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ORIGINAL RESEARCH

Lessons from Coronavirus Disease associated Rhino Orbito Cerebral Mucormycosis: A Case Series from Central India

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ABSTRACT

Aim and Objectives: The aim of our series is to report risk factors, trend of clinical presentation and management of rhino-orbito- cerebral mucormycosis (ROCM) cases among COVID- 19 patients. **Methods:** At our tertiary care hospital, we gathered demographic, clinical and treatment data of first 20 cases of ROCM in COVID 19 who presented to us between April- May 2021. Treatment according to recent guidelines based on Sion Hospital scoring system (SHSS), were chosen between:

1. conservatively with systemic anti fungals ± functional endoscopic sinus surgery (FESS) or
2. ± transcutaneous retrobulbar Amphotericin B (TRAMB)
3. ± exenteration

Results: Seventeen patients were males (mean age of 53.1± 10.6 years). Of these, 75% acquired mucormycosis post recovery from COVID. Mean duration of COVID illness was 17.6± 3.3 days. All patients received steroids and voriconazole during COVID, 85% had 6- 8 days ICU stay within that month, 75% were diabetics and had poor orodental hygiene, 75% received combination of meropenem, doxycycline, piperacillin- tazobactum and meropenem- tazobactum followed by and the rest received doxycycline and ceftriaxone alongside treatment for COVID. Ten percent received tocilizumab. Ninety percent needed oxygen support including 2 Bipap, 12 non rebreathable mask (NRBM) and 5 oxygen mask. As per clinic-radiological assessment, 50% had 3D stage ROCM, rest ranged between 2B- 4D. As per SHSS (mean score of 26± 11), 60% patients were managed conservatively, 35% were given TRAMB and one unilateral exenteration was done. Among these patients, 85% survived, rest succumbed to COVID sequelae. **Conclusion:** Long ICU stay, superantibiotic and immunomodulator overuse, prolonged oxygen support must raise alertness to identify ROCM, especially in immunocompromised patients. Metabolic control, intravenous amphotericin B administration, endoscopic debridement are mainstay treatment. As an adjunct, exenteration is indicated clinicoradiologically, not merely in loss of vision, proptosis and ophthalmoplegia.

Keywords: COVID 19, mucormycosis, ROCM, TRAMB, exenteration, Amphotericin B, posaconazole

INTRODUCTION

Owing to its potential to rapidly generate immunodeficient state, coronavirus disease (COVID) made us susceptible to opportunistic infections. Out of these, rhino orbito cerebral mucormycosis (ROCM) caught our attention nationwide due to high virulence and aggressive course which if unattended caused mortality within a matter of days. The mucorales exist as much as we do in our biota but we only get infected when our immune response becomes inefficient to combat at the point of entry. Mucormycosis had been on an upsurge in India since two decades in the pre

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COVID era with prevalence of 0.14 cases per 1000 population with death toll of 65,500 lives per year. [1] Even with treatment it carries a mortality rate of approximately 50% going as high as 100% in disseminated disease. [2] Among COVID patients its incidence is 1 in 1000. [3] This rise was widely attributed to the role of some age old and certain newer COVID 19 associated predisposing factors. [4]
In order to control this epidemic, awareness regarding frequency and correlation of these factors with severity and response to treatment was needed as much as early intervention in present cases. We aim to share our cases so as to contribute in compilation of our data with others for understanding the recent trend of this disease among COVID patients for better prevention and fewer mortalities in future.

MATERIAL & METHODS

In our series, we share the initial 20 cases which presented alongside second wave of COVID in year 2021 at a tertiary health centre of Central India. It is an epidemiological observational study which adhered to the tenets of the Declaration of Helsinki and written informed consent was obtained from each participant of the study for publication. Each patient was inquired for COVID related history including age, gender, COVID status on acquiring mucormycosis, period of COVID illness, comorbidities, number of days of steroid intake, highest blood sugar level, ICU stay, oxygen support, type of mask, orodental hygiene practices, use of superantibiotics, immunomodulators and voriconazole or echinocandins. On thorough clinical examination and MRI of brain, paranasal sinuses and orbits we assessed the grade of disease and extent of orbital involvement using the proposed staging of ROCM and Sion Hospital scoring system (SHSS), respectively. [5, 6] Thereafter as per proposed guidelines and experiences, the patients were treated with following lines of treatment as per their condition [7]:

1. Conservative medical management with intravenous administration of liposomal Amphotericin B (5- 10 mg/ kg body weight/ day) for patients with any of the following:

a) active COVID infection
b) Lack of fitness for any invasive ophthalmic procedures.

2. Transcutaneous Retrobulbar Amphotericin B injection (TRAMB, lyophilized 1 ml of 3.5 mg/ ml) for selected cases in Operation Theatre fulfilling any of the following:

a) progression of orbital involvement or/ and sudden vision drop within 72 hours of functional endoscopic sinus surgery (FESS).
b) Profound visual deterioration and severe orbital involvement but unfit for exenteration.

3. Exenteration with FESS in same sitting or on worsening at or more than 72 hours post FESS to be planned for those who presented with complete loss of vision with severe orbital involvement with score of equal to or more than 23 as per SHSS with intraconal involvement including angioinvasion with fungal hyphae can be appreciated on magnetic resonance imaging (MRI) [8].

Data analysis was performed using SPSS software (version 21.0, SPSS, Inc.). Descriptive statistics were applied to feature the collected data in form of frequency distribution tables. In inferential statistics, the qualitative data was analyzed by chi square test. It was considered statistically significant if the p value was less than or equal to 0.05.

RESULTS

Among our patients, 17 were males with mean age of 53.1± 10.6 years. Of these, 75% acquired mucormycosis in post COVID recovery phase whereas mean duration of COVID illness was 17.6± 3.3 days. There were 15 diabetics, of which 1 had coexisting hypertensive and rest had steroid induced hyperglycemia as a feature of newly diagnosed diabetes. The mean fasting and post prandial blood sugar during COVID were 231.7 ± 79.4 mg/ ml and 345.7 ± 71.9 mg/ ml. All patients received steroids and voriconazole during COVID, whereas in addition to above, two received tocilizumab. Forty percent of our patients gave history of use of combination of meropenem, doxycycline, piperacillin- tazobactum and meropenem- tazobactum followed by 35 percent who were given meropenem, piperacillin- tazobactum and doxycycline and the rest received doxycycline and ceftriaxone as part of treatment when admitted for COVID. Seventeen patients gave history of ICU stay, noted to be between 6 and 8 days. Ninety percent needed oxygen support including 2 Bipap, 12 non rebreathable mask (NRBM) and 5 oxygen mask. Only five patients maintained good orodental hygiene.
On fundus examination, we found 4 cases of optic neuritis and central retinal artery occlusion (CRAO) each whereas 10 had normal fundus. Due to hazy media, posterior segment could not be assessed for 2 of our patients hence we assigned SHSS of 15 under section for fundus changes. As per clinical and radiological assessment depicted in graph 1, 10 cases presented with 3D stage of ROCM, followed by 2 cases each of stage 2B, 3C and 4B. There were single cases noted of stage 2D, 4A, 4C and 4D each.

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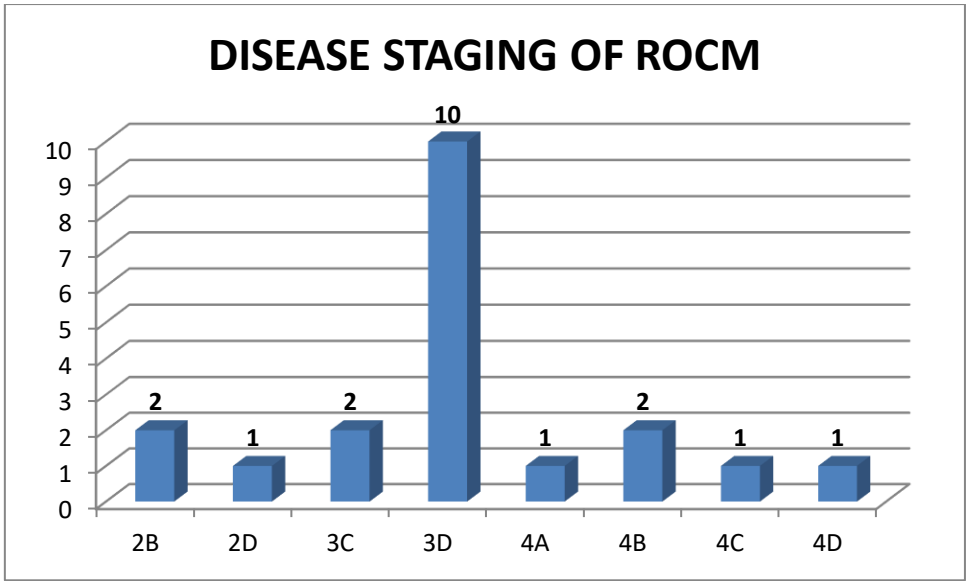
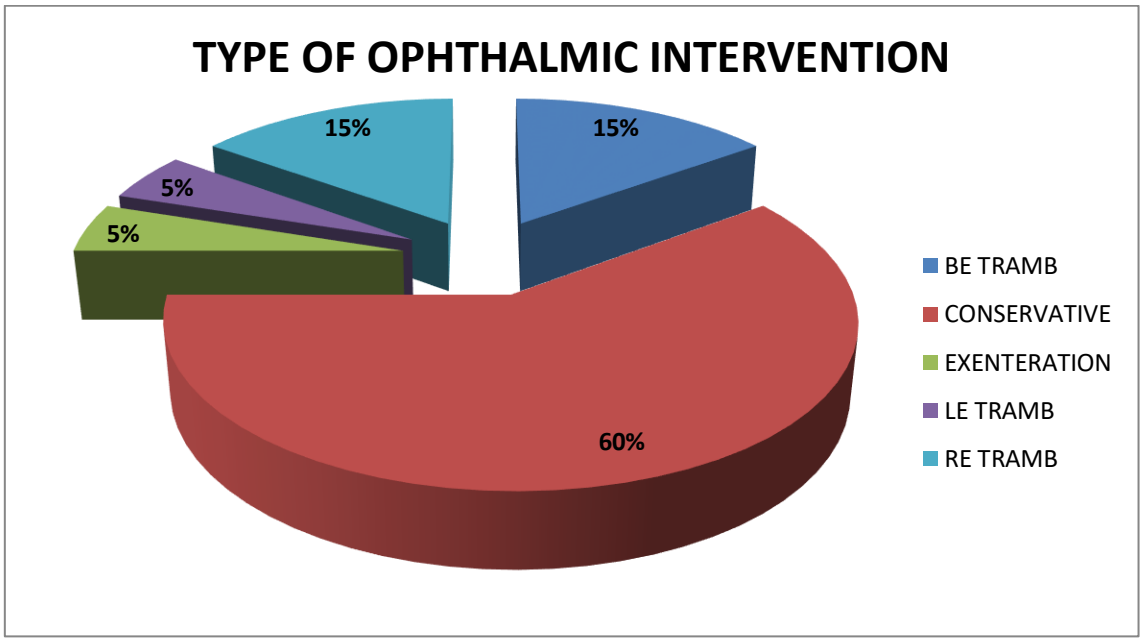


Graph 1: Number of patients- (y axis) in various stages of rhino orbito cerebral mucormycosis (ROCM)- (x axis)

On thorough holistic approach and fitness status, we performed only 1 judicious exenteration with SHSS of 45 and rest were managed by administering 10 mg/ kg daily dose for 2- 3 weeks alongwith TRAMB. For TRAMB we chose 6 patients, of which 5 held SHSS > 23. Among the group of patients who received TRAMB there were 2 deaths due to COVID sequelae. So according to the SHSS (mean score of 26± 11) and ROCM staging, 60% of our patients were managed conservatively, 35% were given TRAMB and one case was undertaken for exenteration as elaborated in pie chart 1. Among these patients, 3 expired and 85% survived.



Pie chart 1: Distribution of percentage of patients as per types of ophthalmic interventions done for orbital involvement in rhino orbito cerebral mucormycosis (ROCM).

DISCUSSION

In accordance with older studies, there is male preponderance affecting young as well as elder population. [2, 3] As established in previous studies we found, the predisposing factors of poor orodental hygiene, use of wet masks, steroid induced uncontrolled sugar levels alongside abuse of superantibiotics and voriconazole favored in creating grounds for uninhibited attack for mucor to grow and spread fiercely in absence of normally defending commensals. [9] As a result the SHSS also was noted to be higher with above factors giving a positive correlation in COVID associated ROCM cases and extent of orbital involvement. Of the 12 cases which

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we managed conservatively, 7 had SHSS of more than 23, which by scoring system only justify exenteration but instead here we emphasize for complete clinical evaluation too.[6]

If ignored, such exenterations may cause lifelong unrequited disfiguration with uncalled deleterious psychological impact or in some cases may cause on table mortality if neurological fitness is not taken into account. Out of these 7 cases, 4 were unfit for exenteration, as 1 was still COVID positive, 2 had bilateral cavernous thrombosis and 1 had episode of seizures just prior to induction. The remaining two showed regression post FESS, as the removal of medial orbital wall with local Amphotericin B wash during FESS and decompression aided in debulking the load of infection in orbits. A higher, longer and continuous intravenous dose of Amphotericin B was successful in these patients except for one who had developed stage 4D during severe COVID illness which limited us from operating any earlier. There were seven patients who we selected for TRAMB, out of which 3 received bilaterally. We observed arrest of disease and stability in post injection visual status in all of them except one patient who showed visual restoration from counting fingers upto 3 feet to 6/6 after 2 days. One of these patients who were given TRAMB who had pre existing meningioma showed orbital disease regression post FESS on repeat MRI but could not survive as mucor invaded central nervous system aggressively. Another patient who acquired ROCM, expired due to severe post COVID multisystemic complications. Last but not the least, a patient who contracted ROCM during COVID illness had worsened to stage 4A ROCM due to lack of Amphotericin B intravenous injection and for whom we performed exenteration alongwith FESS under general anaesthesia as soon he was fit for this intervention. Post operatively with maintenance on oral posaconazole patient was discharged and he has survived with no signs of reactivation. Once resolved completely, rehabilitation with appropriate prosthesis ensures emotional and mental well being for survivors as we did for this patient. These cases need a multidisciplinary approach as per the daily progress. [10]

CONCLUSION

Our series outcomes emphasize on need of strict sugar control, good orodental hygiene and discouraging abuse of superantibiotics during COVID treatment. Prior to and in conjunction to any ophthalmic intervention, the mainstay treatment lies with adequate stable metabolic control, appropriate intravenous Amphotericin B administration and endoscopic debridement (FESS). Regarding exenteration, as against the most common misunderstanding, the two facts are well established and as follows:

1. Only loss of vision, proptosis and ophthalmoplegia are not indications to exenterate. (We have to evaluate rather on basis of clinical features and imaging)
2. Exenteration alone is not a life saving procedure.

Many patients showed regression and even well sustained disease arrest with TRAMB adjunct to multidisciplinary treatment. Only with early diagnosis and appropriate management, we can deal with this condition more effectively.

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