Short Communication

A Cross-Sectional Study of First Hundred Cases of Rhino-Orbital-Cerebral Mucormycosis Admitted at a Tertiary Care Hospital

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Abstract

Background: With the second wave of coronavirus disease (COVID-19) Rhino Orbito Cerebral Mucormycosis (ROCM) has emerged as an epidemic in India. Early suspicion and management can reduce disfigurement and mortality. Objectives: To identify the demographic and clinical profile of ROCM, its association with COVID-19 and other predisposing factors. Methods: Hospital Based Cross Sectional Observational study on first hundred consecutive patients with signs and symptoms and radiological findings suggestive of ROCM. Data collected from patient records and analyzed. Results: Out of hundred, 72 patients were Males, 74 from rural areas, all were above eighteen years age, 35 presented with orbital and 27 with facial manifestations of ROCM. Main predisposing factors were history of COVID-19 (71%), previous hospitalization (48%), in Intensive Care Unit (5%) systemic corticosteroid therapy (48%), Diabetes, uncontrolled (45%) and new (21%). Conclusions: ROCM presented with orbital and facial manifestations. Main predisposing factors were Diabetes, COVID-19 and systemic steroids.

Keywords: Clinical manifestations, COVID-19, mucormycosis, predisposing factors, ROCM

Introduction

Mucormycosis is a rare invasive fungal disease with high mortality if not promptly diagnosed and managed.[1] Rhino-orbital-cerebral mucormycosis (ROCM) is the commonest clinical presentation, caused by the inhalation of spores into the paranasal sinuses of susceptible hosts.[2] Uncontrolled diabetes mellitus (DM), corticosteroid therapy, and other immunosuppressive conditions are known risk factors. Recently coronavirus disease 2019 (COVID-19) pneumonia has also emerged as a predisposing factor.[1]

There was a sudden surge in reporting of ROCM cases from different places in India during the second COVID-19 wave. Rajasthan was the first state to declare mucormycosis an epidemic on May 19, 2021, and by May 21, 2021, seven states and Union Territories had declared mucormycosis an epidemic.[1]

The severity of ROCM is largely dependent on the patient’s immune competency. COVID-19 provides fertile soil for ROCM as the infection itself decreases the patient’s immunity, which is further worsened by treatment with heavy doses of systemic steroids and other immunosuppressive drugs. It worsens pre-existing diabetes and also causes hyperglycemia in previously euglycemic individuals.

There must be a high index of suspicion of ROCM based on symptoms in COVID-19 cases, uncontrolled diabetics, and immuno-compromised individuals if they present with any symptoms suggestive of it.[1]

The lion’s share of available literature on ROCM is from the pre-pandemic time. This study adds to the exiguous literature on the ROCM that emerged as an outbreak after the peak of the second wave of COVID-19 in India. It aims to identify the...
Materials and Methods

A hospital-based cross-sectional observational study was conducted on patients admitted to the mucormycosis wards at Maharana Bhupal General Hospital, RNT Medical College, Udaipur, from May 11, 2021, to June 12, 2021. Four wards, each with 25 beds, were dedicated to the admission of clinically compatible cases of mucormycosis, and the first such case of ROCM was admitted here on May 11, 2021.

Diabetes is a major predisposing condition for ROCM\(^1\) based on this, the sample size was calculated with a prevalence of 50% (Ahmadikia et al.\(^1\)). With a precision of 10% at a 95% confidence interval (CI), the sample size was 96, rounded to 100. We wanted to analyze ROCM at the very onset of the epidemic, to help in projecting future disease burden on health care and timely planning of resources, so the first 100 consecutive patients with compatible clinical manifestations and magnetic resonance imaging (MRI) suggestive of ROCM currently admitted for further management giving informed consent were included in the study. Patients with incomplete medical records and those who left against medical advice (LAMA) or died before MRI could be done, were excluded.

By June 12, 2021, 135 cases were admitted to the dedicated mucormycosis wards; after excluding 35 cases, 100 were selected as study patients. Aseptate hyphae on KOH mount were seen in 31 samples, three of these were culture positive. Thirty-five were negative; reports of 34 patients were awaited. Thirty-five were negative; reports of 34 patients were awaited.

Data were collected from indoor records of the patients on a self-designed pre-tested semi-structured proforma. Information was collected on demographic characteristics, the prominent clinical presentation of ROCM, predisposing conditions such as underlying diabetes mellitus or other immunosuppressive diseases, history of COVID-19 infection, its management with systemic steroids, oxygen supplementation, and immunosuppressant, ICU admission, and duration of hospital stay.

Based on the history of COVID-19, patients were categorized as:

- a. Recovered COVID-19: Patients were either discharged from hospital or in-hospital but 2-weeks had passed post-detection.\(^5\)
- b. Active COVID-19

Diabetes at presentation was categorized as:

- a. New-onset diabetes: Defined by hyperglycemia, confirmed COVID-19, negative history of diabetes, and a history of a normal glycosylated hemoglobin level.\(^6\)
- b. Pre-existing diabetes: Self-reported controlled diabetes (HbA1c <6.5%) or uncontrolled diabetes (HbA1c >6.5%).\(^7\)

The data were analyzed on SPSS version 16 using descriptive statistical methods for analysis. The percentage was calculated for the frequencies and the mean with standard deviation was computed.

The study was initiated after receiving approval from the Ethics Committee of our institution. Full confidentiality of information was maintained and it was used only for research purposes.

Results

The mean age of patients was 41.84 ± 11.2 years, the range being 18 to 81 years. A larger proportion of patients were male (72%), from rural areas (74%) working as farmers and laborers (64%).

Prominent clinical manifestations were orbital with visual problems (27%) and without visual problems (35%), facial pain and puffiness (27%), and headache and nasal congestion (16%); these patients reported to the hospital 3.3 ±0.89 days after the onset of symptoms [Table 1].

Most of the patients (71%) had a history of COVID-19 within the last 3 months, 63 patients had recovered, whereas 8 had an active infection. Symptoms of ROCM appeared 16.25 ± 4.27 days after COVID-19 detection. Seventy-one patients had diabetes, 43 with mainly preexisting uncontrolled diabetes, whereas 21 patients had new-onset diabetes.

COVID-19 was managed with systemic corticosteroids in 48 patients, for 6.2 ± 1.2 days, 43 patients were hospitalized, and 5 of these were in ICU for 12 ± 8.7 days. Oxygen supplementation also emerged as a predisposing factor for ROCM, 21 patients received it for 6.8 ± 1.97 days.

About half (47%) of patients had both COVID-19 and diabetes. Eighteen such patients had received steroids, whereas 10 had received both steroids and oxygen supplementation for COVID

| Table 1: Demographic characteristics and prominent clinical manifestations (n=100) |
|-----------------|-----------------|
| Characteristics | Number          |
| Demographic characteristic | | |
| Age (Mean±SD) in years: | 41.8±11.2 |
| Gender: Male/female | 72/26 |
| Area of residence: Rural/urban | 74/26 |
| Occupation: Farmer and laborer/others | 64/36 |
| Prominent clinical presentation * | | |
| Unilateral swollen and painful eye | 35 |
| Unilateral facial pain and puffiness | 27 |
| Unilateral swollen painful eye with visual problems** | 27 |
| Headache and nasal congestion | 16 |
| Other symptoms | 12 |
| Time (days) since the onset of symptoms and reporting to the hospital (mean±SD) | 3.3±0.9 |

*Main complaint or symptom. Patient’s presented with one or more prominent presentations. **Ptosis, diplopia, loss of vision
management. One patient on steroid therapy had chronic kidney disease (CKD) also [Table 2].

**DISCUSSION**

In the backdrop of the COVID-19 pandemic, there has been a sudden increase in reporting of ROCM cases from different parts of the country.

At our institute, an average of four to five cases reported every day since May 11, 2021. The present study observed male gender predominance[8-10] and a wide age range from 18 years to 81 years, consistent with other studies.[1,8,10] Rural habitats (74%), farmers, and laborers (64%) were more susceptible. Although not proven but activities that involve close contact with soil or dust if avoided, can help in the prevention of mucormycosis.[11]

The prominent clinical manifestations were orbital followed by nasal as reported by Abdollahi et al.[12] whereas a Tamil Nadu study[9] reported them as nasal discharge followed by nasal obstruction and orbital pain. Orbital involvement is usually due to the spread of the disease from the paranasal sinuses; however, there may be no clinical involvement of the sinuses or the nose.[13] In the present study, we assume that some nasal stuffiness and headache might have started early but were ignored by the patients, the alarm being raised only when swelling and pain around the eye or face was noted. None of the patients had the cerebral extension of fungus.

Early reporting and prompt initiation of antifungal treatment and surgical debridement are crucial to save lives and avoid disfigurement. Most (70) patients reported 2–5 days after onset of symptoms, whereas Ahmadikia et al.[1] have reported an interval of 10.1 days. The early reporting in our study is because mucormycosis was declared an epidemic immediately after initial few cases were suspected and mass media played a big role in awareness generation.

Diabetes (72%) was the prominent predisposing factor as observed by other studies.[1,2,5,8] All patients had adult-onset diabetes. Uncontrolled diabetes has an established and strong correlation with invasive mucormycosis.[9] It was observed in 45 study patients, whereas 21 patients had COVID-19 associated, newly detected diabetes. SARS-CoV-2 may cause alterations of glucose metabolism that could complicate the pathophysiology of pre-existing diabetes or lead to new mechanisms of disease.[6] Besides, it is possible that some cases of pre-existing diabetes might have been unmasked while on COVID-19 management, especially in rural patients.

COVID-19 is an independent immunosuppressive condition.[3] The majority (71%) of patients had COVID-associated ROCM. Sixty-three percent had recovered, a few (8%) were active and none presented with symptoms of COVID-19. ROCM manifested late, 2 weeks (16.25 ± 4.27 days) after COVID-19 diagnosis, as observed in a recent multicentric study.[9]

Out of 100, 48 patients received systemic corticosteroids for COVID-19 for a week (6.2 ± 1.2 days), 43 were hospitalized for 2 weeks (12 ± 8.7 days), and 21 received oxygen support for a week (6.8 ± 1.97 Days). Systemic corticosteroids are lifesaving drugs, used in the treatment protocol for moderate and severe COVID-19 cases. Because of their immunosuppressive nature, susceptibility to secondary infections increases. An independent association between corticosteroids use and mucormycosis has been documented.[2] Mucormycosis is also documented as an acquired nosocomial infection.[10] The unexpected increase in hospital admissions during the second COVID wave might have affected the quality of sanitization; however, because of the late-onset of ROCM after COVID detection (at 2 weeks), we cannot comment on it. CKD was identified as an emerging risk factor for mucormycosis in India.[10] It was present in 3% of our study patients.

About half (47) of patients had both COVID-19 and diabetes, and 18 presented with the sinister trinity of uncontrolled diabetes, COVID-19, and systemic steroid for the development of ROCM.

Limitation: The outcome could not be assessed as it was a cross-sectional study. Multicenter prospective studies with a large sample size would give a better insight.

**CONCLUSIONS**

Orbital and facial manifestations of ROCM were the commonest; males above 18 years of age from rural backdrop were more susceptible. COVID-19, diabetes, and the use
of systemic corticosteroids were independent predisposing conditions for ROCM and their combination was treacherous. CKD as a predisposing condition needs attention. Timely suspicion and treatment of predisposing conditions would check the occurrence and severity of ROCM.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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