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Otorhinolaryngology

RHINO-CEREBRO-ORBITAL MUCORMYCOSIS IN COVID19 PANDEMIC- OUR EXPERIENCE IN A TERTIARY CARE INSTITUTE

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ABSTRACT **Introduction-** Mucormycosis seemed to be an emerging infection caused by the fungi of the class of Zygomycetes in India associated with COVID19 infection. This study was done to know the diagnostic modalities, treatment outcome and role of serum ferritin levels as a prognostic marker of mucormycosis patients in our hospital **Materials and Methods-** This observational review study was conducted in the Department of ENT in a tertiary medical college, from 23/05/2021 to 01/09/2021, over 13 admitted patients of age group 40-60yrs with proven rhino-cerebro-orbital mucormycosis. Information on clinical features, microbiological & pathological and radiological findings, treatment, and outcome was extracted from the records obtained from histopathological examination (HPE) and culture & sensitivity reports. Primary outcome at 6weeks was determined.Results and analysis-13 patients were diagnosed with rhino-cerebro-orbital mucormycosis based on microbiological and/or HPE of the clinical samples. Most commonly affected age-group was between 40 years and 60 years. 85% patients had presented with uncontrolled diabetes mellitus and 77% had a history of COVID19 pneumonia. All the patients were put on anti-fungals. 12 patients were managed by combined medical and surgical intervention and among them only 1 patient had undergone orbital exenteration. Only 1 patient died among all of them. **Conclusion-** Mucormycosis is an important differential diagnosis in progressive soft tissue infections and deep organ infection.

KEYWORDS : Mucormycosis, rhino-cerebro-orbital, COVID19

INTRODUCTION-

Mucormycosis (zygomycosis) seemed to be an emerging angioinvasive infection caused by the ubiquitous filamentous fungi of the Mucorales order of the class of Zygomycetes in India associated with 2nd wave of COVID19 infection.

Management of mucormycosis is traditionally multi-modal. It involves the reversal of underlying risk factors, aggressive and often repeated debridement and prompt antifungal treatment.

MATERIALS AND METHODS-

The present study was conducted in the Department of ENT in association with the Department of Pathology, Microbiology and other clinical departments (Medicine/ Ophthalmology/ Radiology) in a tertiary medical college, from 23/05/2021 to 01/09/2021, over 13 admitted patients of age group 40-60yrs. This is a restrospective observational review of patients diagnosed with proven rhino-cerebro-orbital mucormycosis.

All the patients had undergone an MRI Brain/ PNS/ Orbit → diagnostic nasal endoscopy (DNE) guided debridement → tissue sent for KOH mount & culture/ sensitivity (C/S) (in normal saline) and HPE (in formal saline).

Fig-1: DNE was done and guided debridement done by doing middle meatal antrostomy (MMA), anterior & posterior ethmoidectomy and sphenoidotomy and this sample is sent for KOH mount & C/S and HPE

Fig-2: Saboraud's Dextrose Agar Media to grow Mucor

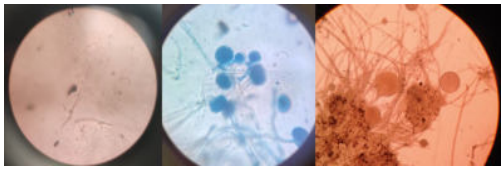


Fig-3: On KOH MOUNT- Microscopic Examination of the debrided tissue revealed Broad Aseptate Filamentous Hyphae (Lctophenol Cotton Blue) (40X) and CULTURE confirmed it to be Mucormycosis.

Information on clinical features, microbiological & pathological and radiological findings, treatment, and outcome was extracted from the records. Primary outcome at 6weeks was determined.

RESULTS AND ANALYSIS-

1. CLINICAL PRESENTATION-

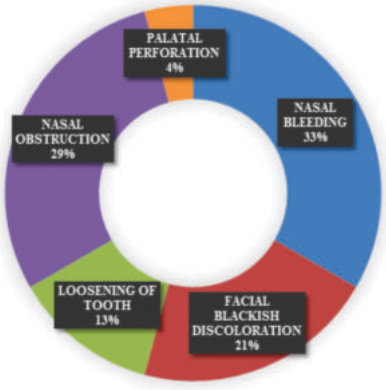


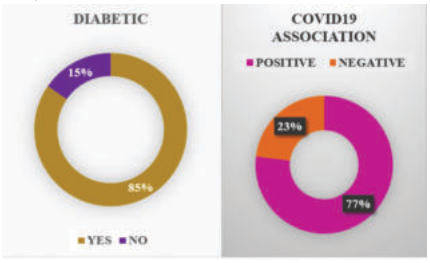
Chart-1

Most of the cases presented with nasal bleeding (33%) followed by nasal obstruction (29%), facial blackish discoloration (21%), loosening of tooth (13%) and also one patient had palatal perforation (4%).

Fig-4: A & B- Facial Blackish Discoloration; C- Palatal Perforation

2. ASSOCIATED FACTORS-

Among all patients, 85% were diabetic and 77% had COVID19 associated (among them 85% were treated with steroid during the illness period).



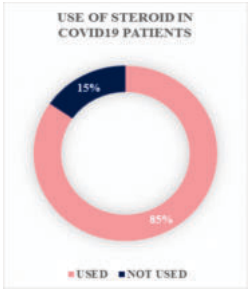
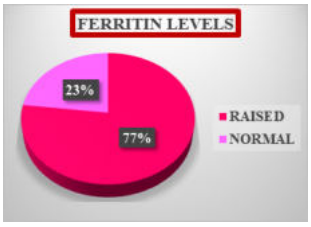


Chart-2

3. ROLE OF FERRITIN AS A PROGNOSTIC MARKER-



The patients of COVID19 pneumonia with raised ferritin levels (77%) had more severe & worse mucormycosis prognosis later on.

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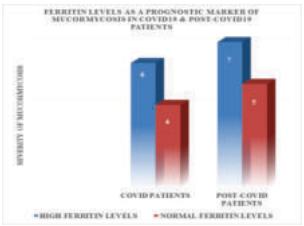

Chart-4

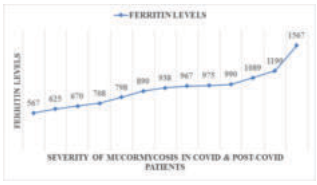

Chart-5

4. MRI REPORTS- On MRI Brain, PNS and Orbit (with Gd contrast and fat suppression)- Ill-defined iso to hypointense soft tissue in then orbit extending to right maxillary and ethmoidal sinuses, likely fungal invasion with orbital involvement.

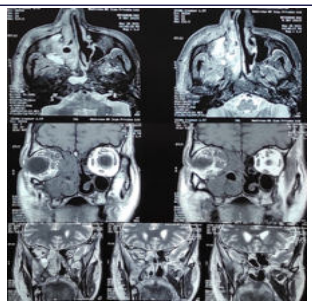

Fig-5

5. SURGICAL MANAGEMENT DONE-

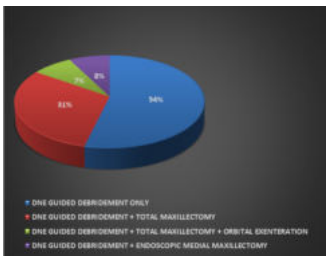

Chart-6

54% patients undergone DNE guided debridement, 31 % had total maxillectomy done and orbital exenteration and endoscopic medial maxillectomy was done for one patient each.

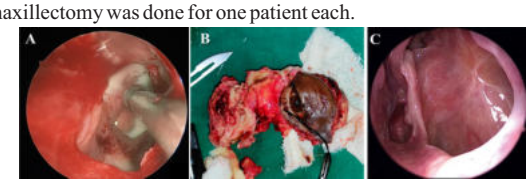

Fig-6: A) DNE guided debridement; B) Total Maxillectomy + Orbital Exenteration; C) Endoscopic Medial Maxillectomy

6. OUTCOMES AT THE TIME OF DISCHARGE

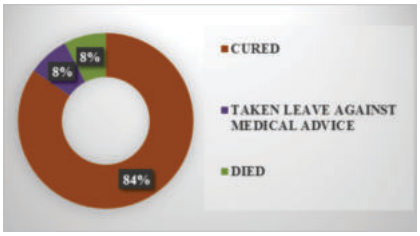

Chart-7

- 11 patients were cured, one had succumbed to death and another one had taken leave against medical advice.
- Patients were declared cured on the basis of last negative histopathological, microbiological (both C/S and KOH Mount) and radiological (MRI) reports.

DISCUSSION-

Rhino-Orbito-Cerebral Mucormycosis (ROCM) may initially present with nasal blockade or congestion, nasal discharge (bloody or brown/ black) with facial pain or numbness or swelling, headache, orbital pain followed by toothache, loosening of maxillary teeth, jaw involvement, blurred or double vision; paresthesia, fever, skin lesions, thrombosis & necrosis (eschar).(1) (2)

The prevalence has been estimated to be 0.005–1.7 per million population worldwide before the pandemic and in India, it is nearly 80 times than in other parts of the world, 0.14 per 1000.(3)

Biochemical alterations underlying COVID19 creating suitable environment for growth & propagation of mucormycosis are mainly immunosupression by drugs or cytokine storm, optimal for secondary growth of opportunistic organisms; endothelial damage and direct alveolar damage-port of entry; raised glucose levels- utilized by sugar fungi; raised ferritin level for optimal growth; raised body temperature- optimal for thermotolerant organisms; prolonged ICU stay with high acuity; hematological alterations; and, reduced pH.(4)

Free available iron is an ideal resource for mucormycosis. Hyperglycemia induced glycosylation of transferrin and ferritin reduces iron binding and increases free iron. Moreover, increase in cytokines in patients with COVID-19 especially IL-6, increases free iron by increasing ferritin levels due to increased synthesis and decreased iron transport. Concomitant acidosis increases free iron furthermore by the same mechanism and additionally by reducing the ability of transferrin to chelate iron.(5)

Serial CT and/or MRI (Gd-enhanced T2 images) may help in assessing the extent and progression of the disease. The definitive diagnosis of fungal infection can be made based on direct microscopy of nasal swab or surgical/ DNE specimens with KOH mount and microbiological/histological confirmation. The presence of broad, non-/ pauci-septate fungal hyphae with right angled branches, necrotising granulomatous inflammation and angio-invasion supports the diagnosis.(6)

The mucormycosis outbreak control is definitely an interdisciplinary approach, requiring an effective communication, awareness, and close coordination within the fraternities like clinicians (dentists, ophthalmologists, ENT specialists, radiologists, pathologists, physicians, infectious disease specialists), research team, environmentalists and hospital administration.(7)

Medical management includes use of Amphotericin B [Liposomal amphotericin B (L-AmB) (preferred treatment)- 5-10mg/kg/day; Amphotericin B deoxycholate (D-AmB)- 1.0-1.5 mg/kg/day; Inj. Amphotericin B Lipid Complex- 5mg/kg/day] [if intolerant to Amphotericin B- Capsofungin/ Posaconazole (300mg twice on day 1, followed by 300mg daily)] for 3-6 weeks, followed by consolidation therapy (posaconazole) for 3-6 months. Adequate hydration to be maintained and renal function and serum potassium to be monitored throughout the course.(8)

Surgical management(9) includes DNE guided debridement, if nose/ sinus involved without any bony erosion of maxilla/ zygoma/ orbital floor; in cases of maxillary involvement, total/ partial maxillectomy to be done; orbital exenteration only indicated in cases of total ophthalmoplegia/ orbital tissue necrosis/ vision loss/ chemosis.

All our patients had undergone either only DNE guided debridement or some forms of radical surgeries associated such as total/ medial/ partial maxillectomy along with the medical management. Only one patient had orbital exenteration done.

Environmental cleanliness (no exposure to decaying organic matters), controlling hyperglycemia and regular glucose monitoring in COVID patients requiring steroid therapy, optimized steroid use, high suspicion and early detection of signs and symptoms of mucormycosis and universal masking will prevent further spread of the disease in the community.(8,9)

CONCLUSION-

- Mucormycosis is an important differential diagnosis in progressive soft tissue infections and deep organ infection.
- COVID19 patients with history of oral/ injectable steroid use and type-2 diabetes mellitus, presenting with nasal obstruction, bleeding, loosening of tooth and/ or facial blackish discoloration should be evaluated for mucormycosis with MRI, microbiological (KOH mount and C/S) and pathological (HPE) evidences.
- Serum ferritin is an important prognostic marker as its raised levels in COVID19 patients predispose them more to mucormycosis.
- Patient should undergo some form of surgical management (endoscopic/ radical as per the extent of the disease) along with medical management (Inj. Amphotericin-B/ T. Posaconazole) to completely get rid of the disease.

DECLARATIONS-

- Funding: None stated by the authors.
- Consent: Informed consent of the patient was obtained for publication of the case.
- Conflict of interest: None stated by the authors.
- Ethical approval: Not required.

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