuria & underlying AKI wasn't advised.

After ruling out all other causes of Pancreatitis with relevant history & investigations, cause was ascertained to Drug Induced Pancreatitis i.e. Danazol.

Eculizumab (Human monoclonal antibody against complement protein C5) can be considered for improvement of Quality of Life & reduce hemolysis in patients of PNH.

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5] D. Ksiqdzyna/ European Journal of Internal Medicine

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Case Report

Evisceration in Ocular Trauma Management

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ABSTRACT :

Despite the eye being surrounded by orbital bones and protective mechanisms such as the blink reflex, it is vulnerable to trauma. The two key issues to consider when presented with a case of ocular trauma are the visual potential of the eye and the risk of sympathetic ophthalmia. The Ocular Trauma Score can be used to assess the visual potential of the injured eye. Surgical management may be either repair or removal of the eye (evisceration or enucleation). Herein we describe a case of ocular trauma and the decision-making process in the management of the injury.

It is also important for non-ophthalmology doctors to be aware of the prognosis and the subsequent management that will ensue. Herein we describe a case of ocular trauma and the decision-making process in the management of the injury.The key issues to address are the visual potential of the eye, risk of sympathetic ophthalmia and informed patient preference. It is important for non-ophthalmology based doctors to correctly identify ocular trauma and they can use the simple Ocular Trauma Score to provide the patient with an idea of their prognosis prior to onward referral to ophthalmologist

BACKGROUND :

Occular trauma is one of the most under-recognized causes of vision loss in the developed world.

The ocular trauma can be used to predict the visual outcome of patients after open-globe ocular trauma.

It is important for doctors to accurately diagnose ocular trauma and penetrating eye injuries to enable prompt referral to ophthalmology for management.

It is important for non-ophthalmology doctors tobe aware of the prognosis and subsequent management that will ensue.

Here in we describe a case of ocular trauma and the decision making process in the management of the injury.

Evisceration

Evisceration is the surgical removal of the contents of the eye, leaving the white part of the eye (the sclera) and the eye muscles intact.

The Ocular Trauma Score (OTS)

The Ocular Trauma Score (OTS), which is used to predict the visual outcome of patients after open-globe ocular trauma. The score's predictive value is used to counsel patients and their families and to manage their expectations.

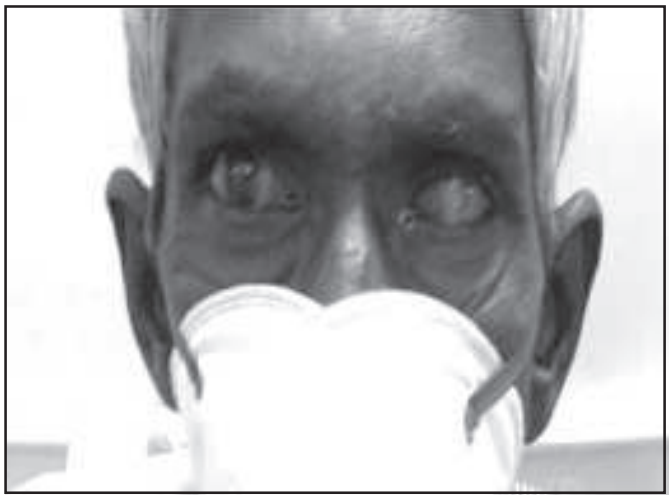
Sympathetic ophthalmia (SO

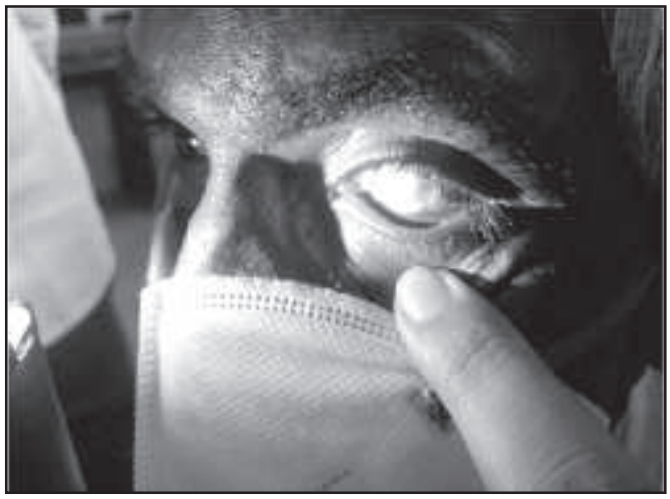
Sympathetic ophthalmia (SO) is a bilateral diffuse granulomatous intraocular inflammation that occurs in most cases within days or months after surgery or penetrating trauma to one eye. The incidence of SO ranges from 0.2 to 0.5% after penetrating ocular injuries and 0.01% after intraocular surgery.

The key issues to address are the visual potential of the eye, risk of sympathetic ophthalmia and informed patient preference. It is important for non-ophthalmology based doctors to correctly identify ocular trauma and they can use the simple Ocular Trauma Score to provide the patient with an idea of their prognosis prior to onward referral to ophthalmologist.

Case Report

A 60 year old male was referred to ophthalmology department i/v/o trauma to eye by a tree branch.Patient came with decreased vision in right eye, history of injury to right eye by a tree branch. On examination patient's visual acuity in right eye[affected eye] was no perception to light.Anterior segment of right eye showed signs of cornea melt and bluish shining tissue just beneath the cornea.After examination he was diagnosed with pseudocorna in right eye with cicatricial uveal tissue, anterior staphyloma..There was ocular hypotony with subconjunctival heamhorrage. Patient had history of chronic alcoholism, S/P surgery for sigmoid volvulus 1 month back. Patient had generalized swelling of hands and feet. On admission patient's haemoglobin count was 4.0, platelet-64,000, RFT and LFT were deranged. Patient would need systemic management for stabilization of all conditions to get fitness for evisceration surgery. Patient was diagnosed with Chronic Kidney Disease and went through 2 rounds of dialysis. Post the 2nd round of dialysis his haemoglobin reached 12gms/dl and other vitals were stable. Patient was given fitness for Right eye Evisceration under general Anaesthesia under High risk. Prior to further intervention a number of issues neede to be considered in consultation with the patient, principally the visual potential of eye and the risk of sympathetic ophthalmia.





Investigation

Occular Trauma Score

Raw score sum	OTS score	NPL	PL/HM	1/200–10/200	20/200 to 20/50	>20/40

Table 1. [1] [2] [3]
Computational method for deriving the OTS score

Initial visual factor	Raw points	
Raw score sum = sum of raw points		
A. Initial raw score (based on initial visual acuity)	NPL =	60
	PL or HM =	70
	1/200 to 19/200 =	80
	20/200 to 20/50 =	90
	> 20/40 =	100
B. Globe rupture		–23
C. Endophthalmitis		–17
D. Perforating injury		–14
E. Retinal detachment		–11
F. Relative afferent pupillary defect (RAPD)		–10

Table 2. [1] [2] [3]
Estimated probability of follow-up visual acuity category at 6 month

Raw score sum	OTS score	NPL	PL/HM	1/200–10/200	20/200 to 20/50	>20/40
0–44 1	73%	17%	7%	2%	1%	
45–65	2	28%	26%	18%	13%	15%
66–80	3	2%	11%	15%	28%	44%
81–91	4	1%	2%	2%	21%	74%
92–100	5	0%	1%	2%	5%	92%

NPL = Nil Perception of Light; PL= Perception of Light; HM = Hand Movements

Discussion

Timeline of Events:

1. Decide on eye removal surgery.
2. Day of surgery.

3.1 Week follow up after surgery.

4.2 Months follow up with occuloplasty surgeon.

5. Start prosthesis fitting with occuloplasty surgeon
6. Life with an ocular prosthesis.

An evisceration removes the intraocular contents (light blue) while preserving the remaining scleral shell, extraocular muscle attachments, and surrounding orbital tissues.[8][9][10]Evisceration is a surgical options for severely traumatised eyes to reduce the risk of sympathetic ophthalmia.

It has been suggested that the chances of developing sympathetic ophthalmia are very low when surgery is performed within 10 days of the initial trauma.[8]

However, evisceration has not always been a favourable treatment option. In 1887, Frost[9] reported a series of patients who developed sympathetic ophthalmia following evisceration. Furthermore, in 1974, Green *et a*[10] reported four cases of sympathetic ophthalmia following evisceration but did not document how many eviscerations were performed. However, more recent large-scale retrospective analyses have reported no cases of sympathetic ophthalmia following evisceration.[10]The choice of procedure requires an active discussion with the patient, considering risks and benefits of each procedure.

An evisceration is not indicated in the presence of uveal malignancy. It is important to give the patient time following the primary repair to make an informed decision with regard to their treatment options and to come to terms with the prospect of living without an eye. In the present case, the patient opted for an evisceration procedure.

Steps in evisceration surgery.[10] a. Sclera is cut 360 degrees around the surgical limbus. b. The scleral rim attached to cornea is grasped with forceps and the intraocular contents are removed with an evisceration spoon. c. The uveal contents and cornea are prepared to submit to pathology. d. The scleral shell is scrubbed with alcohol to remove residual uvea. e. Relaxing incisions are cut in the sclera. f. A spherical implant is placed into the scleral shell, scleral dog-ears are trimmed, and

sclera is closed with simple interrupted 5-0 polyglactin sutures. g. Tenon capsule is closed with a running 5-0 polyglactin suture. Conjunctiva is closed with a running 6-0 plain gut suture. h. A conformer is placed behind the eyelids.

Sympathetic Ophthalmitis

Sympathetic ophthalmia (SO)

Sympathetic ophthalmia (SO) is a bilateral diffuse granulomatous intraocular inflammation that occurs in most cases within days or months after surgery or penetrating trauma to one eye. The incidence of SO ranges from 0.2 to 0.5% after penetrating ocular injuries and 0.01% after intraocular surgery.

Very rarely, sympathetic ophthalmia occurs as early as 1 week or as late as 30 years after the initial injury or surgery.

The incidence is difficult to determine due to its rarity. The estimated incidence is 0.1% following intraocular surgery and 0.2–0.5% (2–5 in 1000) for open globe injuries.[3] In 2000, Kilmartin *et*[6] *al* reported that retinal surgery was the main risk factor for the development of sympathetic ophthalmia. The incidence of sympathetic ophthalmia following penetrating trauma was 0.14%.[7] It would appear, however, that evisceration after severe ocular trauma is an acceptable option with a low risk of sympathetic ophthalmia.

Conclusion:

Surgical decision-making in ocular trauma is largely based on surgeon preference and experience along with patient's preference. We recommend evisceration over in cases of reliable patient follow-up due to the low incidence of sympathetic ophthalmia. The key issues to address are the visual potential of the eye, risk of sympathetic ophthalmia and informed patient preference. It is important for non-ophthalmology based doctors to correctly identify ocular trauma and they can use the simple Ocular Trauma Score to provide the patient with an idea of their prognosis prior to onward referral to ophthalmology

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