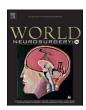
ELSEVIER

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x





Pott's puffy tumor: An unusual complication of rhino-orbito-cerebral mucormycosis

Ananth P. Abraham ^a, Abi Manesh ^b, Soumya Regi ^c, Joy S. Michael ^d, R Hemanth Kumar ^e, Meera Thomas ^e, Lisa Mary Cherian ^f, Lalee Varghese ^f, Regi Kurien ^f, Ranjith K. Moorthy ^a, Bijesh Ravindran Nair ^a, Vedantam Rajshekhar ^a, Vedantam Rupa ^{f,*}

- ^a Departments of Neurological Sciences, Christian Medical College Vellore, Tamil Nadu, India
- ^b Departments of Infectious Diseases, Christian Medical College Vellore, Tamil Nadu, India
- ^c Departments of Radiology, Christian Medical College Vellore, Tamil Nadu, India
- ^d Departments of Microbiology, Christian Medical College Vellore, Tamil Nadu, India
- ^e Departments of Pathology, Christian Medical College Vellore, Tamil Nadu, India
- f Departments of Otorhinolaryngology, Christian Medical College Vellore, Tamil Nadu, India

ARTICLE INFO

Keywords: Mucormycosis COVID-19 frontal Osteomyelitis Pott's puffy tumor

ABSTRACT

Objective: To describe clinicoradiological features and surgical outcomes in a series of nine patients with rhino-orbito-cerebral mucormycosis (ROCM) who presented with Pott's puffy tumor (ROCM-PPT)

Methods: The records of nine patients with ROCM-PPT seen between March 2020 and December 2021 were analysed. Clinical features, radiology, histopathology, operative findings, management and outcome were noted. Frontal sinus pneumatisation and outflow tract configuration was compared between patients and controls with ROCM and no PPT.

Results: ROCM-PPT was diagnosed in 9 of 284 (3.2 %) patients with ROCM seen during the study period. There were six (66.7 %) males and the median age was 54 (IQR 46–60) years. Eight (88.9 %) patients had diabetes mellitus and seven (77.8 %) had been COVID-19 positive. Radiological features of osteomyelitis, subperiosteal abscess formation and dural enhancement were seen in all patients. No significant differences in pneumatisation or frontal sinus outflow tract configuration were noted between patients and controls. All patients underwent a craniectomy with frontal bone debridement and frontal sinus exteriorisation. All patients were treated with antifungal agents for several months. All patients had symptomatic improvement at a median follow-up of 21 (IQR 18–23) months. Repeat CT/MRI scans showed disease regression/resolution in six out of eight (75 %) patients with follow-up imaging, and stable disease in two others.

Conclusions: ROCM-PPT is a rare, delayed complication of mucormycosis that was seen in larger numbers during the recent COVID-19 pandemic. Aggressive debridement of osteomyelitic bone and antifungal therapy results in a good outcome.

1. Introduction

Pott's puffy tumor (PPT), a condition first described by Sir Percival Pott in 1768, has been described as a rare complication of partially treated frontal sinusitis or forehead trauma which is seen predominantly in adolescents. PPT presents as a "doughy" swelling on the forehead caused by osteomyelitis of the underlying frontal bone with subperiosteal abscess formation. Both Gram-positive and Gram-negative bacteria have been reported to cause PPT. In a contemporary review

of a large series of patients with PPT, a fungal etiology was not identified in even a single case. $^2\,$

Sinonasal mucormycosis is a potentially fatal infection caused by angioinvasive fungi of the order *Mucorales*, the commonest infective species being *Rhizopus* and *Mucor*.³ The disease is typically seen among diabetics and immunosuppressed patients. Two recent studies (of mostly diabetic patients) published in the pre-coronavirus disease (COVID-19) era, reported mortality rates of 24 % and 32 %.^{4,5} While intraorbital and intracranial extension of the disease as well as skull-base osteomyelitis

^{*} Corresponding author. Department of Otorhinolaryngology, Christian Medical College Vellore, Tamil Nadu, India, 632004. E-mail addresses: rupavedantam@cmcvellore.ac.in, rupavedantam@gmail.com (V. Rupa).

have been well documented, rhino-orbito-cerebral mucormycosis (ROCM) presenting with PPT (ROCM-PPT) had been reported only once in the pre-COVID-19 era. During the COVID-19 pandemic, however, a few cases of ROCM with frontal bone osteomyelitis were described, chiefly from India, where sinonasal mucormycosis had reached epidemic proportions. As ROCM-PPT is an uncommon complication of sinonasal mucormycosis and the predisposing factors for this are unclear, we reviewed our records of patients with ROCM treated during the pandemic to analyze the clinicoradiological features and outcome of those patients diagnosed with ROCM-PPT to better understand the disease and its causative factors. To the best of our knowledge, this is the largest published series of patients with ROCM-PPT.

2. Methods

2.1. Patient cohort

We retrospectively reviewed the hospital records of 284 patients with ROCM admitted in the Department of Otorhinolaryngology between March 2020 and December 2021 and identified nine patients who were diagnosed with ROCM-PPT between July and December 2021.

2.2. Case definition

Diagnosis of ROCM-PPT was made in patients with ROCM who presented with forehead swelling and had radiological findings of frontal bone erosion with contrast enhancement of the overlying scalp. These clinico-radiological findings were corroborated by intraoperative findings of sub-periosteal abscess formation with necrotic, osteomyelitic bone and histopathological confirmation of fungal osteomyelitis.

2.3. Demographic variables

The demographic variables collected were age, gender, nature and duration of symptoms, presence of comorbid illnesses, history of COVID-19 infection, and history of steroid intake. Details of previous medical and surgical treatment were also documented.

2.4. Radiological assessment

All patients diagnosed with ROCM-PPT underwent contrastenhanced magnetic resonance imaging (MRI) and thin-slice (2 mm) computerized tomography (CT). The extent of frontal bone osteomyelitis, presence of intracranial disease, and degree of frontal sinus involvement was noted.

In order to ascertain the degree of pneumatisation of the frontal sinuses and anatomy of the frontal sinus outflow tract in these patients (which might have predisposed to the development of ROCM-PPT), CT findings were analyzed. Based on the degree of frontal sinus

pneumatisation, as described by Yazici et al, ¹⁶ CT findings were categorized into three types. Type 1 had minimal or no pneumatisation, Type 2 had intermediate pneumatisation and Type 3 (hyperplastic) had extensive pneumatisation, extending lateral to the mid-orbital line (Fig. 1). Kuhn cell configuration and opacification of agger nasi cells were also noted. ¹⁷ The CT findings of these nine patients were compared with eight age- and sex-matched patients with ROCM and frontal sinus disease but no PPT.

2.5. Surgical management of ROCM-PPT

All patients with ROCM-PPT underwent craniectomy and debridement of diseased bone. In five patients, synchronous endoscopic sinus surgery using a previously published protocol, was performed.⁴

Cranial surgery was performed using a bicoronal scalp reflected anteriorly till the supraorbital ridges. Osteomyelitic frontal bone along with the orbital roof (if involved) was debrided with rongeurs till normal bone was reached all around. After complete excision of the mucosa in both frontal sinuses, the sinus cavities were filled and obliterated with fat harvested from the thigh. The frontal sinuses were then exteriorized using a pedicled pericranial graft or fascia lata graft. No reconstruction of the bony defect was performed as our policy has been to avoid insertion of a foreign body/implant in the acute phase when infection is active and disease is contiguous with the paranasal sinuses.

2.6. Medical management of ROCM-PPT

Antifungal therapy included 1-1.5~mg/kg/day of conventional or liposomal amphotericin B for two to three weeks, followed by 300–400 mg/day of oral posaconazole for 3–6 months. Renal function was monitored during therapy. Dose and duration of posaconazole was titrated based on the patient's clinical and radiological response to therapy.

2.7. Follow-up protocol

Patients were asked to review every month in a combined Otorhinolaryngology and Infectious Diseases outpatient clinic for the first three months and then every three months for a year. Visits to the Neurosurgery clinic were scheduled a month after surgery, six months after surgery and one year after surgery. Annual visits thereafter to both clinics were recommended. Relevant blood investigations, nasal endoscopy and repeat imaging with CT/MRI were ordered as appropriate. Patients who were unable to attend the outpatient clinics were followed up via telephonic interviews.

Clinical response to treatment was defined as resolution of presenting symptoms and signs. Resolution of disease on radiology was defined as no residual osteomyelitic bone or contrast enhancement on CT and/or MRI. Disease regression was defined as a reduction in disease burden on

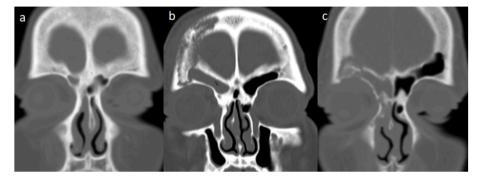


Fig. 1. Yazici classification of frontal sinus pneumatisation: Representative preoperative non-contrast enhanced CT scans from our patient series showing **(a)** Type 1 (aplastic/hypoplastic) frontal sinus pneumatization, **(b)** Type 2 (medium) frontal sinus pneumatisation and **(c)** Type 3 (hyperplastic) frontal sinus pneumatisation.

CT/MRI compared with the initial scans.

2.8. Statistical analysis

Data were entered into a Microsoft Excel database and analyzed using SPSS version 25.0 (Armonk, NY: IBM Corp). Frequency and percentage were used for categorical variables. Mean \pm standard deviation (SD) or median with inter-quartile range (IQR) was used for continuous variables as applicable. Categorical variables were compared using either the Fisher's exact test or Chi-square test. Continuous variables were compared using Student's t-test. A p value of t0.05 was considered significant.

2.9. Ethical considerations

This retrospective study was approved by the Institutional Review Board of our institution (IRB Min No. 14642, dated 27th April 2022)..

3. Results

3.1. Demographic profile (Table 1)

There were six (66.7 %) males and the median age was 54 (IQR 46–60) years (range, 32–65 years). Eight (88.9 %) patients were diabetic. Seven (77.8 %) had a history of recent COVID-19 infection, four of whom received steroid therapy.

3.2. Clinical features

All nine patients presented with diffuse, non-tender forehead swellings extending from the supraorbital ridge to just above the hair line. The swelling crossed the midline in seven patients and was lateralized to one side in two. Four had associated headache. One patient had a discharging midline sinus. The median time between endoscopic sinus surgery done for the nasal disease and presentation with ROCM-PPT for the five previously operated patients was 5 (IQR 3–5) months (range, 1–9 months). The median time interval between COVID-19 infection and PPT was 3.5 (IQR 2–5) months (range, 2–5 months).

Table 1 Clinical features and outcomes of patients with ROCM-PPT.

Patient History of Previous endonasal Antifungal Antifungal Follow-up Clinical Radiological Diabetes Fungal (years)/ COVID-19/ surgery/interval therapy prior to culture therapy duration outcome number outcome gender months between surgery and ROCM-PPT following (months) diagnosis of ROCMbefore diagnosis/ surgery for ROCM-PPT duration ROCM-PPT PPT (months) 1 AmB x 14 days 32/F Yes Yes/4 Not performed No Sterile 23 Resolved Regression Posa x 5.5 mo 2 55/M Yes Yes/2 AmB x 13 days Sterile AmB x 14 days 23 Resolved Resolved Posa x 9 days Posa x 4.5 mo 3 Not performed AmB + Posa x 5 Resolved Resolved 61/F Yes/2 Sterile AmB x 23 days 23 Yes days Posa x 5 mo 59/M Yes/5 Resolved No post-op 4 Yes No No Sterile AmB x 14 days 5 Posa x 4.5 mo imaging Yes/3.5 AmB x 10 days Resolved Stable residue 5 54/M Yes Yes/3 Sterile Posa x 9 mo 21 Posa x 2.5 mo 6 46/M Yes/3 Not performed Posa x 20 days Sterile AmB x 14 days Resolved Regression 21 Posa x 5.5 mo 7 48/M Yes Yes/5 Yes/5 AmB x 14 days Sterile Posa x 7 mo 20 Resolved Stable residue Posa x 4.5 mo 8 65/M Yes No Yes/9 AmB x 28 days Sterile Posa x 6 mo 17 Resolved Regression Posa x 8 mo 46/M No Yes/5 Not performed No R. arrhizus AmB x 14 days 19 Resolved Regression Posa x 4.5 mo

Abbreviations: ROCM-PPT – rhino-orbito-cerebral mucormycosis with Pott's puffy tumour, HPE – histopathological examination, AmB – amphotericin B, Posa – posaconazole.

3.3. Previous management (Table 1)

Five patients had undergone endoscopic sinus debridement (three elsewhere and two at our institution) before presenting with features of PPT. Six patients were administered antifungal therapy after diagnosis of ROCM. This included four previously operated patients. Two of these patients had subsequently discontinued antifungal therapy within a month, while the remaining four (two who had undergone prior surgery and two who had not) were on posaconazole at the time of presentation with ROCM-PPT..

3.4. Radiology (Table 2)

Of the 284 patients with ROCM seen during the study period, 28 (9.9 %) were found to have frontal bone osteomyelitis. However, only nine (3.2 %) of 284 patients developed ROCM-PPT. These nine patients had erosion of both outer and inner tables of the frontal bone with mottling and sequestrum formation along with thickening and enhancement of the overlying scalp and underlying dura (Fig. 2A). The affected frontal sinuses were also completely opacified. Nineteen (6.7 %) patients had relatively small areas of frontal osteomyelitis without PPT (Fig. 2B). One patient had bilateral cavernous sinus involvement with partial right internal carotid artery thrombosis (Fig. 2C) and another had a very small frontal lobe abscess adjacent to the convexity dura (Fig. 2D).

On comparing the CT findings of the nine patients who developed ROCM-PPT with eight age- and sex-matched controls (ROCM patients with frontal sinus disease but no osteomyelitis) from our hospital, none of the controls were found to have bilateral frontal sinus disease compared to 78 % among the cases (p=0.002). While mucosal thickening alone was seen in the frontal sinuses of the controls, complete opacification of the sinus (100 %) with erosion of the surrounding bone (78 %) were seen only amongst the cases (p<0.001). Various morphological parameters of the frontal sinus outflow tract including agger nasi involvement, presence of different types of Kuhn cells, frontal sinus ostium and frontal sinus beak dimensions, and degree of pneumatisation of the frontal sinus showed no significant differences between cases and controls.

Table 2CT findings of the frontal sinus in patients with ROCM-PPT and controls.

	Cases (n = 9) N (%)	Controls ^a (n = 8) N (%)	p value
Frontal sinus disease			
Unilateral disease	2 (22.2)	8 (100)	0.002
Mucosal thickening only	0 (0)	8 (100)	< 0.001
Complete opacification (any side)	2 (22.2)	0 (0)	
Erosion of frontal sinus walls (any side)	7 (77.8)	0 (0)	
Agger nasi cell			
Opacified (any side)	1 (11.1)	2 (25)	NS
Aerated (both sides)	7 (77.8)	6 (75)	
Not discernible (both sides)	1 (11.1)	0	
Kuhn cell type			
Type 1	4 (44.4)	1 (12.5)	NS
Type 2	0 (0)	1 (12.5)	
Type 3	1 (11.1)	3 (37.5)	
Mixed	1 (11.1)	1 (12.5)	
Absent	2 (22.2)	2 (25)	
Not discernible	1 (11.1)	0 (0)	
Frontal beak dimensions (at site of	maximum proj	ection) ^b	
Mean \pm SD (mm)	7.8 ± 1.3		NS
Range (mm)	6-9.3	7–10	
Frontal ostium dimensions at same	site as beak ^c		
Mean \pm SD (mm)	5.3 ± 1.4	5.1 ± 1.5	NS
Range (mm)	4-6.8	3–7	
Yacizi classification of frontal sinus	S		
Type 1	3 (33.3)	0 (0)	NS
Type 2	3 (33.3)	6 (75)	
Type 3	3 (33.3)	2 (25)	
Type of frontal bone osteomyelitis			
Lateral	2 (22.2)	NA	NA
Central	7 (77.8)	NA	

Abbreviations: ROCM-PPT – rhino-orbito-cerebral mucormycosis with Pott's puffy tumor, NS – not significant, SD – standard deviation, NA-not applicable.

3.5. Surgical management

Endoscopic examination of the sinuses during surgery showed either edematous polypoid mucosa or necrotic mucosa in all patients. All necrotic and polypoid mucosa was excised and histopathologically studied. In patients who had undergone prior surgery at our institution with no obvious frontal sinus disease on CT, a Draf 1 procedure had been performed. In patients with evidence of frontal sinus mucosal thickening who had undergone prior surgery at our institution, Draf 2a had been performed. In patients who presented with ROCM-PPT without prior surgery as well as all those who had undergone prior surgery, a combined approach debridement with Draf 3 was performed.

The mean duration of the cranial surgery was 141 min (range, 120–180 min) and the mean blood loss was 342 ml (range, 100–500 ml). Subperiosteal abscess formation was noted in all operated patients. Five patients had small dural tears during surgery due to dense adherence of the diseased dura to the inner table of the skull. One of them developed postoperative CSF rhinorrhoea, which subsided with bed rest and lumbar subarachnoid drain. No other surgery-related complications occurred. Fig. 3 shows the intraoperative findings of one of the patients.

3.6. Histopathological examination and cultures

Histopathological examination revealed bone invasion by broad aseptate hyphae and necrosis in all patients. A positive culture was noted in only one patient and the isolate was *Rhizopus arrhizus*. This patient had not had prior surgery and had not received antifungal therapy.

3.7. Antifungal therapy (Table 1)

After surgery for ROCM-PPT, six patients received two weeks of intravenous amphotericin B followed by oral posaconazole, while three patients continued to take posaconazole that they had been taking before presentation. Two patients with good renal function had a second course of amphotericin B when they presented with ROCM-PPT. The mean duration of administration of postoperative antifungal therapy was 6 ± 1.3 months (range, 5–9 months).

3.8. Outcome (Table 1)

The median duration of follow-up after surgery was 21 (IQR 18–23) months (range, 5–23 months). All nine patients were alive at follow-up and had resolution of clinical symptoms. Among the eight patients with follow-up radiological imaging, six (75 %) had disease regression or resolution (Fig. 4) while two who were on treatment had stable residual disease (Fig. 5).

4. Discussion

Sinonasal mucormycosis typically presents as ROCM with rapid onset of features of orbital cellulitis and/or intracranial involvement in diabetics or immunosuppressed patients. During the COVID-19 pandemic we noted a disproportionate number of patients with orbital and intracranial involvement. ^{18–20} Significant cranial vault osteomyelitis secondary to ROCM was also seen, albeit less frequently. ^{7–9,12,13,21,22} However, presentation as PPT has been rarely described during either the pre-pandemic or pandemic eras, ¹¹ both publications being single case reports in adult patients.

4.1. Pathophysiology and probable risk factors

We observed that calvarial osteomyelitis involving the frontal bone appeared to be a delayed manifestation of mucormycosis in almost 10 % of patients in our series, nine (3 %) of whom progressed to develop ROCM-PPT. A likely mechanism in these patients is that angioinvasion by Mucor/Rhizopus species leads to the formation of thrombi within the blood vessels with subsequent infarction and necrosis of the surrounding tissues.²³ Bone necrosis, which occurs in osteomyelitis, restricts the ability of systemic antifungals to reach the target areas, causing further cell death. COVID-19 induced vascular thrombosis and vasculitis with resultant necrosis is another possible mechanism by which osteonecrosis occurs.²⁴ Diabetes mellitus is known to provide a favourable environment for the growth of Mucorales. 25 The reduced pH of the blood and hyperglycemia in these patients result in the impaired ability of phagocytes to kill the fungal spores and instead promote their growth by diminishing the iron-binding capacity of transferrin. Increased free iron concentration in the serum has been shown to prolong survival of Mucorales, especially Rhizopus oryzae. 25

Five of the nine patients in our series had previously undergone debridement of the paranasal sinuses (including the frontal sinus) for sinus involvement. These patients developed frontal bone osteomyelitis several weeks after initial surgery and institution of antifungal therapy. While it may be surmised that incomplete frontal sinus clearance may have been the cause of persistent disease in these patients, the degree of frontal sinus involvement and surgery done were similar to several such patients with mucormycosis both during the COVID-19 pandemic and in the pre-pandemic period.^{4,20} In other words, the same technique of frontal sinusotomy was followed for all ROCM patients operated at our institute during the pandemic and only two patients developed osteomyelitis progressing to PPT (the remaining seven were either operated elsewhere or had PPT at presentation). Hence, it is unlikely that inadequate frontal sinus clearance is the main cause for the development of the disease. Furthermore, since 4 (44 %) of our patients had PPT at presentation, the role of incomplete frontal sinus clearance as a possible

^a Controls include all patients with ROCM with no frontal osteomyelitis.

b Could not be measured in 3 patients with ROCM-PPT.

^c Could not be measured in 5 patients with ROCM-PPT.

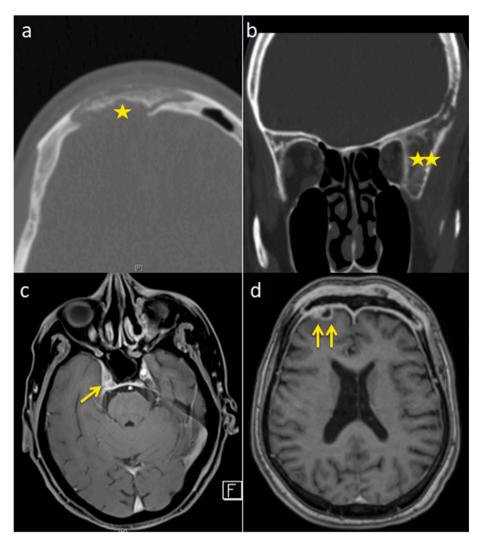


Fig. 2. Pre-operative imaging: (a) Plain axial CT of a 32-year-old female showing osteomyelitis of the right side of the frontal bone and sequestrum formation (single star) with PPT. (b) Plain coronal CT of a 67-year-old male showing osteomyelitis of the left frontal bone adjacent to the frontal sinus (double star) without PPT. (c) Axial gadolinium enhanced T1-weighted MRI in a 65-year-old male showing fungal disease in the right cavernous sinus chronic partial thrombosis (single arrow). (d) Axial gadolinium enhanced T1-weighted MRI in a 61-year-old female showing thickening and enhancement of the bilateral frontal dural with a small underlying right frontal abscess (double arrow).

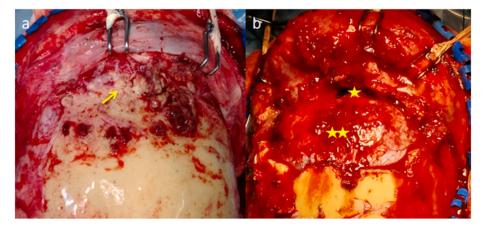


Fig. 3. Intra-operative photographs: (a) Photograph after elevation of the bicoronal scalp flap showing inflamed scalp and diseased frontal bone with pockets of subperiosteal pus formation (arrow) (b) Post-debridement picture showing underlying intact dura (single star) and open frontal sinuses cleared of diseased mucosa with well-visualised sinus ostia (double star).

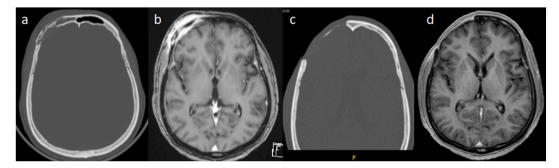


Fig. 4. Illustrative case: This 55-year-old male presented with headache and epiphora for three days. He had undergone endoscopic debridement of the paranasal sinuses elsewhere a month earlier. He had also been started on antifungal therapy at the same center. (a) Axial CT of the paranasal sinuses shows osteomyelitis of the right side of the frontal bone and roof of the orbit. (b) Axial gadolinium enhanced T1-weighted MRI of the brain shows disease involving the right frontal scalp, bone and underlying dura. (c, d) Contrast enhanced T1-weighted axial MRI and axial CT done 5 months after surgery shows right frontal craniectomy defect with no evidence of residual disease.

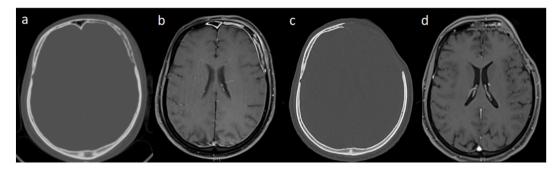


Fig. 5. Illustrative case: This 46-year-old male presented with headache, left sided forehead swelling and intermittent nasal discharge for six months. (a) Axial CT of the paranasal sinuses shows extensive osteomyelitis of the left frontal bone, more on the left side (b) Axial gadolinium enhanced T1-weighted MRI of the brain shows involvement of the left frontal convexity dura. (c, d) Contrast-enhanced T1-weighted axial MRI and axial CT done 6 months following surgery showing a left frontal craniectomy defect with partial remission of disease. The patient was continued on antifungal therapy.

cause is unlikely.

In order to ascertain whether either the degree of pneumatisation of the frontal sinus or incomplete clearance of the frontal sinus outflow tract may have had a role to play in the development of PPT, we compared radiological features in both patients and controls (Table 2). However, our analysis showed that both pneumatisation as well as the disposition of the frontal sinus outflow tract was similar in both cases and controls.

In the absence of anatomical factors or inadequate surgery at the first instance predisposing to the development of ROCM-PPT, we speculate that impaired phagocytosis due to diabetes mellitus and prior COVID-19 infection causing more aggressive disease or gradually progressive impact of COVID-19 induced avascular necrosis may be causative factors in these patients.

4.2. Management

Our results show that the ideal treatment ROCM-PPT is surgical debridement of necrotic bone via a combined open (craniectomy) and endoscopic approach along with appropriate antifungal therapy. Unlike bacterial PPT which can occasionally be managed conservatively, surgical exploration is mandatory in patients with ROCM-PPT. The extent of surgery required in patients with frontal osteomyelitis without PPT is controversial. In a series of four cases with fungal frontal osteomyelitis (without PPT), the authors describe using a Lynch Howarth incision in combination with endoscopic resection of diseased bone and mucosa. ¹⁰ However, all four patients had erosion of only the anterior wall of the frontal sinus. Other series have described a craniotomy approach for similar cases. ^{7–9} Our own experience with 19 patients with ROCM and frontal osteomyelitis without PPT showed that there was no need to

re-explore patients via either an open or endoscopic approach if the initial endoscopic debridement using a standard protocol was performed and followed up with antifungal therapy and regular cavity cleaning of the operated sinuses. We applied the same protocol for the management of patients with extensive skull base osteomyelitis too, with good outcomes. Radiological evidence of osteomyelitis in the absence of progressive inflammatory symptoms like pain, swelling or headache does not warrant surgical exploration. The radiological features of osteomyelitis sometimes persist for several months to years.

During the COVID-19 pandemic a greater proportion of patients with intracranial, intradural disease were seen than in the pre-pandemic era. ^{18,20} Patients with ROCM and intradural disease in the form of large abscesses often require craniotomy and excision. The prognosis in these patients is, however, poor. In contrast, patients with ROCM-PPT underwent craniotomy and debridement and had a good outcome because the disease was largely extradural. It should be noted that debridement could result in CSF leak because the dura is often densely adherent to diseased bone. Intraoperative repair of the dural defect and measures to control any postoperative CSF leak help to prevent potentially fatal secondary meningitis.

5. Limitations of the study

This study has the inherent limitations of any retrospective study with suboptimal follow up in one out of nine patients. Even among the eight patients with follow-up >1 year, radiological disease clearance was observed only in two. Further follow-up therefore is required to determine the long-term outcome of patients with ROCM-PPT.

6. Conclusions

ROCM-PPT is an unusual complication of sinonasal mucormycosis that we encountered for the first time during the COVID-19 pandemic. Unlike ROCM with intradural extension, patients with ROCM-PPT have favourable long-term outcomes with aggressive debridement of osteomyelitic bone and disease clearance from the frontal sinuses. No variations in frontal sinus pneumatisation or outflow tract anatomy were found to predispose to ROCM-PPT.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Availability of data

The data of this study are available from the corresponding author, upon reasonable request.

CRediT authorship contribution statement

Ananth P. Abraham: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Abi Manesh:** Writing – review & editing, Validation, Methodology. Soumva Regi: Writing – review & editing, Validation, Data curation. Joy S. Michael: Writing - review & editing, Resources. R Hemanth Kumar: Writing - review & editing, Resources. Meera Thomas: Writing - review & editing, Resources. Lisa Mary Cherian: Writing - review & editing. Lalee Varghese: Writing - review & editing. Regi Kurien: Writing - review & editing. Ranjith K. Moorthy: Writing - review & editing, Supervision, Conceptualization. Bijesh Ravindran Nair: Writing – review & editing. **Vedantam Rajshekhar:** Writing – review & editing, Supervision, Conceptualization. Vedantam Rupa: Writing -Supervision, review & editing, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- Koltsidopoulos P, Papageorgiou E, Skoulakis C. Pott's puffy tumor in children: a review of the literature. *Laryngoscope*. 2020;130:225–231. https://doi.org/10.1002/larv.27757.
- Rohde RL, North LM, Murray M, Khalili S, Poetker DM. Pott's puffy tumor: a comprehensive review of the literature. Am J Otolaryngol. 2022;43, 103529. https://doi.org/10.1016/j.amjoto.2022.103529.
- Petrikkos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP. Epidemiology and clinical manifestations of mucormycosis. *Clin Infect Dis*. 2012;54: \$23–\$34. https://doi.org/10.1093/cid/cir866.
- Malleshappa V, Rupa V, Varghese L, Kurien R. Avoiding repeated surgery in patients with acute invasive fungal sinusitis. Eur Arch Oto-Rhino-Laryngol. 2020;277: 1667–1674. https://doi.org/10.1007/s00405-020-05879-v.
- Varghese L, Malleshappa V, Yadav BK, Kurien R, Rupa V. Risk factors and predictors of mortality in acute invasive fungal sinusitis - a single-institution experience.

- J Laryngol Otol. 2022;136:1320–1327. https://doi.org/10.1017/
- Effat KG, Karam M, El-Kabani A. Pott's puffy tumour caused by mucormycosis. *J Laryngol Otol.* 2005;119:643–645. https://doi.org/10.1258/0022215054516304.
- Mavani SB, Joshi SJ. Frontal bone osteomyelitis: a dreaded complication of post-COVID mucormycosis. *Neurol India*. 2022;70:1283–1284. https://doi.org/10.4103/ 0028-3886-349670
- Mehta R, Rao KN, Nagarkar NM, Sharma A, Kumar B, P K. Outcomes of open frontofacial resection for fungal osteomyelitis of frontal bone. Rambam Maimonides Med J. 2022;13, e0025. https://doi.org/10.5041/RMMJ.10484.
- Chugh A, Punia P, Gotecha S, Rege I, Shinde V. Post mucormycosis frontal bone osteonecrosis: "A road less traveled during the pandemic.". World Neurosurg. 2023; 172:e335–e342. https://doi.org/10.1016/j.wneu.2023.01.023.
- Arora N, Wadhera R, Professor O, et al. Isolated frontal sinus mucormycosis post covid 19-external approaches revisited. *Indian J Otolaryngol Head Neck Surg.* 2023. https://doi.org/10.1007/s12070-023-03684-7.
- Arora RD, Thangaraju P. Pott's puffy tumor in coronavirus disease-2019 associated mucormycosis. Rev Soc Bras Med Trop. 2022;55:e0669–e2021. https://doi.org/ 10.1590/0037-8682-0669-2021.
- Das AK, Mani SK, Singh SK. Surgical management of post-COVID invasive rhinoorbito- cerebral mucormycosis and its outcomes: role of neurosurgeons in a tertiary care center. Surg Neurol Int. 2022;13:335. https://doi.org/10.25259/SNI_374_2022.
- Kulkarni P, Beeraka D, Tanwar M, Kim U, Ganesan RM, Saini P. Frontal osteomyelitis post-COVID-19 associated mucormycosis. *Indian J Ophthalmol*. 2023; 71:2906–2910. https://doi.org/10.4103/IJO.IJO_3117_22.
- Chakravarty S, Nagarkar NM, Mehta R, et al. Skull base involvement in covid associated rhino-orbital-cerebral mucormycosis: a comprehensive analysis. *Indian J Otolaryngol Head Neck Surg.* 2023;75:1826–1838. https://doi.org/10.1007/s12070-023-03717-1.
- Eswaran S, Balan SK, Saravanam PK. Acute fulminant mucormycosis triggered by covid 19 infection in a young patient. *Indian J Otolaryngol Head Neck Surg.* 2022;74: 3442–3446. https://doi.org/10.1007/s12070-021-02689-4.
- Yazici D. The effect of frontal sinus pneumatization on anatomic variants of paranasal sinuses. Eur Arch Oto-Rhino-Laryngol. 2019;276:1049–1056. https://doi. org/10.1007/s00405-018-5259-y.
- Bent JP, Cuilty-Siller C, Kuhn FA. The frontal cell as a cause of frontal sinus obstruction. Am J Rhinol. 1994;8:185–192. https://doi.org/10.2500/ 105065894781874278.
- Sen M, Honavar SG, Bansal R, et al. Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India - collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. Indian J Ophthalmol. 2021;69:1670–1692. https://doi.org/ 10.4103/ijo.IJO 1565 21.
- Meher R, Wadhwa V, Kumar V, et al. COVID associated mucormycosis: a preliminary study from a dedicated COVID Hospital in Delhi. Am J Otolaryngol. 2022;43, 103220. https://doi.org/10.1016/j.amjoto.2021.103220.
- Cherian LM, Varghese L, Rupa V, et al. Rhino-orbito-cerebral mucormycosis: patient characteristics in pre-COVID-19 and COVID-19 period. *Rhinology*. 2022;60:427–434. https://doi.org/10.4193/Rhin22.099.
- de Guimarães JA, Boasquevisque GS, Gaspar GG, et al. Progressive chronic calvarial osteomyelitis in rhino-orbital mucormycosis associated with COVID-19. *Orbit.* 2022; 0:1–7. https://doi.org/10.1080/01676830.2022.2080233.
- Ebada HA, Abd El-Fattah AM, Tawfik A. Management of frontal sinus fungal osteomyelitis in the COVID 19 era: a case series. *J Cranio-Maxillo-Fac Surg.* 2022;50: 692–698. https://doi.org/10.1016/j.jcms.2022.07.010.
- Chan LL, Singh S, Jones D, Diaz EM, Ginsberg LE. Imaging of mucormycosis skull base osteomyelitis. AJNR Am J Neuroradiol. 2000;21:828–831.
- Ackermann M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in covid-19. N Engl J Med. 2020;383:120–128. https://doi.org/10.1056/NEJMoa2015432.
- Rammaert B, Lanternier F, Poirée S, Kania R, Lortholary O. Diabetes and mucormycosis: a complex interplay. *Diabetes Metab.* 2012;38:193–204. https://doi. org/10.1016/j.diabet.2012.01.002.

Abbreviations list

COVID-19 -: Coronavirus disease 2019

CT \rightarrow computerized tomography

MRI -: magnetic resonance imaging

PPT -: Pott's puffy tumour

ROCM -: rhino-orbito-cerebral mucormycosis

ROCM-PPT -: rhino-orbito-cerebral mucormycosis presenting with Pott's puffy tumour