Section: ENT

Original Research Article

RETROSPECTIVE STUDY OF OCCURRENCE AND ASSOCIATED PATHOGENESIS OF FACIAL NERVE PALSY IN RHINO-ORBITAL MUCORMYCOSIS

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Abstract

Background: Cephalic mucormycosis has two forms of which rhino-orbito-cerebral form is a fatal variety and rhino paranasal sinuses form generally follows a benign clinical course. We have witnessed a post covid epidemic of mucormycosis which is followed by many complications, one rare complication of which is facial nerve paresis/palsy. The purpose behind this study is to note the facial nerve paresis/palsy occurrence and to establish it's probable pathophysiology in development of facial palsy. **Methodology:** It is an retrospective study conducted at Bharati Vidyapeeth (Deemed to be University)- Medical College and Hospital, Sangli during the period of 6 months In the department of Otorhinolaryngology. We got total of 113 KOH/HPE positive mucormycosis cases and out of which clinically 13 cases had Lower Motor Neurone facial nerve palsy, all 13 cases were included in our study which had undergone thorough clinical and radiological evaluation. **Results:** The mean age of our study participants was 56.23 years with 11 males (84.62%) and 2 females (15.38%). We observed that the facial nerve palsy was seen in right side in 8 cases (61.54%). The majority of the cases had grade 4 facial paresis as seen in 7 cases (53.85%). 11 were Covid-19 positive (84.62%), PPF/ITF involvement was seen in 12 cases (92.31%). Schirmer's Test was severe in 9 cases (69.23%), moderate in 2 cases (15.38%). We found radiologically a significant positive correlation between the PPF and ITF involvement in Mucormycosis cases who developed FNP. ($p<0.05$) **Conclusion:** Facial nerve palsy is an unusual but yet significant presentation of rhino orbital mucormycosis; Hence should not be misdiagnosed with other diseases like cerebrovascular accident leading to delay in treatment. From our study we can infer that involvement of PPF/ITF can act as reservoir and route of spread of mucormycosis to facial nerve suggesting a positive correlation between them.

INTRODUCTION

The American pathologist R. D. Baker is credited with coining the word "mucormycosis." According to published research, there are roughly 1.7 cases of mucormycosis per 1,000,000 people per year.[1] It is a fulminant, opportunistic fungus brought on by Rhizopus species of the order Mucorales. Immunocompromised patients are primarily affected, particularly those with uncontrolled diabetic mellitus (DM). Patients who have undergone an organ transplant, hematopoietic stem cell transplant, neutropenia, or cancer are also at a higher risk.[2] The disease may present in six distinct ways, including pulmonary, cutaneous, gastro-intestinal, ocular, and disseminated, depending on the area afflicted. The most prevalent kind, rhino-orbital cerebral mucormycosis (ROCM), accounts for 30 to 50% of cases.[3] Nasal congestion, headaches, retro-orbital pain, orbital edoema, ophthalmoplegia, and visual impairment in diabetes individuals are typical symptoms of RCM. Mucormycosis is additionally associated to several cranial nerve palsies. Patients with rhino-orbital-cerebral Mucormycosis uncommonly presents with facial nerve paralysis, which accounts

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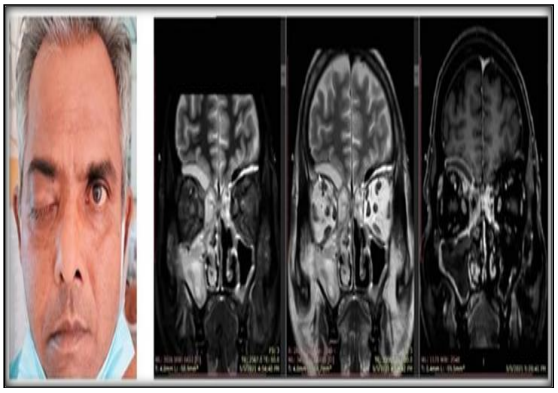
for 11% of cases. The emotional health and quality of life (QOL) are negatively impacted by facial palsy.[4] Very few studies have been done in relationship to the occurrence of facial nerve palsy and in establishing it's probable pathogenesis behind it with respect to mucormycosis. As it's important to note that facial nerve palsy can be a presenting complaint of mucormycosis patient and hence suggests the need of studying it's associations prompt diagnosis and early interventions.

MATERIAL AND METHODS

Retrospective study was conducted at Bharati Vidyapeeth (Deemed to be University) Medical college and Hospital which is a tertiary care teaching hospital and research institute in duration of 6 months after getting Ethical Committee approval (no:BV(DU)MC&H/SANGLI/IEC/514/23). Total of 113 positive cases for Rhino-orbital mucormycosis were studied out of which 13 patients had lower motor neurone facial nerve palsy. These 13 patients were selected for the study after taking their informed written consent. All 13 patients had undergone thorough clinical examination,diagnostic nasal endoscopy and topodiagnostic tests for identifying the level of facial nerve lesion .Following which they were subjected to imaging modalities like CT/MRI scans with contrast to establish its possible pathogenesis behind development of FNP.

Patients' illustrations
Patient with Right facial palsy
Case-1

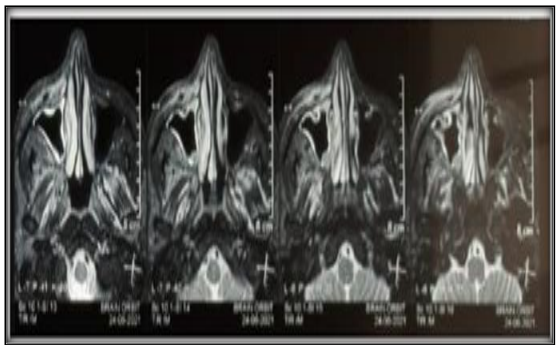


MRIPNS+ ORBIT(P+c) A) CORONAL STIR B) CORONAL T2C) CORONAL TIFS(P+C)

MRI WITH FADOLINIUM CONTRAST of BRAIN WITH PNS WITH ORBITQL CUTS:

A and B – Heterogeneous T2/ STIR hyperintense complete opacification of right frontal, ethmoidal and maxillary sinus causing complete obliteration of right fronto-ethmoidal and right osteo-meatal unit. It show T2 hypointense areas within likely s/o Hyphae/ Inspissated secretions. On post-contrast T1WI it show peripheral contrast enhancement of sinus walls and bilateral inferior turbinates.

Case-1



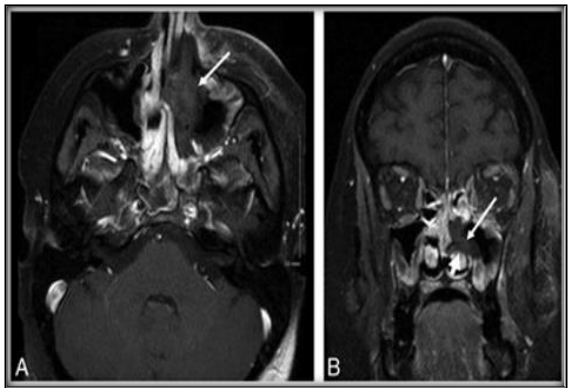
MRI NS STIR Axis images show:
Circumferential STIR Hyperintense signal in right maxillary sinus with adjacent inflammatory changes in right premaxillary region, retroantral, pterygopalatine fossa region and infratemporal fossa region

Patient with left facial palsy

MRI PNS STIR Axial images show:

STIR hyperintense opacification of left maxillary sinus with similar intensity seen involving left inferior turbinate with adjacent extensive soft tissue swelling over left premaxillary, nasal region, soft tissue infiltrates are also seen in retroantral and infratemporal fossa region An ill-defined STIR hypointense soft tissue lesion is seen arising from left maxillary sinus, eroding anterior wall and extending into premaxillary sinus; consistent with fungal infection.

Case-2



AXIAL CORONAL MRI PNS (T1FS P+C):

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Large ill-defined non-enhancing soft tissue lesion is seen extending from left maxillary sinus into left nasal cavity infilterating medial wall of left maxillary sinus left nasal turbinates and nasal septum s/o Nacrosis (Also known as " Black turbinates sign") -seen in acute invasing fungal rhinosinusitis.
Homogeneously enhancing reactive mucosal thickening in rest of paranasal sinuses are noted.

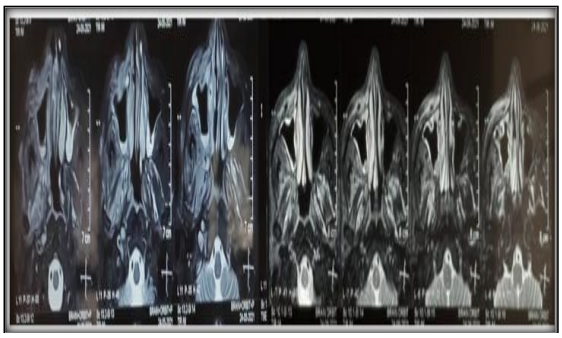
Case 3

MRI PNS STIR Axial images show:

Heterogeneously hyperintense mucosal thickening is noted in bilateral maxillary sinus on STIR axial sequences likely secondary to inspissated secretions/ fungal hyphae.
Mild STIR hyperintense soft tissue swelling is noted in right premaxillary and check region

Extensive involvement of right retroantral region, infratemporal fossa region and right pterygoid muscles. Soft tissue infillterates also seen involving right pterygopalatine fossa and sphenopalatine
Foramen.
Mild oedematous right inferior nasal turbinate, nasal septum and posterior nasopharyngeal wall is also noted.

Case 3



MRI PNS STIR Axial images show:

Extensive STIR hyperintense fat stranding is noted in right premaxillary and cheek region, retrantral region, infratemporal fossa region and right pterygoid muscles, soft tissue infiltrates also seen involving right pterygopalatine fossa and sphenopalatine foramen.

RESULTS

We studied a total of 113 mucormycosis positive cases for the occurrence of facial nerve palsy. We observed that 13 out of total 113 cases who had facial nerve palsy. Therefore, the overall incidence of facial nerve paralysis in mucormycosis cases in our study was 11.5%.

Table 1: Summary of the total 13 cases in our study

SR No.	AGE/GENDER	COMORB.	FNP	GRADE	Covid h/o	HPE	CHEEK	ORBIT	MRI findings
1)	48/M	DM	R	4	Y	Y	N	CHEMOSIS	ITF
2)	68/M	DM	R	4	Y	Y	Y	-	PPF, ITF
3)	71/M	DM	L	5	Y	Y	Y	-	PPF, PPS
4)	75/M	DM	R	3	Y	Y	-	LOV, EOM, PTOSIS	PPF, ITF, PALATE
5)	41 /M	DM	L	4	Y	Y	-	PERINEURITIS, PTOSIS	PPF, ITF
6)	71/M	DM	L	5	N	Y	Y	-	PPF, ITF
7)	55/F	DM	L	4	Y	Y	Y	PTOSIS	PPF, ITF
8)	52/M	DM	R	4	Y	Y		EOM, LOV	ORBITAL APEX
9)	40/M	DM	L	3	N	Y	-	EOM, LOV	ITF
10)	35/M	DM	R	5	Y	Y		PTOSIS, CHEMOSIS	PPF,
11)	65/M	DM	R	4	Y	Y			PPF, ITF
12)	55/F	DM	R	4	Y	Y	Y	-	PPF, ITF
13)	55/M	DM	R	5	Y	Y	Y	PTOSIS	PPF

ITF- Infratemporal fossa PPF- Pterygopaltine fossa EOM – Extra ocular muscle LOV-Loss of vision FNP – facial nerve palsy. We observed that the mean age of our study participants was 56.23 ± 13.04 years.
There were 11 males (84.62%) and 2 females (15.38%) in our study. All our 13 cases had diabetes mellitus as comorbidity (100%).

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Table 2: House-Brackmann classification of facial nerve function

Grade	Number of Cases	Percentage
Grade 3	2	15.38
Grade 4	7	53.85
Grade 5	4	30.77

We observed that majority of the cases had grade 4 paralysis as seen in 7 cases (53.85%) followed by grade 5 paralysis ass seen in 4 cases (30.77%) and grade 3 paralysis was seen in 2 cases (15.38%). We found that out of 13 cases, 11 were Covid-19 positive (84.62%) and rest 2 were Covid-19 negative (15.38%).

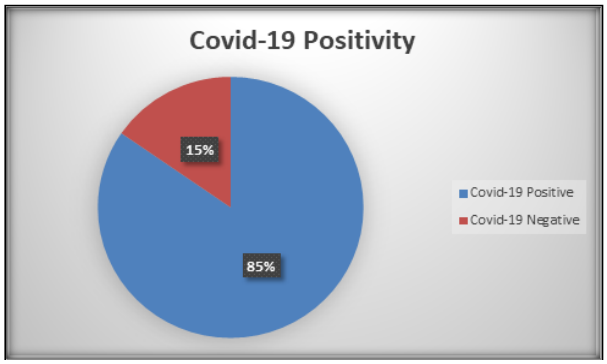

Figure 1: Covid-19 Positivity

Table 3: Summary of study findings

Study Parameters	Number of cases	Percentage
PPF/ITF involvement	12	92.31%
PPF involvement	10	76.92%
ITF involvement	9	69.23%
Cheek Involvement	6	46.15%
EOM Restriction	6	46.15%
Ptosis	5	38.46%
Stapedial Reflex present	13	100%
Loss of Vision	3	23.08%
Cerebral involvement	2	15.38%
Palate involvement	1	7.69%
Sense of taste affected	0	0%

We observed that PPF/ITF involvement was seen in 12 cases (92.31%), Pterygopalatine fossa (PPF) involvement was observed in 10 cases (76.92%), Infratemporal fossa (ITF) involvement in 9 cases (69.23%), Cheeks were involved in 6 cases (46.15%), Extra ocular movement (EOM) restriction was seen in 6 cases (46.15%). We observed that ptosis was seen in 5 cases (38.46%), Stapedial reflex was seen in all cases (100%), loss of vision in 3 cases (23.08%), palate was involved in one case (7.69%) and no intracranial involvement noted. We observed that all the 13 cases had intact sense of taste.

Table 4: Schirmer's Test

Schirmer's Test	Number of cases	Percentage
Severe	9	69.23%
Moderate	2	15.38%
Mild	1	7.69%
Normal	1	7.69%

We observed that the Schirmer's Test was severe in 9 cases (69.23%), moderate in 2 cases (15.38%) and mild in 1 case (7.69%). It was normal in one case (7.69%).

Table 5: Correlation of PPF and ITF involvement with FNP in total mucormycosis cases

	FNP present	FNP Absent	Total	P value
PPF involved	10	12	22	<0.001
PPF not involved	3	88	91	
Total	13	100	113	
ITF involved	9	14	23	<0.001
ITF not involved	4	86	90	
Total	13	100	113	

Significant correlation ($p<0.05$)

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We studied the correlation between the PPF and ITF involvement and presence of Facial nerve paralysis in our study.

We observed that out of 13 cases with Facial nerve paralysis, 10 cases had PPF involvement (76.92%) and 9 cases had ITF involvement (69.23%). While out of the rest 100 cases without FNP, only 12 had PPF involvement (12%) and 14 had ITF involvement (14%).

Thus we found a significant correlation between the PPF and ITF involvement in Mucormycosis cases and presence of FNP. ($p<0.05$).

DISCUSSION

The world has experienced two major waves of Covid-19 disease since last 2 years, the smaller after waves with new variants are still on the rise everywhere. We observed many complications and secondary infections associated with this disease one of the most important of which is mucormycosis infection. We studied the facial nerve paralysis in these mucormycosis cases and tried to study its occurrence and its probable pathogenesis for the involvement of it.

Mucormycosis is an opportunistic infection that can be fatal in patients with metabolic acidosis, iron overload, immune deficiency syndrome, organ transplant, fasting, burns, and those on steroids or deferoxamine.[7,8] All of these factors influence the development of hyphae and the germination of spores.[9] COVID-19 is a major trigger that raises the risk of mucormycosis. Mucormycosis became an epidemic in the pandemic of COVID-19.

Presentation of mucormycosis as the facial nerve palsy has been reported previously in few isolated cases. The involvement of the various tissues in our rhino-cerebral area can lead to the clinical presentation mimicking other conditions like the cerebro vascular accidents (CVA). The aim of this study was to further highlight the involvement of facial nerve paresis as a presenting feature in rhino orbital mucormycosis.

We observed an unusual presentation of facial nerve palsy as cranial nerve II, III, IV, V and VI are most commonly affected cranial nerves in the mucormycosis cases.

The probable involvement of Facial nerve in the mucormycosis infection can be explained as –

Bony Erosion > Spread from maxillary sinus to pterygopalatine fossa > to infratemporal fossa
By bony erosion > Spread from maxillary sinus to premaxillary space to cheek region
By bony erosion > Floor of sphenoid sinus is involved > Vidian nerve and GSPN involvement
It can also be incidental and it also could be non-specific as in Bell's Palsy.

In our study, we evaluated a total of 113 mucormycosis positive cases for the occurrence of facial nerve palsy. We observed that 13 out of total 113 cases had facial nerve paralysis. Therefore, the incidence of facial nerve paralysis in mucormycosis cases in our study was 11.5%.

In a similar study by **R Mehta *et al.***, they studied a total of 196 cases of mucor mycosis out of which 17 cases had facial nerve paralysis with an incidence of 8.67%, litter less than our study findings.[10]

M Gautam *et al.* studied a total of 300 patients with post-COVID-19 mucormycosis cases. Out of which 30 (10%) patients were found to have FNP, similar to our study. All were lower motor neuron (LMN) type and were associated with corneal complications.[11]

YM Reddy *et al.* studied 300 cases of patients with past history of being treated for coronavirus disease and who presented to our department with symptoms of invasive fungal sinusitis.[12]

We observed that the mean age of our study participants was 56.23 ± 13.04 years.

There were 11 males (84.62%) and 2 females (15.38%) in our study.

All our 13 cases had diabetes as comorbidity (100%).

In a similar study by **R Mehta *et al.***, they observed that all cases Diabetes or Hypertension as comorbidities. The mean age of 17 cases with FPN cases. There were 9 males (52.9%) and 8 females (47.1%).[10]

M Gautam *et al.* reported that all 30 patients in their study had hyperglycemia on admission, with 14 known cases and 16 newly diagnosed cases of diabetes.[11]

YM Reddy *et al.* reported that out of total 300 cases, 227 (75.6%) were males and 73 (24.33%) were females, with ratio between males to females to be 3.1:1. The age of the patients ranged from 18 to 80 years with a mean age of 47.05 ± 10.7 years.[12]

We observed that the facial nerve palsy was seen in right side in 8 cases (61.54%) and in left side in rest 5 cases (38.46%).

R Mehta *et al.* also reported less number in left sided facial nerve which were 35.3% as compared to right sided FNP with 64.7% cases.[10]

In our study all were diabetic and most of them had history of COVID -19 or COVID positive status stating probable positive relationship in development of FNP more in these patients than not having, but it cannot be confirmed considering the small number of cases that we have and other study limitations.

We observed that majority of the cases had grade 4 paresis as seen in 7 cases (53.85%) followed by

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grade 5 paralysis ass seen in 4 cases (30.77%) and grade 3 paralysis was seen in 2 cases (15.38%).

Similar findings were reported by **R Mehta *et al.*** with Grade 4 and Grade 5 paralysis seen in 4 cases each (23.53%).[10]

We found that out of 13 cases, 11 were Covid-19 positive (84.62%) and rest 2 were Covid-19 negative (15.38%).

Buil JB *et al.* reported that though most of the cases of mucor mycosis are because of Covid-19, there is a possibility that it may be seen in previously undiagnosed cases of Covid-19 or in negative cases because of associated comorbidities and community spread of mucormycosis.[13]

We observed that PPF/ITF involvement was seen in 12 cases (92.31%), Pterygopalatine fossa (PPF) involvement was observed in 10 cases (76.92%), Infratemporal fossa (ITF) involvement in 9 cases (69.23%), Cheeks were involved in 6 cases (46.15%), Extra ocular movement (EOM) restriction was seen in 6 cases (46.15%). We observed that ptosis was seen in 5 cases (38.46%), Stapedial reflex was seen in all cases (100%), loss of vision in 3 cases (23.08%), no cerebral involvement and palate was involved in one case (7.69%).

Similar kind of presentation was observed by other studies including **R Mehta *et al.*** and **YM Reddy *et al.*[10]**

We observed that the Schirmer's Test was severe in 9 cases (69.23%), moderate in 2 cases (15.38%) and mild in 1 case (7.69%). It was normal in one case (7.69%).

M Aljhali *et al.* also reported that the Schirmer's Test was commonly seen as severe in their cases.[14]

Correlation of PPF and ITF involvement with FNP in total mucormycosis cases

We found a significant correlation between the PPF and ITF involvement in Mucormycosis cases and presence of FNP. ($p<0.05$) Thus proving the correlation between the clinical diagnosis and radiological confirmation of FNP in mucor positive cases.

We observed that out of 13 cases with Facial nerve paralysis, 10 cases had PPF involvement (76.92%) and 9 cases had ITF involvement (69.23%). While out of the rest 100 cases without FNP, only 12 had PPF involvement (12%) and 14 had ITF involvement (14%).

M Gautam *et al.* also reported that the clinical localization of FNP in mucor patients significantly correlated with the radiological findings with a *P* value of 0.0127.[11]

M Aljhali *et al.* also found similar clinico-radiological correlation in their cases.[14]

Rhizopus oryzae is the root cause of 60% of all cases and 90% of rhinocerebral cases. Numerous tissues may be affected in the rhinocerebral region, which could lead to clinical symptoms that resemble cerebrovascular accidents (CVA).[8]

Mucormycosis is a pathology brought on by fungi spores that enter the host through inhalation. These spores germinate, forming hyphae that enter blood arteries, resulting in thrombosis, which eventually obstructs veins and results in ischemia. The angioinvasion with fungal spores results in black necrotic eschar, which causes infection to quickly spread throughout the surrounding area.[10] The ethmoidal, angular, and lacrimal arteries allow the fungus to enter the nasal cavity and then travel to the sinus canals where it invades the palate, orbit, and intracranially.[11] Sino-naso-orbito cerebral mucormycosis can manifest with meningitis, cavernous sinus thrombosis, frontal and medial temporal abscess, and facial nerve paralysis. The pathophysiology and real causation of facial nerve palsy are both unknown. A few authors claimed that bone erosion to the infratemporal fossa via the maxillary sinus to the pterygopalatine fossa may disrupt the nerve entering the stylomastoid foramen. The retroglobal and infratemporal areas of the orbit are believed to be reached by mucor from the pterygopalatine fossa.[11]

As a result, the orbital apex, inferior orbital fissure, and infratemporal fossa can all become infected from the pterygopalatine fossa. In several experiments, it was discovered that Mucorales species move via peripheral nerves.[8] The pterygopalatine fossa is a likely site for perineural invasion due to its closeness to the cranial tissues and the existence of several vascular and neural tissue lineages.[6]

The facial nerve palsy might be accidental and vague, like Bell's palsy, according to another theory. Cases of mucormycosis spreading to the middle ear through the Eustachian tube and facial nerve have been reported.[7] A single involvement may manifest along the intracanalicular facial nerve's nerve sheath within the temporal bone.[13] This explains facial nerve affection without the involvement of any other cranial nerves, as seen in some of the current investigation of patients. The condition of the resistance arteries, which can result in oedema and localised facial nerve ischemia, is another factor contributing to facial nerve palsy in diabetics. Palsy might develop if this damaged the nerve's blood supply.[14] .Involvement of the floor of sphenoid sinus via Vidian nerve ,which is continuation of the greater superficial petrosal nerve(GSPN) is also a viable alternative.In our series contrast enchanced MRI of paranasal sinuses ,orbit and brain was performed as preferred imaging modality .It helps in early detection of a soft tissue involvement and in cases of facial nerve involvement widening of the ptergopalatine fossa and perineural invasion was noted.

The consequence of FNP and prognosis of the patients is yet to be noticed and confirmed from our case series.It is interesting to find FNP as an unusual presentation of an rare disease

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mucormycosis.Our concerns our very few studies have been done in this field and published.

CONCLUSION

Rhino-orbital mucormycosis being an aggressive disease should be promptly diagnosed and treated. Facial nerve palsy is an unusual presentation of mucormycosis; Hence should not be misdiagnosed with other diseases like cerebrovascular accident, hence thorough clinical examination and use of diagnostic modalities like Diagnostic Nasal endoscopy, topodiagnostic test for facial nerve function and contrast enchanced MRI scan should be carried out for early diagnosis .It's was inferred from our study that majority of cases of mucormycosis with FNP had involvement of infratemporal /pterygopalatine fossa noted on MRI scans leading to establish probable pathogenesis behind the spread and association with significant correlation. In this study, the authors emphasise facial nerve paresis as a sign of rhino- orbital mucormycosis. Treatment includes antifungal medications, reversing aggravating potential dangers, and quick surgical debridement. The prognosis for the recovery of facial nerve function in our series is still cannot be commented upon and more time is required for follow-up. A small case series cannot be used to draw conclusions about the impact of facial nerve palsy on the outcomes of mucormycosis patients because it has not yet been demonstrated. For this, we advise doing a thorough investigation encompassing more extensive mucormycosis research with a multicentric approach involving a larger sample size.

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