FUNGAL OSTEOMYELITIS OF FRONTAL BONE FOLLOWING COVID ASSOCIATED MUCORMYCOSIS

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Abstract

Introduction - The second wave of COVID 19 lead to resurgence of opportunistic infections due to injudicious use of steroids. Sinonasal Mucormycosis was declared as an epidemic during the pandemic. The mucormycosis was managed effectively by surgical debridement along with systemic amphotericin B. Now, following the initial treatment of mucormycosis there is a resurgence, in the form of fungal osteomyelitis of the frontal bone. Methods – the prospective study included the cases from ten patients with fungal osteomyelitis of frontal bone due to mucormycosis, all the patients underwent surgical debridement of sequestrum and involucrum with systemic antifungals. Results - The average duration of the recurrence was 22 days following the initial treatment Range (10 days to 33 days). Extracranial bossing following outer frontal cortex erosion in 30% of cases, bicortical erosion in 30%, bifrontal involvement (20%), dural involvement (30%), brain parenchymal involvement and prefrontal cortex (20%) case. All cases underwent debridement of entire sequestrous bone and involucrum till normal bone was identified. The mean duration of admission was 4 weeks (3 to 6 weeks). All treated patients are currently alive without disease, confirmed by CECT. Conclusion - The successful treatment of fungal osteomyelitis due to mucormycosis requires four pronged approach (1) early detection (2) multidisciplinary management of comorbidities (3) surgical debridement of necrotic bone and (4) adequate systemic antifungal therapy. Long term outcomes of fungal osteomyelitis of frontal bone are yet to be established

Introduction

In the early 2021 started with mutation of SARS CoV2 and emergence of B.1.617.1 or Delta variant leading to a deadly resurgence of the disease. This highly virulent strain led to increased mortality due to its high infectivity and virulence[1]. Outbreak of new opportunistic infection mucormycosis was seen among the post covid patients. These secondary fungal infections or coinfections are critical challenges increasing the patient's morbidity and mortality. India has reported the highest number of mucormycosis cases in the world, especially following the second wave of the pandemic[2]. Mucormycosis was declared as an epidemic by the Government of India[3] due to surge in the cases. The mucormycosis was managed effectively by surgical debridement along with systemic amphotericin B through the multidisciplinary teams in hospitals across India[4]. Now, following the initial treatment of mucormycosis there is a resurgence, in the form of fungal osteomyelitis of the frontal bone. This form of presentation has not been previous recognized, with only a very few case reports describing it. The resurgence of this disease is attributed to the incomplete clearance, inadequate amphotericin dosing, comorbidities, immune status and previous disease extent[4,5].

Here in this article, we describe the presentation, clinical features, radiological, intraoperative findings, and post operative outcomes following the management of frontal osteomyelitis of fungal origin.

Subjects and methods

This is a prospective, single-centre, interventional study at "Blinded for review". This cross-sectional study has included the patients presenting with recurrence in the frontal bone following the initial treatment of covid associated mucormycosis by surgical debridement and systemic amphotericin B . ten patients admitted and treated at our centre from 1st July 2021 to 30th September 2021 were included in the data analysis. A detailed proforma to record the demographic data, clinical presentation, investigations, points in pathogenesis, and pathogenesis of the management in each patient. The data analysis was performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. The Institutional Research Cell approval was obtained for the study under reference OW/RC/AIIMS-RPR/2021/571. STROBE guidelines has been utilized for data reporting.

A check nasal endoscopy was done to look for other focus of infection in the sinonasal cavity. A complimentary cross sectional radiological imaging was performed to look for the disease extent and to determine the intracranial spread. The patients were planned for appropriate open surgical debridement based on the disease extent. An intraoperative fungal KOH smear was performed to determine the mucormycosis. After the ablative surgery, a definitive permanent plastic reconstruction procedure was deferred due to the possibility of disease recurrence and contaminated surgical field. The patients were restarted on Liposomal Amphotericin B, irrespective of the previous cumulative dosing. High-risk patients were started on a prophylactic dose of low molecular weight heparin from the 1st postoperative day to reduce the incidence of thromboembolism[6,7]. The patients were started on isotonic saline nasal douching to clear the slough and debris upon nasal pack removal. Early recovery after surgery (ERAS) guidelines were strictly followed. All patients received pulmonary conditioning exercises, incentive spirometry, and chest physiotherapy. The patients were considered for discharge if they were clinically stable with reasonable control of comorbidities, completed their target dosage of amphotericin B and had no radiological evidence of disease.

Results

A total of ten patients were admitted for recurrent frontal osteomyelitis following initial treatment of covid associated sinonasal mucormycosis. A total of eight patients (80%) were diagnosed with recurrent Mucormycosis by KOH mount of pus from the frontal bone osteomyelitis sent intraoperatively (Fungal elements/broad aseptate hyphae). Nine patients were male (90%) and one female (10%). All the patients (100%) had previously diagnosed sinonasal mucormycosis and previous history of COVID 19 infection. 3 patients (30%) had previously undergone orbital exenteration for CAM.

The average duration of the recurrence was 22 days following the initial treatment Range (10 days to 33 days). The patients presented with frontal headache (100%), frontal bulge (60%), discharging sinus near the medial canthus (10%) (Figure -1), and fever (40%). The diagnostic nasal endoscopy commonly revealed mucosalization of the nasal cavity with mild polypoidal changes in the opened sinuses, there was evidence of pus discharge from the frontal ostium in 30% cases and 40% cases had frontal outflow tract obstruction. Retrospective radiographic review of these patients showed partial to complete opacification frontal sinus in 30% of cases during the initial disease presentation. 30% of patients had undergone debridement of frontal sinus during the initial surgery for CAM.

CECT scan was done to look at the bony status and a complimentary MRI scan was done to look for the soft tissue extent (intraorbital, orbital apex and intracranial extension) and as problem solving tool. The cross sectional imaging revealed extracranial bossing following outer frontal cortex erosion in 30% of cases (Figure -2), bicortical erosion in 30%, bifrontal involvement (20%), Dural involvement (30%), brain parenchymal involvement and prefrontal cortex (20%) case (Table -1).

Open surgical debridement was preferred due to recurrent nature of the disease and for adequate disease clearance. Bifrontal craniotomy with complete debridement of the frontal bone and pericranial flap was

done in 7 patients (70%), ipsilateral supraorbital craniotomy was done for 2 patients (20%), intraoperative CSF leak was seen in 2 patients (20%) and was repaired by primary closure with onlay pericranial flap. reconstruction with free flaps and alloplastic materials were not done due to the possibility of seeding in the graft and foreign body reaction. Frank pus was seen in all the patients after exteriorizing the frontal sinus. Bony sequestrum and involucrum was seen along the frontal bone in all the cases (Figure -3). Debridement entailed removal of entire sequestrous bone and a part of involucrum till normal bone was identified.

None of the patients had post operative CSF leak. A closed suction drain was placed in the cavity, removed if drain was less than 25ml. Nasal tamponade packing was removed on postoperatively following 48h.

No patients had neurological deficits following the surgery, 2 patients had local wound collection which needed exploration and evacuation under anaesthesia (Clavein Dindo Grade 3b). All the patients received prophylactic broad spectrum antibiotic coverage and antifungal treatment with Amphotericin B. Amphotericin B was continued till radiological disease clearance. The mean duration of admission was 4 weeks (3 to 6 weeks). All treated patients are currently alive without disease, confirmed by CECT.

Discussion

Only a handful of case reports have described about the frontal sinus osteomyelitis following mucormycosis[8–11]. Mucormycosis usually affects the nose and paranasal sinuses; the disease can spread via direct extension or by hematogenous spread. Hossieni and colleagues[12] initially have described about the routes of spread of mucormycosis. We hypothesize the following pathway for the spread of mucormycosis into the frontal sinus –

1. Via the ethmoidal air cells by direct extension, leading to frontal outflow tract obstruction.
2. By erosion of frontal sinus floor from superior part of the orbit.
3. Perineural spread along the supraorbital or supratrochlear nerves.
4. Along the anterior ethmoidal arteries.
5. Direct spread to the brain through the roof of the ethmoid and cribriform plate to skull base/frontal bone to Basi frontal lobe.
6. Disease tracking along the Orbital apex.

In acute osteomyelitis, the patient is toxic with tender swelling over the bone involved, called Pott's puffy tumour. The Pott's puffy tumour was initially described as complication of acute bacterial frontal sinusitis. The successful management of frontal bone osteomyelitis entails removal of the entire sequestrum and debriding the involucrum till the normal bony architecture is reached. Frontal sinus obliteration with the fat, muscle and alloplastic materials have been tried with varying success. In the setting of mucormycosis, it is utmost important to clear all the disease till the fresh bleeding is observed. The main crux of frontal sinus cranialization or obliteration in the mucormycosis setting is to ensure complete elimination of disease and dead space, formation of a protective barrier for the intracranial spread and with the ability to reassess clincoradiologically for disease recurrence. The use of alloplastic materials is usually not recommended in the settings of severe infection[13].

The disease is more susceptible to complete endoscopic surgical resection along with bony debridement if detected early[14]. Because antifungal medication alone will not suffice, all grossly diseased tissue must be excised. Debridement should be repeated until a healthy tissue margin is found, and it should be done at regular intervals, if necessary. Sinus surgery, wide resection of necrotic soft tissue and bone, and exenteration of the orbit, if necessary, are examples of more comprehensive surgical treatments[15,16]. According to the available literature, patients with intracranial extension are less likely to react to radical surgery, and their prognosis is poor[17]. However, if surgery is done early on, the chances of survival increase significantly[14]. It is well established that the management of comorbid conditions is crucial in the successful management of mucormycosis. It is also the single most crucial factor determining the overall prognosis of the patient[18].

As per the AMBILOAD trial[19], higher dose preparations of amphotericin B does not improve the overall outcome compared to the conventional dosing. Before amphotericin B dosage, factors such as existing diabetic and hypertension-induced nephropathy must be kept in mind. There is no strict consensus on the duration and the target dosage of amphotericin B therapy[20], especially in the recurrent setting. Based on our institutional expert multidisciplinary team recommendations, we have titrated the target dose based on the extent of the disease, comorbidities, and response to therapy.

The overall better outcomes in this study can be attributed to the early detection, prompt surgical debridement, prolonged amphotericin B and strict management of comorbidities, In a recent systematic review, 80% mortality was seen with CNS involvement[21]; Among the patients who have survived the CNS, debridement has the minimal or early invasion of the dura and brain.

Long term outcomes of fungal osteomyelitis of frontal bone are not well established.

Conclusion

The successful treatment of fungal osteomyelitis due to mucormycosis requires four pronged approach (1) early detection (2) multidisciplinary management of comorbidities (3) surgical debridement of necrotic bone and (4) adequate systemic antifungal therapy. Long term outcomes of fungal osteomyelitis of frontal bone are yet to be established, hence close follow up at regular intervals and disease surveillance is paramount importance.

Table – 1: Case Description

Age
62
52
30
43
33
40
45
43
46
39

M – Male, F – Female, DM – Diabetes Mellites, HTN – Hypertension, SN – Sinonasal, SNP – Sinonasopalatal, SNO – Sino

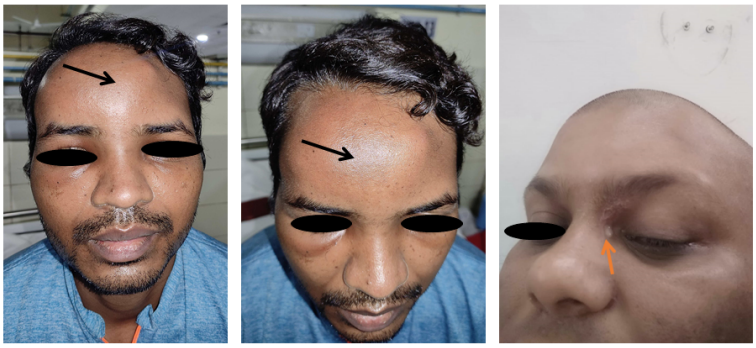

Figure - 1: Panel A and B showing frontal bossing (Black arrow), Panel C showing fronto-cutaneous fistula with pus discharge (Red arrow)

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