Original Research Article

Rhinoorbital mucormycosis in COVID-19 pandemic: presentation and course of disease: An observational study

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A R T I C L E  I N F O

Article history:
Received 16-06-2021
Accepted 06-07-2021
Available online 03-01-2022

Keywords:
COVID 19
Mucormycosis
Prevention

A B S T R A C T

Purpose: During the second wave of covid 19[SARS- Co V-2] pandemic, there is a sudden increase in number of mucormycosis infection cases in India. The present study is an attempt to understand the presentation, course and outcome of rhino orbital mucormycosis in a group of patients who reported to Ophthalmology and Otorhinolaryngology department of our Govt. District Hospital (secondary referral centre) for enhancing measures for prevention and management.

Materials and Methods: Patients who reported to our Government district hospital with signs or symptoms suggestive of rhino orbital mucormycosis during May-June 2021 were included in the study with consent of ethical committee, patients and patient’s relatives. Total 17 cases were reported and followed. Clinical examination was done for all the patients. History of the presenting complaints and underlying illness with COVID -19 was elicited. Underlying comorbid status was recorded. Patients were followed as all of them were referred to higher centre for further management as per the guidelines issued by directorate medical and health services, rajasthan, Jaipur.

Results: 13(76.4%) patients were from rural and 4 (23.5%) were from urban area. 11(64.7%) patients had RT-PCR +ve, 6 had RT-PCR _ve, 2 did not have RT-PCR report. 15(88.7%) patients had high blood sugar at presentation mean being 315.7mg%. 9 (52.9%) developed mucormycosis during their treatment for COVID in hospital. 8(47.05%) presented in OPD. 9 patients had treatment with inhalational O2 while 8 patients did not have treatment with O2. Death rate was high (70.5%) among our patients. Patients who survived (29.4%) had only initial symptoms and signs at presentation therefore could be managed earlier. None of our patient had vaccination for COVID.

Conclusion: Our study was done at secondary referral centre, all the previous studies were done at tertiary referral centres; therefore it shows the course of disease mainly among rural population ; most of them presented very late and had poor outcomes. It shows the need of more awareness about COVID and mucormycosis among people especially in rural areas. High blood sugar either due to treatment with steroids or pre existing is a major risk factor for Rhino orbital mucormycosis. Being RT- PCR negative for COVID 19 does not rule out the associated possible complication of Rhino orbital mucormycosis. Early diagnosis and management remains the key factor for managing Rhino orbital mucormycosis.

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1. Introduction

Second wave of COVID-19 pandemic in India has affected a large number of people so the associated bacterial and fungal infection cases are also high.1 Cases with symptoms and signs suggestive of rhinoorbital mucormycosis suddenly
increased that was previously seldomly reported. Sen et al. studied 6 patients with COVID-19 who developed rhino-orbital mucormycosis. Recently Sarcar et al. reported 10 cases of clinically diagnosed orbital mucormycosis with concurrent COVID-19 illness.

The term ‘Mucormycosis’ denote the acute or subacute rapidly progressing infection caused by the angioinvasive fungi in the order of ‘Mucorales’. The ubiquitous fungi often thrive on decaying plant debris and soil. The most common genera causing human infection include Rhizopus, Lichtheimia, Apophysomyces, Mucor and Rhizomucor. The most common clinical presentation is Rhino-orbital cerebral mucormycosis. Rhinocerebral mucormycosis almost always occurs in immunocompromised individuals, including uncontrolled diabetes mellitus with acidosis or keto acidosis, steroid therapy, organ transplant recipients, chemotherapy, hematologic dyscrasias, retroviral disease and malnourishment.

The rapidly growing saprophytic fungi release a large number of spores in the environment. These sporangiospores are commonly inhaled by the host, in hosts with normal immune status, the ciliary system directs the spores towards the pharynx, thereby eliminating them via the GI system. The spores might also get colonized in the oral mucosa, nose, throat and paranasal sinuses. Mucorales do not cause disease in host with normal immune status, the ciliary system directs the spores towards the pharynx, thereby eliminating them via the GI system where phagocytosis could effectively contain the invasion and infection. When phagocytosis is impaired due to immune deficiency, the germination of spores into hyphae with resultant angioinvasion is initiated. The initial site of infection in Rhinocerebral cerebral mucormycosis is the nasal turbinates. An acute episode of sinusitis progresses into pan sinus involvement within a few days with contiguous spread to orbit, palate and brain resulting in severe tissue ischemia and necrosis due to the angioinvasive nature of the fungi. This mechanism is facilitated by high amount of Iron and Glucose in serum.

The presenting symptoms of rhino orbital cerebral mucormycosis include headache, facial pain, eye pain, facial numbness, diplopia with varying degrees of ophthalmoplegia, ptosis, proptosis, vision loss with and without papilloedema, nasal discharge, epistaxis and loosening of teeth. Black discoloration of skin and mucosa along with ulceration and discharge from nose and palatal mucosa are characteristic of mucormycosis. CT Scan can demonstrate the nature and extent of soft tissue abnormalities in the sinuses, orbits and brain. Mucosal thickening of sinuses along with opacification is often noted. MRI is more helpful over the CT in clearly delineating vascular invasion, intracranial spread and also in the assessment of early perineural spread. A T2 weighted MRI with fat saturation sequences or short T1 inversion recovery is ideal. Definite diagnosis is arrived at by tissue biopsy.

Rhino orbital mucormycosis is an medical and surgical emergency. Amphotericin B has become the gold standard for the systemic treatment. Liposomal amphotericin B is the first choice of treatment as it crosses the blood brain barrier more effectively. Surgical debridement of local necrotic tissue (paranasal sinuses and orbital exenteration) are done to reduce fungal load.

As the patients reported in our study were mostly from rural area, the awareness about the disease and data availability was limited. Therefore our study largely represents the presentation and course of disease among rural population.

2. Materials and Methods

We recruited a cluster of 17 patients with signs or symptoms suggestive of rhino-orbital mucormycosis who reported to Ophthalmology and Otorhinolaryngology departments of our Government district hospital after obtaining consent from patients. Their demographic profile was noted. Clinical examination was done. SpO2 blood sugar, treatment history with O2 and steroids was recorded. CT-PNS, orbit and head were done. All the patients were referred to tertiary level centres. Patients were followed for their management and outcome. At tertiary level MRI of paranasal sinuses, orbits and brain (plain and contrast) were obtained. Endoscopic tissue biopsy was done for final diagnosis. Endoscopic sinus debridement or orbital exenteration were done as per the requirement. Intravenous liposomal amphotericin B was used for the medical management.

3. Results

Case no. 1,2,3,4,5,10,11,12 and 17 total 9 developed symptoms during their treatment for COVID in hospital. All these patients were on intravenous steroids and O2. 7 out of these 9 patients had spO2 below 90%. All these 7 patients died within 7 days from the onset of symptoms of mucormycosis. One patient out of these 9 admitted patients had spO2 97%, had orbital exenteration done and was on Amphotericin B but expired during 3rd week of treatment. Remaining one patient had orbital exenteration and was on Amphotericin B till the last follow up.
<table>
<thead>
<tr>
<th>Case no.</th>
<th>Ag/sex</th>
<th>R/U COVID</th>
<th>COVID Related symptoms, Spo₂</th>
<th>Treatment with inhalational O₂</th>
<th>Blood sugar (mg%)</th>
<th>Orbital symptoms and signs</th>
<th>Radiologic findings</th>
<th>Treatment received for Mucormycosis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45/M</td>
<td>R</td>
<td>+ve</td>
<td>ICU, Spo₂ 75%</td>
<td>+</td>
<td>240</td>
<td>RE/orbital cellulitis</td>
<td>MRI –Rt. Orbital cellulitis and Optic Neuritis, Cavernous sinus thrombosis</td>
<td>Death</td>
</tr>
<tr>
<td>2</td>
<td>80/F</td>
<td>U</td>
<td>+ve</td>
<td>ICU, Spo₂ 70%</td>
<td>+</td>
<td>320</td>
<td>RE/Orbital cellulitis</td>
<td>MRI –Rt. Orbital cellulitis and Optic neuritis</td>
<td>Death</td>
</tr>
<tr>
<td>3</td>
<td>75/F</td>
<td>R</td>
<td>-ve</td>
<td>Fever, dyspnoea Spo₂ 80%</td>
<td>+</td>
<td>285</td>
<td>RE/Orbital cellulitis</td>
<td>NA</td>
<td>Death</td>
</tr>
<tr>
<td>4</td>
<td>45/F</td>
<td>U</td>
<td>+ve</td>
<td>Fever, dyspnoea Spo₂ 85%</td>
<td>+</td>
<td>280</td>
<td>RE/Orbital cellulitis</td>
<td>MRI –Rt. Orbital cellulitis</td>
<td>Death</td>
</tr>
<tr>
<td>5</td>
<td>70/M</td>
<td>R</td>
<td>+</td>
<td>Fever, Dyspnoea Spo₂ 85%</td>
<td>+</td>
<td>310</td>
<td>RE/Orbital cellulitis</td>
<td>MRI –Rt. Orbital cellulitis with Optic neuritis</td>
<td>Death</td>
</tr>
<tr>
<td>6</td>
<td>45/M</td>
<td>R</td>
<td>-ve</td>
<td>Fever Spo₂ 95%</td>
<td>_</td>
<td>500</td>
<td>RE/Orbital cellulitis PL _ve</td>
<td>MRI –Rt. Orbital Cellulitis</td>
<td>Death</td>
</tr>
<tr>
<td>7</td>
<td>65/M</td>
<td>R</td>
<td>-ve</td>
<td>Fever Spo₂ 95%</td>
<td>_</td>
<td>500</td>
<td>LE/Orbital cellulitis</td>
<td>MRI –Lt. Orbital cellulitis, Cavernous sinus Thrombosis</td>
<td>Death</td>
</tr>
<tr>
<td>8</td>
<td>54/F</td>
<td>R</td>
<td>_ve</td>
<td>Fever, breathlessness, anosmia</td>
<td>_</td>
<td>500</td>
<td>LE/Orbital Cellulitis</td>
<td>MRI –Lt. Orbital cellulitis</td>
<td>Death</td>
</tr>
<tr>
<td>9</td>
<td>70/F</td>
<td>R</td>
<td>_ve</td>
<td>Fever, dyspnea, Spo₂ 75%</td>
<td>_</td>
<td>380</td>
<td>LE/ C/O pain at presentation, paraesthesia over Lt. heek progressed to Lt. 6th nerve palsy</td>
<td>MRI –+ve</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Continued on next page
<table>
<thead>
<tr>
<th>No.</th>
<th>Age</th>
<th>Sex</th>
<th>Site of Infection</th>
<th>Clinical Findings</th>
<th>Investigations</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>70/F</td>
<td>R</td>
<td>+ve</td>
<td>Fever, Spo2 90%</td>
<td>+ 340</td>
<td>CT PNS- Pansinusitis</td>
<td>Sinus debridement followed by Amph. B</td>
</tr>
<tr>
<td>11</td>
<td>60/M</td>
<td>U</td>
<td>+ve</td>
<td>Fever</td>
<td>+ 199</td>
<td>LE/Proptosis and chemosis</td>
<td>CT PNS- Pansinusitis, MRI- +ve</td>
</tr>
<tr>
<td>12</td>
<td>50/M</td>
<td>R</td>
<td>+ve</td>
<td>Admitted in ICU Spo2 54%</td>
<td>+ 360</td>
<td>LE/ Eyelid swelling Progressed to orbital cellulitis</td>
<td>NA</td>
</tr>
<tr>
<td>13</td>
<td>50/M</td>
<td>R</td>
<td>NA, +ve after death</td>
<td>NIL</td>
<td>_ 240</td>
<td>RE/ Orbital cellulitis</td>
<td>MRI - +ve</td>
</tr>
<tr>
<td>14</td>
<td>61/F</td>
<td>R</td>
<td>+ve</td>
<td>Fever</td>
<td>+ 70</td>
<td>RE/ Sudden loss of vision, PL_ve</td>
<td>CT PNS- Maxillary sinusitis</td>
</tr>
<tr>
<td>15</td>
<td>65/F</td>
<td>R</td>
<td>_ve</td>
<td>Fever CRP- 53 Spo2 95%</td>
<td>+ 400</td>
<td>B/L Orbital cellulitis with facial swelling and eschar over lt. cheek</td>
<td>MRI- +ve</td>
</tr>
<tr>
<td>16</td>
<td>34/M</td>
<td>U</td>
<td>NA, vomiting</td>
<td>Fever</td>
<td>_ 123</td>
<td>B/L conjunctival congestion</td>
<td>CT PNS- Sphenoidal sinusitis</td>
</tr>
<tr>
<td>17</td>
<td>62/M</td>
<td>R</td>
<td>+ve</td>
<td>Fever</td>
<td>+ 320</td>
<td>LE/ Orbital cellulitis</td>
<td>MRI- Rhino orbital mucormycosis</td>
</tr>
</tbody>
</table>

Ag-Age, M-Male, F-Female, R- Rural, U- urban, MRI- +ve=MRI- +ve for Rhinoorbital mucormycosis, RE-Right eye, LE-Left eye, Orb. Ext.-Orbital Exentration, Amph. B- Liposomal Amphotericin B
8 patients presented in OPD, they did not have history of treatment with O₂. 6 out of these 8 patients were on oral steroids. 5 out of these 8 OPD patients had orbital cellulitis at presentation. 4 of these 5 died within 1 week while on treatment for mucormycosis. One out of these 8 patients had acute presentation with right orbital cellulitis and nasal bleeding, blood sugar was 240 mg/dl and spo₂ was 95%. MRI was positive for rhino-orbital mucormycosis. He had no history of any type of illness or treatment in the past. He died before having any treatment for mucormycosis. Duration of his onset of symptoms and death was only 4 days. RT-PCR done after death was negative. Another one patient was 34 yr male with vomiting, diarrhea and bilateral conjunctival congestion at presentation. CT-PNS showed sphenoidal sinusitis. His blood sugar level was 123 mg/dl and spo₂ was 97%. He was immediately referred; was diagnosed to have rhino-orbital mucormycosis and was managed accordingly with Intravenous Amphotericin B. This patient survived and improved with timely intervention.

4. Observations

Total 17 patients were enrolled in our study. 13 (76.4%) patients were from rural area and remaining 4 (23.5%) were from urban area.

Mean age of presentation was 58.88 years

9/17 (52.9%) of patients were already admitted in COVID wards and developed mucormycosis during treatment of COVID. Other 8/17 (47.05%) cases, reported in OPD and never had treatment with inhalational O₂. Therefore role of inhalational O₂ in causing rhino-orbital mucormycosis remains doubtful in our study.

6 patients had RT-PCR report negative but developed symptoms and signs of Rhino orbital mucormycosis in due course. 2 patients did not get RT-PCR test done. It shows that patients can develop associated complications of COVID 19 even if they are reported negative in RT-PCR.

12 enrolled patients (12/17 i.e 70.5%) died and 5 patients survived till the last follow up in our study. This denotes a high death rate in mucormycosis patients. Out of 12 patients who died 10 (90.9%) had orbital cellulitis at presentation. Out of these 10 cases 2 cases presented in OPD; were immediately referred to higher centre but died before receiving any treatment for mucormycosis. 2 cases out of these 10 had orbital exentration followed by liposomal amphotericin B, 5 had received amphotericin B for 2-3 days and remaining 1 died at home within 7 days without receiving any treatment. This shows poor prognosis of patients once orbital cellulitis sets in.

5. Discussion

15 (82.3%) cases had high blood sugar at presentation. Our finding correlates with the fact that mucormycosis infection is facilitated by high blood sugar. The early flag sign and symptoms reported in our study were:

1. Paresthesia over cheek and ipsilateral eye pain
2. Bilateral conjunctival congestion
3. Eye lid swelling
4. Headache

Any patient with these symptoms must have CT PNS done; if CT PNS shows mucosal thickening in any of the paranasal sinuses immediate further management must be done.

6. Conclusion

Rhino-orbital mucormycosis showed acute onset and rapid progression in all the patients. High index of suspicion
is necessary for early diagnosis and treatment to avoid high mortality and morbidity as it showed acute onset and rapid progression even in patients with mild symptoms of COVID. Prevention of COVID infection especially in patients with Diabetes remains the only way to avoid associated mortality, morbidity, social and economic upheavals. Wide social awareness about the preventive measures, early symptoms and available management is of paramount importance especially in rural and remote areas of India.

7. Source of Funding
None.

8. Conflict of Interest
The authors declare no conflict of interest.

9. Acknowledgement
We would like to acknowledge support of Dr. Anju Kochar, SP Medical College and Hospital, Bikaner for providing follow up details of our patients.

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