

## Ophthalmology

**KEYWORDS:** Social Media, Common Mental Disorders, 12 Item GHQ, Beck Depression Inventory

## RHINO ORBITAL CEREBRAL MUCORMYCOSIS ASSOCIATION WITH CAVERNOUS SINUS THROMBOSIS IN DIABETES MELLITUS PATIENTS



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OF PURE MEDICAL RESEARCH**ABSTRACT****INTRODUCTION:**

- Rhino-orbital-cerebral-mucormycosis (ROCM), previously referred to as orbital zygomycosis, refers to the presentation of pathologic symptoms in the orbit as a result of fungal infections caused by fungi in the order Mucorales, most commonly by the species *Rhizopus oryzae*. ROCM usually occurs in an immunocompromised host and presents with initial symptoms such as vision loss, ptosis, diplopia, and external ophthalmoplegia. Left untreated, ROCM can progress to acute vision loss and death.
- A chronic immunocompromised is the most common predisposing condition for ROCM (e.g. HIV, diabetes mellitus II, organ transplant recipients taking immunosuppressants, deferoxamine treatment).
- The primary species responsible for the development of ROCM is the fungus *Rhizopus oryzae*. This fungus is a fast growing, aseptate filamentous fungus that is responsible for nearly 90% of all rhinocerebral cases.
- Like most diseases of fungal origin, mucormycosis is usually introduced to the body through inhalation of spores. The two characteristics most often responsible for the proliferation and development include its propensity for induction of angiogenesis and rapid growth rate.
- One critical step that allows for angioinvasion to occur is the penetration of and damage to the endothelial cells and extracellular matrix proteins lining the blood vessels. One receptor that is known to be involved in the penetration process is a protein known as glucose-regulated protein (GRP78)
- ROCM can spread to the brain through the cribriform plate and orbital apex, causing potential complications such as internal carotid artery occlusion, cranial nerve palsy, chiasmal infarction, intracranial aneurysm, fungal meningitis, cavernous sinus thrombosis and even death.

The classical clinical progression of CROM includes three stages:

- Stage I: Infection of the nasal mucosa and sinuses.
- Stage II: Orbital involvement (orbital apex syndrome, superior orbital fissure syndrome).
- Stage III: Cerebral involvement in which intracranial spread occurs via one of the following routes:

1. Ophthalmic artery.
2. Superior orbital fissure. Spreading via this route may cause sinus

thrombosis and internal carotid artery thrombotic occlusion.

3. Cribriform plate. The spread of the infection to the frontal lobes and to the cavernous sinus occurs via perivascular and perineural channels through the cribriform plate and the orbital apex, respectively.

- Cavernous sinus thrombosis is one of the most severe complication of ROCM.
- During second wave of novel covid 19 pandemic the incidence of cavernous sinus thrombosis in a diabetic patients with ROCM is being increasing with rapid spread.
- Here we have a case series of 25 patients diagnosed with ROCM associated with diabetes amongs 57 mucormycosis patients.
- We have started our study from 10th april 2021 to 12th June 2021.
- We have included the time of presentation, age, sex ratio, associated other systemic illnesses, clinical features, treatment outcome and mortality rate.

**METHODOLOGY:**

- A retrospective, non comparative study of 25 patients with ROCM and diabetes mellitus [10th april 2021 to 12th June 2021] have done.
- 16 women and 9 men with a mean age of 54.0(SD) years (range 35-70 years) were studied. 18 patients had type 2 diabetes mellitus and 7 had secondary diabetes mellitus.
- Amongs 25 patients 16 were presented to our institute within 1 month of starting clinical symptoms and other 9 patients were presented within 2 weeks of starting symptoms.
- All patients had history of covid 19 and were presented with diminished vision with associated symptoms of watering, redness, eyeache, chemosis.

**EXAMINATION –****Ocular manifestation –**

External ophthalmoplegia	87 %
Vision loss	84 %
Proptosis	81 %
Chemosis	78 %
Ptosis	50 %

Other ocular manifestations – watering, redness, eyeache, diplopia

Non Ocular manifestation –

Sinusitis	100 %
Nasal discharge	74 %
Infranuclear 6th nerve palsy	46 %

Palate involvement	15 %
Cerebral lobe involvement	20 %

Orbital involvement was observed in (85%) of patients with cavernous sinus thrombosis in (50%), and internal carotid occlusion in (4%).

On computed tomography/magnetic resonance (Contrast Enhanced) imaging, all patients had evidence of paranasal sinuses involvement.

Ethmoid	86 %
Maxillary	80 %
Shenoid & frontal	17 %
Pansinusitis	14 %

Cavernous sinus thrombosis	50 %
Internal carotid artery occlusion	4 %

#### Diagnosis:

The diagnosis of mucormycosis was based on-

1. Direct microscopy of aspirate/crusts from the nasal/sinus mucosa.

The finding of aseptate hyphae with right angled branching was considered pathognomonic for determining the morphology of the mucor.

2. MRI ( Contrast Enhanced ) Brain + Orbit + PNS

3. CT Scan Brain + Orbit + PNS

#### Treatment :

1. Systemic amphotericin B with total doses varying from 3.0–3.5 g for approximately 30 days depending on general condition of the patients.

It was given under physician coverage.

None of these patients had any significant untoward events with amphotericin B treatment.

2. TRAMB –Transcutaneous retrobulbar injection of amphotericin B ( 3.5mg/ml )- given for 5 days/ 7 days/9 days depending on ocular manifestation of the patients.

Progression of TRAMB therapy –

Out of 25 patients 15 patients improved and 10 patients underwent orbital exenteration surgery.

Other sx – FESS (25/25), Frontotemporal craniotomy (2/25),Maxillectomy (2/25)

3. other medical management was done by physician ( ex- inj. Heparin, inj.insulin, higher antibiotics IV)

#### Discussion :

- ROCM typically originates in the nasal or oral mucosa, spreads to the paranasal sinuses, and enters the orbit via the ethmoid and maxillary sinuses or via the nasolacrimal duct. Intracerebral extension may occur from the orbit via orbital apex, orbital vessels, or via cribriform plate. Diabetes predisposes to this infection, as is seen in the majority of instances of ROCM.

- Yohai et al reviewed 145 case reports of ROCM, 60% of them had diabetes, and analysed their ophthalmic and nonophthalmic signs and symptoms occurring at any time during the course of disease.1 Similarly Ferry and Abedi reported 16 cases of ROCM; 13 (81%) of them had diabetes.

- Cavernous sinus thrombosis due to mucormycosis is typically associated with vision loss as was seen in our patients.

- Overall it seems that orbital manifestations were more common in our patients than reported in the literature. This could be due to delay in admission, thereby permitting spread of infection to the orbital tissue. Orbital manifestations are due to ischaemic necrosis of the intraorbital cranial nerves, orbital cellulitis, or rarely ocular invasion by Mucorales.

- In our patients there were 50 % involvement of cavernous sinus thrombosis in diabetes mellitus patients.
- Computed tomography or magnetic resonance imaging are useful modalities to assess the extent of the disease. In our study paranasal sinuses were involved in all patients, with ethmoid and maxillary being the most frequent.
- Cavernous sinus thrombosis usually results from spread of infection from the orbit and appears as a filling defect within the enhancing sinus or as a lateral convexity.
- Early diagnosis with direct microscopy using KOH staining will be helpful for starting early treatment with systemic amphotericin B under physician coverage, and it will help to delay the progression of fungal infection.
- If Patient diagnosed with Cavernous sinus thrombosis on MRI (Contrast enhanced) Brain, with Vision loss and painful eye then orbital exenteration will be the mainstay surgical management.
- Medical management includes inj. Heparin, inj. Insulin, higher IV antibiotics to prevent secondary infections.
- In our patients there was Unilateral involvement of the Cavernous sinus thrombosis, although there are high chances of involvement of bilateral cavernous sinus thrombosis if diagnosis delayed, and then it can lead to high mortality

#### Conclusion:

- Here we have done a study on 25 diabetes mellitus patients with covid -19 positive with cavernous sinus involvement. It is suggesting that there are high chances of CVT in DM patients, and high chances of mortality with CVT ( UL/ BL) in DM patients with covid -19 positive.
- Early institutional admission with prompt treatment (Medical + Surgical) under combine care ( Physician, Ophthalmologist, Neurosurgeon, ENT surgeon) with early diagnosis with KOH staining and MRI ( C+ E) Brain + Orbit + PNS can prevent CVT in covid patients and hence can decrease the mortality.

#### Conflict of interest:

No conflict of interest

#### Figures :

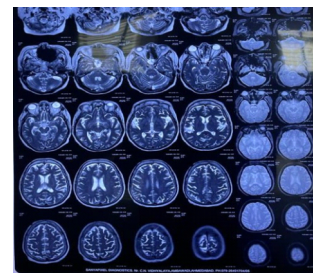


Figure – 1

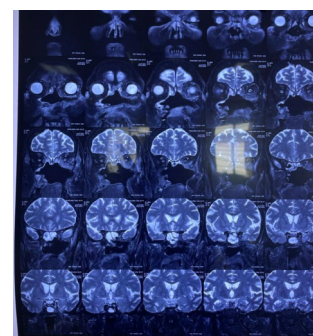


Figure-2

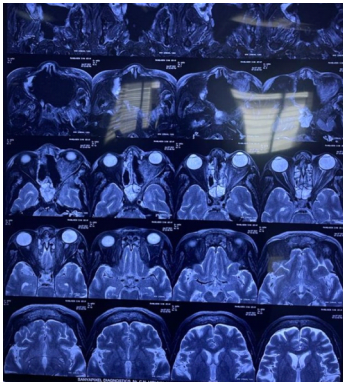


Figure-3

**Figure 1- Post maxillectomy intracranial extension with involvement of left eye**

**Figure 2 & Figure 3- Left sided CVT in post maxillectomy patient**

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