Treatment outcome of rhino-orbital-cerebral mucormycosis patients: a retrospective institutional study

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Authors
Treatment Outcome of Rhino-Orbital-Cerebral Mucormycosis Patients: A Retrospective Institutional Study

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Abstract

Introduction: Rhino-orbital-cerebral mucormycosis is an acute fungal infection characterized by fungal hyphal invasion of blood vessels resulting in thrombosis and infarction of the nasal, paranasal sinus, orbital, and cerebral tissues.

Patients and methods: This was a retrospective study conducted on 80 patients with biopsy-proven mucormycosis. The study was carried out in the Mucormycosis Ward of a Tertiary Care Medical College and Hospital during a period of 6 months from May 2021 to October 2021.

Results: Among 80 patients, 50 (62.5%) were males and 37 (37.5%) were females. Of the patients, 53.75% were in the age group of 31–70 years. Primary clinical presentation was facial pain/swelling/paresthesia in 75 (93.75%) followed by nasal obstruction in 50 (62.5%) patients and orbital symptoms — pain/edema/blurring of vision in 46 (57.5%) patients. Forty-six patients were known cases of diabetes mellitus and 42 patients had a previous history of coronavirus disease 2019 infection-associated comorbidities. As per staging of the disease, 36 patients were of stage III (involvement of the orbit), 22 patients of stage-II (involvement of paranasal sinuses), 16 patients of stage IV (involvement of central nervous system), and six patients were in stage I (involvement of nasal mucosa). Forty patients were treated by the modified Denker’s procedure, 30 patients by endoscopic debridement, eight patients by the modified Denker’s procedure with orbital exenteration, one patient by the modified Denker’s procedure with inferior maxillectomy, and one patient by total maxillectomy. All the patients were also given amphotericin injection. Out of 80 patients, 64 patients survived with sequelae, while 16 patients expired till date.

Keywords: Coronavirus disease 2019, Immunocompetent, Mucormycosis, Rhino-orbito-cerebral, Treatment outcome

1. Introduction

Rhino-orbital-cerebral mucormycosis (ROCM) is an acute, often fatal, fungal infection caused by members of the class Zygomycetes and the order Mucorales [1]. The genus Rhizopus accounts for most cases of ROCM. The disease is characterized by fungal hyphal invasion of blood vessels resulting in thrombosis and infarction of the nasal, paranasal sinus, orbital, and cerebral tissues. The most common comorbidities include diabetes mellitus, lymphoid malignancy, burn, severe trauma, renal failure, and steroid therapy [2,3]. Common clinical findings include rhinitis, periorbital and facial swelling, facial and mucosal necrosis, ophthalmoplegia, multiple cranial nerve palsies, facial pain, and headache. Definitive diagnosis is made by demonstration of fungal hyphae in tissue specimens. The mainstay of treatment is aggressive surgical debridement of infected tissue and administration of amphotericin-B. The mortality rate due to ROCM is very high due to its rapid spread [4]. Early diagnosis and treatment are imperative in the successful management of patients afflicted with this devastating sight-threatening and life-threatening disease.
2. Patients and Methods

A retrospective study was carried out in the Mucormycosis Ward of a Tertiary Care Medical College and Hospital during a period of 6 months from May 2021 to October 2021. A total of 80 biopsy-proven mucormycosis patients were included in the study. Each of these patients were subjected to complete history and thorough ENT examination after obtaining proper written informed consent. The relevant data were collected with regard to age and sex, clinical presentation, radiological findings, and treatment outcome of patients.

3. Results

The data were analyzed statistically and the following observations were made. Among 80 patients, 50 (62.5%) were males and 37 (42.5%) were females. Maximum patients were found in the fifth and sixth decade of life with 22 (27.5%) and 21 (26.25%) patients in the age group of 51–60 and 61–70 years, respectively (Tables 1 and 2).

Graph showing age distribution of study participants
Primary clinical presentation was facial pain/swelling/paresthesia in 75 (93.75%) patients followed by nasal obstruction in 50 (62.5%) patients and orbital symptoms like pain/edema/blurring of vision in 46 (57.5%) patients (Table 3, Figs. 1 and 2).

Forty-six patients were previously diagnosed cases of diabetes mellitus, while 42 patients had a previous history of coronavirus disease 2019 infection-associated comorbidity (Table 4).

Pie chart showing associated comorbidities of ROCM patients
Association between different groups is good and significant with comorbidities.

\[ \chi^2 = 33.98 \]

\[ P \text{ value less than } 0.0001 \ (0.0000002) \]

DF-3
Inference: highly significant
Radiological findings revealed that 28 patients had their disease limited to the nose and paranasal sinus, 41 patients had involvement of nose and paranasal sinus along with orbit and skull base while 11 patients had intracranial extension of disease (Table 5, Fig. 3).

Graph showing involvement as per radiological findings of ROCM patients
Association between radiological findings of the ROCM patients is good with significant relationship.

\[ \chi^2 = 9.622 \]

\[ P \text{ value less than } 0.008138 \]

Inference: significant
Majority of the patients presented with advanced stage of disease. Stage III (involvement of orbit)

Table 1. Distribution of patients according to age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01–20</td>
<td>01 (1.25)</td>
</tr>
<tr>
<td>21–30</td>
<td>07 (8.75)</td>
</tr>
<tr>
<td>31–40</td>
<td>12 (15)</td>
</tr>
<tr>
<td>41–50</td>
<td>13 (16.25)</td>
</tr>
<tr>
<td>51–60</td>
<td>22 (27.5)</td>
</tr>
<tr>
<td>61–70</td>
<td>21 (26.25)</td>
</tr>
<tr>
<td>71–80</td>
<td>02 (2.5)</td>
</tr>
<tr>
<td>81–90</td>
<td>02 (2.5)</td>
</tr>
<tr>
<td>&gt;91</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 2. Distribution of patients according to sex

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>50 (62.5)</td>
</tr>
<tr>
<td>Female</td>
<td>30 (37.5)</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 3. Presenting complaints of rhino-orbital-cerebral mucormycosis patients

<table>
<thead>
<tr>
<th>Presenting complaints</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial pain/swelling/paresthesia</td>
<td>75 (93.75)</td>
</tr>
<tr>
<td>Nasal obstruction</td>
<td>50 (62.5)</td>
</tr>
<tr>
<td>Orbital symptoms – pain/edema/blurring of vision</td>
<td>46 (57.5)</td>
</tr>
<tr>
<td>CNS symptoms – altered sensorium/seizure/paresis/paralysis</td>
<td>07 (8.75)</td>
</tr>
</tbody>
</table>

CNS, central nervous system.

Fig. 1. Involvement orbit due to mucormycosis.
presentation in 36 patients, stage-II (involvement of paranasal sinuses) in 22 patients, stage IV (involvement of central nervous system (CNS)) in 16 patients, and only six patients came to the hospital with early spread in stage I (involvement of nasal mucosa) (Table 6, Figs. 4 and 5).

Bar chart showing staging of ROCM patients. Association between stagings is good with significant relationship to each other.

\[ \chi^2 = 12.65 \]

DF-3

P value less than 0.005459.

Inference: significant.

Forty patients were treated by the modified Denker’s procedure, 30 patients by endoscopic debridement, eight patients by the modified Denker’s procedure with orbital exenteration, one patient by the modified Denker’s procedure with inferior maxillectomy and one patient by total maxillectomy. All the patients were also subjected to amphotericin injection coverage (Table 7).

Pie chart showing the surgical procedure performed.

Out of 80 patients, 64 patients survived with sequelae, while 16 patients succumbed to the disease (Table 8).

Bar chart showing short-term treatment outcome of the patients.

4. Discussion

Mucormycosis is a rare filamentous and fatal fungal infection mostly encountered among immunosuppressed patients [5,6]. The most common risk factors accompanied with mucormycosis are diabetes mellitus, especially ketoacidosis, immunosuppressive conditions like hematologic malignancies and organ transplantations [7–9]. In our study among 80 patients, 50 (62.5%) were males and 37 (46.25%) were females. Of the patients, 53.75% were in the age group of 51–70 years. Analogous conclusions were made by Jiang et al. [10] where out of 11 cases of ROCM, eight were males and three females. The mean age was 53.7 years (range, 45–60 years).

In the present study, primary clinical presentation was facial pain/swelling/paresthesia in 75 (93.75%) patients followed by nasal obstruction in 50(62.5%) patients and orbital symptoms – pain/edema/blurring of vision in 46 (57.5%) patients. Forty-six patients had the comorbidity of diabetes mellitus, while 42 patients had previous history of coronavirus disease 2019 infection-associated comorbidities. Fouad et al. [11] corroborated similar findings. In their study, out of the 12 ROCM cases identified, five had a concurrent positive reverse transcription-PCR test result for severe acute respiratory syndrome coronavirus 2, one had a prior positive result, while six had neither concurrent nor prior positive test results. Nine of the 12 cases had poorly controlled diabetes mellitus, and two cases had a hematological malignancy [11].

In our study, the clinical staging of the disease at presentation was stage III (involvement of orbit) in 36 patients. Stage II (involvement of paranasal sinuses) in 22 patients, stage IV (involvement of CNS)
in 16 patients, and stage I (involvement of nasal mucosa) in only six patients. Forty patients were treated by the modified Denker’s procedure + injection amphotericin, 30 patients by endoscopic debridement + injection amphotericin, eight patients by the modified Denker’s procedure with orbital exenteration + injection amphotericin, one patient by the modified Denker’s procedure with inferior maxillectomy + injection amphotericin. Out of 80 patients, 64 patients survived with sequelae while 16 patients expired till date. Dave et al. [12] in their study – a retrospective multi-centric interventional case series of 58 eyes with ROCM – found that

<table>
<thead>
<tr>
<th>Staging</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I (involvement of nasal mucosa)</td>
<td>6 (7.5)</td>
</tr>
<tr>
<td>Stage II (involvement of paranasal sinuses)</td>
<td>22 (27.5)</td>
</tr>
<tr>
<td>Stage III (involvement of orbit)</td>
<td>36 (45)</td>
</tr>
<tr>
<td>Stage IV (involvement of CNS)</td>
<td>16 (20)</td>
</tr>
</tbody>
</table>

CNS, central nervous system.
the duration between the diagnosis of coronavirus disease 2019 and ROCM was 16 ± 21 days (median, 8 days). Thirty-six (62%) eyes had no vision at presentation. Imaging revealed paranasal sinus involvement (100%), orbital apex involvement (41%), cavernous sinus involvement (30%), and CNS involvement (33%). All the patients were treated with systemic liposomal amphotericin B and sinus debridement. Twenty-two (38%) eyes underwent exenteration. One eye underwent transcutaneous retrobulbar amphotericin-B. The mean follow-up duration was 5.62 ± 0.78 months (median, 6).

Favorable outcome was seen in 35 (60%) cases. Presence of uncontrolled diabetes (P = 0.001), orbital apex involvement (P = 0.04), CNS involvement (P = 0.04), and history of steroid use (P < 0.0001) resulted in unfavorable outcomes. CNS involvement was the only factor predicting mortality (P = 0.03). Mortality was seen in 20 (34%) patients [12].

5. Conclusion

ROCM following coronavirus disease 2019 has a severe, emergent, and fatal infection requiring multidisciplinary management. Delay in the treatment due to late presentation and CNS-associated complications were major determinants of the survival outcome in these patients.

Ethics statement

The study was approved by the Institutional Ethics committee.

Conflicts of interest

None declared.

References