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COVID-19 Associated Rhino Orbital Mucormycosis-Case Report (Post COVID Psunami of Black Fungus)

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Abstract: ***Coronavirus disease 2019 (COVID-19) is known to be associated with a myriad of viral, fungal, and bacterial co-infections. Rhino-orbital mucormycosis is a rare, an aggressive angio-invasive fungal infection which tends to affect patients with a history of diabetes (especially with ketoacidosis), chronic steroid use and on immunosuppressive drugs. It involves paranasal sinuses and orbital cavity, and may extend into the cerebral parenchyma. Clinical presentations include regional facial, paranasal sinus, dental and orbital pain, orbital edema, proptosis, decreased vision and ophthalmoplegia. Contrasted computed tomography (CT) of the orbits and/or paranasal sinuses and Magneticresonance imaging (MRI) can be helpful in diagnosis. Early recognition of symptoms and prompt initiation of treatment, both with intravenous lipid-soluble amphoteracin and aggressive surgical debridement are crucial in improving clinical outcomes.***

Keywords: Rhino-orbital mucormycosis, angio- invasive

1. Introduction

Rhino-orbital cerebral mucormycosis is an uncommon infection caused by the angiotropic fungus belonging to the order Mucorales. Zygomycetes are irregularly branched pauciseptate molds that reproduce sexually via the formation of zygospores. Subsequently, zygospores are divided into Mucorales and Entomopthorales. [(1).] Mucorales, are commonly found in the soil, on plant surfaces, decaying fruits, veggies and animal manure. Mostly mucor molds are incapable of infecting humans because they do not grow at body temperature. However, thermo tolerant species, such as those isolated from COVID-19 - associated mucormycosis (CAM) cases in India, can cause opportunistic infection; and when they do, it's serious. ([2])

Mucormycosis involves invasion of the blood vessels by fungal hyphae, causes necrotizing vacuities and thrombosis resulting in extensive tissue infarcts and necrosis. It is a systemic infection with a fulminant course and a high mortality risk that can affect lungs, kidney, bone, bladder, gastrointestinal tract, skin, heart and brain etc. Rhino-orbital mucormycosis is a dreaded condition with mortality rate of approximately 50% even with treatment. The disease usually starts in the nose and sinuses after inhalation of fungal spores. It proliferates and spreads to the paranasal sinuses and then to the orbit by direct extension or through hematogenous route. It can also spread to the brain. Mucormycosis is known to affect immunocompromised patients particularly those with uncontrolled diabetes (60%) [(3)]. Moreover, it is surging as a COVID-19 associated infection at unprecedented rates throughout India and raising alarm bells around the world. Suspicion or diagnosis of rhino-orbital cerebral mucormycosis is a medical as well as surgical emergency. [(2)] A high index of suspicion among caregivers, a rapid workup, and early initiation of amphotericin and surgical debridement in all suspected cases are a must for improved outcomes.

Epidemiology

There is an increase in the incidence of mucormycosisglobally; it is significantly higher in the Asian continent, especially in India and China. The Leading International Fungal Education (LIFE) portal estimates the annual global prevalence of mucormycosis approximately as 10, 000 cases without including Indian data and 910, 000 cases annually including Indian data. [(4)] Systematic review of available literature on COVID-19 Associated Mucormycosis (CAM) (till 14 May 2021), revealed that most cases were reported from India (72%). The majority of the patients were male (78%) and had diabetes mellitus (85%). Rhino-orbital mucormycosis was most common (42%), followed by rhino-orbito-cerebral mucormycosis (24%). [(5)]

Risk factors

Almost all patients with mucormycosis have some underlying disease that predisposes to the infection and influences the clinical presentation. [(1)]

- Diabetes mellitus, particularly with ketoacidosis-commonest risk factor (36%)
- Hematologic cancers (17%),
- Hematopoietic stem cell or solid organ transplant (12%).

Others:

- COVID-19 infection: both as a co-infection and as sequelae.
- Treatment with glucocorticoids
- Treatment with deferoxamine
- Iron overload
- AIDS
- Intravenous drugabuse
- Trauma/burns
- Malnutrition

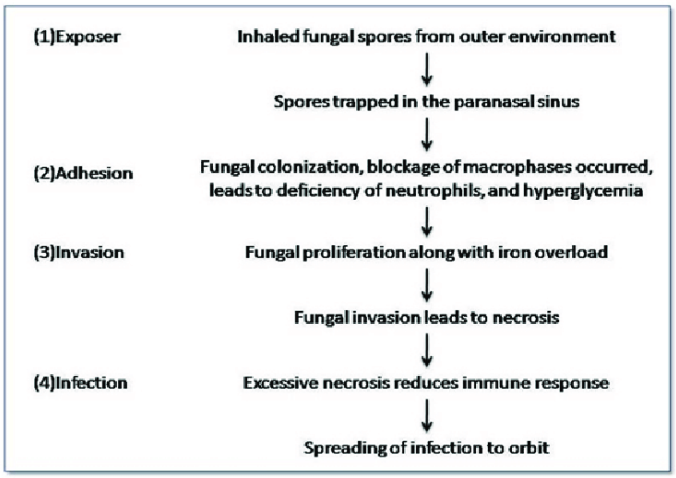
Etiology

The most common genera causing human infections include *Rhizopusarrhizus*. *Lichtheimia*, *Apophysomyces*, *Mucor*, and *Rhizomucor*. The most commonly isolated mucormycosis species in the world is *Rhizopus arrhizus*, though *Apophysomyces variabilis* is most common in Asia, and *Lichtheimia* species is predominant in Europe. [(1).] The

commonest etiology for rhino-orbital cerebral mucormycosis is *Rhizopus arrhizus.*

Pathophysiology

Pathogenesis includes microbial infection, inflammation, malignancy and tissue breakdown to cause disease. A pathogen must successfully achieve four steps or stages of pathogenesis: Exposure (contact), Adhesion (colonization), Invasion, and Infection [6]. When host inhales the spores produced by Mucorales from the environment, it colonizes at paranasal sinus and nasal cavity; It invades and occludes vascular lumina, forms a characteristic black eschar on paranasal sinus and causes infection. The disease, through the ethmoid and maxillary sinuses, spreads to the paranasal sinuses into the orbit and then to the cranial cavity by way of the orbital apex, cribriform plate, orbital nerves or orbital vessels. Epithelial cells and phagocytic cells help in host defence mechanism, but Mucorales spores trap the nasal epithelial cells coming in contact with GRP78 (Glucose-regulated Protein) through fungal spore coat protein CotH3 and harm the primary cell lining and predisposes to disease. Germination is supported by high glucose, low oxygen concentration, high iron levels and acidic medium, and then germinates into hyphae. [6]



Clinical Manifestations [7]

The symptoms of rhino-orbital mucormycosis are often non-specific with varying spectrum and severity. Background history of diabetes mellitus or underlying immunosuppression is usually revealed. **Initial symptoms:** Fever, headache, nausea, and generalized weakness **Facial symptoms:** Pain and numbness. **Nasal symptoms:** Nasal stuffiness & Mucoid, purulent, blood-tinged or black nasal discharge **Orbital symptoms:** Periorbital or retro-orbital pain, double or blurred vision, and partial or complete loss of vision in one or both eyes might progress to blindness Painful ptosis, abscess of eyelids, and corneal numbness with edema.

Clinical assessment & Diagnostic findings [1]

Examination of the eyes: Tenderness and swelling of the eyelids, evidence of vitritis and/or endophthalmitis, optic disc edema, ophthalmoplegia, fixed pupils, and nystagmus. Presence of superior orbital fissure syndrome and superior ophthalmic vein thrombosis. Cranial nerve palsies with varying involvement of II, III, IV, V, VI, and VII nerves are common. ***Nasal or palatine findings****:* Grey or reddish mucosa, which progresses to black areas of eschar as necrosis ensues. Eschar may be seen in the nasal septum, palate, eyelid, face, or orbital areas.

Diagnostic findings

Blood studies: May show a high blood sugar reading with/without evidence of acidosis or ketoacidosis. dyselectrolytemia, Complete blood cell count: To rule out a neutropenic state. Iron studies: To rule out suspected iron overload states in the form of low total iron-binding capacity and high ferritin values.

Urine: Presence of ketone bodies.

Endoscopic evaluation: of sinuses performed to look for tissue necrosis and to obtain specimens

Radiological Imaging

Computed tomography (CT) scan: Sinuses mucosal thickening with obliteration of osteo-meatal complexes, along with presence of cavernous sinus thrombosis.

MRI: Clearly delineate early vascular invasion, intracranial spread, and also assessment for early perineural spread.

Tissue Specimen: Characteristic ribbon-shaped non-septate or pauciseptate, irregularly branching hyphae seen. Fresh tissue specimens subjected to PCR techniques often show high sensitivity and specificity in the diagnosis.

Management [7]

Management of rhino-orbital cerebral mucormycosis is a medical as well as surgical emergency. Early recognition and initiation of appropriate treatment is of paramount importance with regards to outcomes.

1) ***Reversal of immunosuppressive state:*** Rapid correction of underlying systemic derangements such as hyperglycemia, metabolic ketoacidosis, hypoxia, dyselectrolytemiaand tapering of corticosteroids or

immuno-suppressive medications should be pursued if possible.

2) ***Early antifungal administration:*** **Inj. Liposomal amphotericin B**: is the first choice of treatment, as it crosses the blood-brain barrier more effectively. It should be initiated as soon as the diagnosis is suspected. IV Amphotericin (liposomal) is administered in the dose of 5-10 mg per Kg body weight per day for several weeks.
3) ***Step-down therapy:*** based on the achievement of clinical improvement, the Amphotericin is usually stepped down to oral Posaconazole or Isavuconazole.
   - Posaconazole, a triazole that inhibits growth of the fungus, an adjunctive or alternative treatment for mucormycosis.
     Oral posaconazole (delayed-release tablet) is given at a dose of 300mg twice daily on the first day, followed by 300 mg once daily for one week. Serum trough concentration of oral Posaconazole needs to be monitored after a week of treatment and has to be kept at least above 1 mcg/ml.
   - Oral Isavuconazole is given at a dose of 200 mg, thrice daily for two days, followed by 200 mg once daily.
     IV or oral Posaconazole or Isavuconazole has been used as salvage therapy in certain patients who do not tolerate Amphotericin or who do not respond to it
4) ***Surgical Intervention:*** Early aggressive surgical debridement is important for successful management of invasive fungal disease.
   a) ***Orbital decompression***: Extensive resection of infected and necrotic tissues as a part of source control and reduction of fungal load. Extending debridement until freshly bleeding, viable tissue is encountered is a generally accepted principle.
   b) ***Exenteration:*** Necessary to reduce the fungal load and prevent cerebral involvement and the fatal progression of the disease. Orbital exenteration is done in cases with no visual potential, where the disease is limited to the orbit without or minimal extension to the cavernous sinus. c) ***Local instillation:*** Amphotericin is also used for local instillation or irrigation of debrided cavities in surgical management.

Nursing Care

Nursing management of a patient with Rhino orbital mucormycosis is presented using a case report.

Case Report

Mr. X, 48 year old male got re-admitted **(Third admission)** with the complaints of sudden, painless decreased vision with periorbital pain on the left eye since one day. He is a known case of type II Diabetes Mellitus since three years and on oral ant diabetic drugs (OADS). He was found taking Tab. Posaconazole 100mg once a day instead of the prescribed dose 300mg once in a day. **On Examination:** PR: 84/mt, BP: 120/80 mmHg, Spo2 99% on Room air. PICCLE: Negative, JVP not elevated. No carotid bruit, CVS: normal S1 & S2 present. No murmur noted. RES: Normal vesicular breath sounds. Abdomen: Soft, no masses palpable. CNS: GCS: 15/15. ***Ophthalmic:*** Tenderness and swelling of the eyelids, evidence of endophthalmitis, optic disc edema, and nystagmus. ***Nasal:*** Presence of Eschar on the nasal septum. **Investigations findings: *CT PNS:*** Left orbital cellulitis, suspicious thrombosis of the left ophthalmic artery and cavernous sinus. No obvious skull base/bones erosions or intracranial extension. ***MRI Brain with Contrast:*** Involvement of the left orbital apex and left inferior rectus muscle. He was diagnosed with acute invasive rhino-orbital mucormycosis with left cavernous sinus thrombosis. He underwent left orbital exenteration. He was reinitiated on IV Conventional Amphoterecin B for 10 days followed by Tab. Posaconazole 300mg once daily for 14 days. He was discharged with OADS and advised to have regular eye dressing in oculoplasty clinic.

He was hospitalized twice with symptoms suggestive of mucormycosis. During **First admission**, he was treated as clinical COVID-19 with Oxygen, IV Steroids, and anticoagulant. **Second admission:** His SpO2; 88%, HbA1 C-13.2 and was found to be COVID positive. He was initiated on Insulin along with OADS. He was treated with Oxygen, 1-2 litres, and surgical intervention: Bilateral Rhino-orbital sinonasal debridement. He was prescribed Inj. Amphotericin once in a day for 14 days. Tab. Posaconazole 300mg once in a day was prescribed from 12th day of Inj. Amphotericin and was advised to continue for two weeks.

Nursing Diagnosis:

1) Acute pain related to increase orbital cavity pressure, secondary to inflammation of the orbital cavity and surgical intervention

Interventions:

- Assessed the characteristics of pain such as site, frequency, intensity, aggravating, relieving factors and pain score
- Positioned him in propped up position to relieve pressure
- Administered Inj. Febrinil 1gm IV every 6 hourly on the first and second post operative day followed by Tab. Paracetamol 1gm PRN
- Offered emotional support

Evaluation: Pain score was monitored every 4 hourly. The pain was minimized as evidenced by reduction in pain score and normal vital signs.

2) Infection, actual related to invasion of micro organism Interventions:

- Monitored vital signs every 4 hourly
- Monitored blood counts
- Administered antifungal as per the order
- Strict asepsis was followed while administering injections and handling invasive lines

Evaluation: Inj. Amphotericin 1gm IV, OD 10 days was administered followed by step down therapy Tab. Posaconazole 300 mg OD for 14 days.

3) Deficient knowledge regarding disease condition, treatment regimen, home care and follow up related to lack of knowledge. Interventions:

- Assessed the level of knowledge

- Explained the disease condition and treatment in simple terms
- Explained about regular follow up, medications, ocular prosthesis, regular ocular dressing, detection and prevention of complications such as wound infection and impaired glucose level
- Encouraged them to clarify doubts and reinforced the information.

Evaluation: He verbalized his understanding about all the instructions given to him and also expressed his confidence towards home care and follow up.

4) Ineffective coping individual and family related to surgical outcome, recurrent admission and financial crisis Interventions:

- Developed good rapport
- Allowed to ventilate their feelings
- Encouraged them to identify their strength
- Cleared their doubts
- Exercised non judgmental attitude
- Provided spiritual support with counseling

Evaluation: Mr. X and his wife were depressed. With adequate counseling and spiritual support, their coping was improved.

5) Impaired body image related to surgery. Intervention:

- Developed good rapport by answering the questions with simple and clear instruction
- Assessed emotional status regarding change in the physical appearance
- Explained about wound care and prosthesis

Evaluation: Mr. X, could not accept the body image change of having eye enucleated and placing prosthesis.

6) Potential for complication Interventions:

Hemorrhage:

- Monitored vital signs
- Assessed for oozing / bleeding from the surgical site
- Observed the dressing and ensured occlusive dressing

Wound infection:

- Monitored vital signs and signs of infection
- Maintained strict aseptic technique while dressing the wound
- Changed dressings daily
- Ensured good personal hygiene

Impaired glucose level:

- Monitored blood glucose level four times in a day
- Administered OADS as per the order
- Administered insulin as per the GRBS value
- Provided 1600 Kcal diabetic diet

Evaluation: Mr., X did not have bleeding from the operated site. Had wound gapping along with discharge. Wound was cleaned regularly using antiseptic solution and he was prescribed with Tab. Ciprofloxacin 500mg BD for five days. Wound was resutured. His blood sugar value was maintained within acceptable limit with OADS, along with Insulin, 1600kcal diabetic diet and additional insulin as PRN.

2. Conclusion

Possibly the most feared infection in all of infectious diseases is mucormycosis. It's an extremely morbid and deadly fungal infection. Rhino-orbital cerebral mucormycosis almost and always occurs in immune-compromised persons, including uncontrolled diabetes mellitus, especially with acidosis or ketoacidosis. The incidence is likely to rise, both as a co-infection and as a sequelae of COVID-19. Early diagnosis and management with appropriate and aggressive antifungal and orbital exploration, decompression, or exenteration can improve survival. Once rhino-orbital cerebral mucormycosis is diagnosed, the patients and family need to be adequately counseled regarding poor prognosis, and the pros and cons of extensive surgical debridement, including the potential for severe disfigurement after the procedure.

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