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Radiographic Involvement of Maxillofacial Region in Mucormycosis Secondary to COVID-19 Using Magnetic Resonance Imaging: A Cross-Sectional Observational Study

[1]Swati Jitendra Rathod, [2]Jitendra Kerba Rathod,[3]Manisha Naiknaware and [4]Rajendra Bohra

[1]Department of Dentistry, M.G.M. Medical College and Hospital, Aurangabad.(Affiliated To MGMIHS, Navi Mumbai) Maharashtra, India

[2-4]Department of Otorhinolaryngology, M.G.M. Medical College and Hospital, Aurangabad. (Affiliated To MGMIHS, Navi Mumbai) Maharashtra, India

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Corresponding Author
Jitendra Kerba Rathod, Department of Otorhinolaryngology, M.G.M. Medical College and Hospital, Aurangabad. (Affiliated To MGMIHS, Navi Mumbai) Maharashtra, India

Author Designation
[1]Associate Professor
[2]Professor
[3]Assistant Professor
[4]Professor and Dean

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Abstract
At the end of second wave of COVID 19, Mucormycosis was the new challenge the whole world was facing. The purpose of the study is to check anatomical involvement of maxillofacial region in Mucormycosis patients using MRI also to know and understand the severity of Mucormycosis secondary to COVID-19.This is a cross - sectional observational study. This study was conducted on 40 patients reported to the department of Radiology for MRI brain, orbit and PNS with provisional diagnosis of Mucormycosis. The radiographic involvement and commonly affected area were noted. The collected data was entered in MS Excel sheet and for analysis SPSS version 25th was used. The qualitative data was represented in frequency and percentage. Quantitative data was represented in mean and standard deviation. Out of 40 patients 28 were male and 12 were female. All the patients were in the age group of 30-80 with the mean age 55.37±12.78 years. The Erosion was seen as 20% in medial wall of right maxillary sinus, 17.5% in medial wall of left maxillary sinus and postero-lateral wall of right maxillary sinus each, 12.5% in Bilateral medial wall of maxillary sinus, 7.5% in inferior wall of left orbit and hard palate each. 5.0% in nasal septum, 2.5% inferior wall of right orbit, bilateral cribriform plates and bilateral inferior wall of orbit individually. The mucosal thickening was observed as 67.5% in bilateral maxillary sinus followed by 37.5% in right and 25% in left maxillary sinus, 55% in bilateral frontal sinus, 52.5% in Sphenoid sinus, 15% in nasal cavity on both side, 12.5% on left and 7.5 % on right side of nasal cavity, 12.5% in bilateral ethmoid, 5% in right and left frontal sinus each. Out of 40 patients 2 had proptosis in left eye and 1 on each right and bilateral eyes. A generalised soft tissue swelling and edema was seen on maxillofacial region. Other involvement like acute infract in left optic nerve (5%), left optic neuritis (5%), right optic neuritis (2.5%), deviated nasal septum with convexity towards right side (7.5%), left optic perineuritis (2.5%), osteonecrosis with osteomyelitis involving bilateral greater wing of sphenoid (2.5%), left zygomatic process of maxilla (2.5%), left pterygoid plate (2.5%) were also noted. the present study shows the systematic approach to study the involvement of maxillofacial region and surrounding structure. This study also helps in nature and spread of the disease.

INTRODUCTION

At the end of the second wave of COVID-19 pandemic the whole world was facing to the new challenge like Mucormycosis. Mucormycosis is a rare but serious fungal infection caused by molds known as mucurmycets[1]. The mode of infection is through inhalation of spores, inoculation of fungi into abrasion or cuts on the skin and consumption of contaminated food. The hyphae cause invasion of blood vessels, resulting in tissue infarction and necrosis[2,3]. Elderly especially with chronic diabetics, Immune -compromised state such as patients on long term corticosteroid therapy and immunosuppressant are more prone to this disesse[4,5,6]. The majority of cases were seen in India during second wave of COVID-19[7]. Rhino-orbital-cerebral mucormycosis is the most common, highly lethal, invasive opportunistic fungal infection of the nose and paranasal sinuses (PNS) associated with COVID 19 that can also invade the orbit and brain[8].

Because of sudden increase in the cases of post COVID Mucormycosis in a tertiary health care centre, the burden on pathological investigations and radiology have also increased for early detection of disease. This study was done to check the commonly involved anatomical structure in Rhino-orbital-cerebral mucormycosis for better understanding of the disease and its spread.

MATERIALS AND METHODS

This is a cross-sectional observational study. This study was conducted on 40 patients reported to the department of Radiology for MRI brain, orbit and PNS with provisional diagnosis of Mucormycosis. Inclusion criteria were selected such as, Patients whose KOH mount was positive; history of COVID-19 infection, long term hospitalization due to COVID 19. Patients came with a complaint of pain and numbness over face/ sinuses region, with sudden mobility of teeth and numbness in jaw region, multiple draining sinuses and gingival inflammation in jaw maxillary or mandibular region. Pain and swelling over orbital and periorbital region, blurring of vision. Trauma to face and paranasal sinus area, chronic cases of generalised mobile tooth or chronic generalized periodontitis and any other pathology like cyst and tumour of paranasal sinuses area were excluded from the study.

MRI brain, orbit and PNS was performed using T1, T2, FLAIR, DWI, GRE, STIR, PD Fat-Sat Sequences in multiple planes using 1.5T MRI machine. The orbits were subsequently scanned using a high -resolution small FOV sequences.Radiographic involvement and commonly affected area were observed and only positive findings were noted. Data were analysed using percentage of total cases. The collected data was entered in MS Excel sheet and for analysis SPSS version 25th was used. The qualitative data was represented in frequency and percentage. Quantitative data was represented in mean and standard deviation.

RESULTS AND DISCUSSIONS

Out of 40 patients 28 were male and 12 were female. All the patients were in the age group of 30-80 with the mean age 55.37±12.78 years (Table 1). The Erosion was seen as 20% in medial wall of right maxillary sinus, 17.5% in medial wall of left maxillary sinus and postero-lateral wall of right maxillary sinus

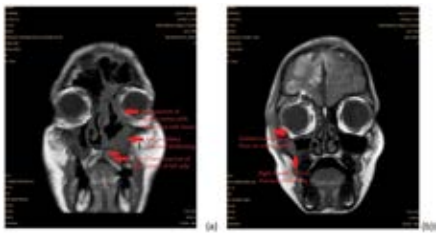

Fig. 1: Involvement of medial rectus with extra-coronal soft tissue, left maxillary mucosal thickening and loss of fatty marrow of hard palate of left side. T1Wi coronal section (a).Orbital involvement floor of orbit erosion, Right maxillary sinus mucosal thickening, T1Wi coronal section (b).

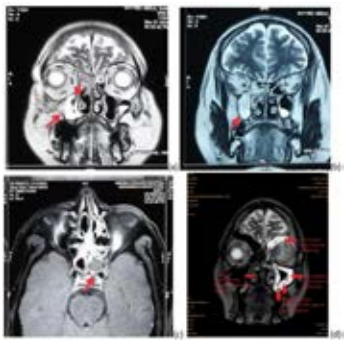

Fig. 2: Right maxillary sinus mucosal thickness with few tiny T2 hypointensity, T2Wi coronal section (a,b). Mucosal thickness in left sphenoidal sinus appearing as isointense on T1Wi axial view (c). Left frontal sinus mucosal thickening, left maxillary sinus mucosal thickening, hypointensities associated with sign of fungal hyphae in left maxillary sinus, Turbinate hypointensity secondary to fungal element T2Wi coronal section (d).

each, 12.5% in Bilateral medial wall of maxillary sinus, 7.5% in inferior wall of left orbit and hard palate each. 5.0% in nasal septum, 2.5% inferior wall of right orbit, bilateral cribriform plates and bilateral inferior wall of orbit individually (Table 2)(Fig. 1). The mucosal thickening was observed as 67.5% in bilateral maxillary sinus followed by 37.5% in right and 25% in left

Table 1: Distribution of patients according to Demographic profile

		No. of patients(n = 40)	Percentage
Age-group	31-40	05	12.5
	41-50	08	20.0
	51-60	14	35.0
	61-70	07	17.5
	>70	06	15.0
	Mean±SD	55.37±12.78 years	
Gender	Male	28	70.0
	Female	12	30.0

Table 2: Distribution of patients according to Erosion

Erosion	No. of patients(n = 40)	Percentage
Medial Wall of Left Maxillary sinus	07	17.5
Bilateral Medial Wall of Maxillary sinus	05	12.5
Medial Wall of Right Maxillary sinus	08	20.0
Inferior Wall of Left Orbit	03	7.5
Inferior Wall of Right Orbit	01	2.5
Hard Palate	03	7.5
Bilateral Cribriform Plates	01	2.5
bilateral Inferior Wall of Orbit	01	2.5
Nasal Septum	02	5.0
Posterolateral Wall 0f Right Maxillary Sinus	07	17.5

Table 3: Distribution of patients according to Mucosal Thickening (Polypoid)

Mucosal Thickening (Polypoid)	No. of patients(n = 40)	Percentage
Bilateral Ethmoid	05	12.5
Bilateral Maxillary Sinus	27	67.5
Sphenoid Sinus	21	52.5
Right Maxillary Sinus	15	37.5
Left Maxillary Sinus	10	25.0
Bilateral Frontal Sinus	22	55.0
Left frontal sinus	02	5.0
Right frontal sinus	02	5.0
Nasal Cavity On Left Side	05	12.5
Nasal Cavity On Right Side	03	7.5
Nasal Cavity On Both Side	06	15.0

Table 4: Distribution of patients according to Proptosis

Proptosis	No. of patients(n = 40)	Percentage
Right eye	01	2.5
Left eye	02	5.0
Bilateral eyes	01	2.5

Table 5: Distribution of patients according to Edema

Edema	No. of patients(n = 40)	Percentage
Clivus	01	2.5
Left preseptal soft tissue edema	01	2.5
Medial and lateral recti of right eye	01	2.5
Right optic nerve	01	2.5
Retro maxillary fat pad and muscle of mastications on left side	01	2.5
Retro maxillary fat pad and muscle of mastications on Right side	01	2.5
Retro maxillary fat pad and muscles of mastication on both side	01	2.5
mild soft tissue edema in left maxillo-facial region	01	2.5
Pre-maxillary region	01	2.5
Left optic nerve	01	2.5
Medial rectus muscle	01	2.5
Right masticatory muscle	01	2.5
Periorbital edema on left side	01	2.5
Retroantral region on both sides	01	2.5

Table 6: Distribution of patients according to soft tissue swelling

soft tissue swelling	No. of patients(n = 40)	Percentage
bilateral maxillofacial region	02	5.0
maxillofacial region on right side	02	5.0
Retro maxillary	01	2.5
retroantral and masticatory space region	01	2.5
Intra and Extra coronal fat pad on right side	01	2.5
Left preseptal and maxillo facial region	03	7.5
pre-maxillary and retroantral region	01	2.5
Right preseptal and maxillo facial region	02	5.0

Table 7: Distribution of patients according to other involvement

other involvement	No. of patients(n = 40)	Percentage
Acute Infract In Left Optic Nerve	02	5.0
left optic neuritis	02	5.0
Right optic neuritis	01	2.5
deviated nasal septum with convexity towards right side	03	7.5
Left optic perineuritis	01	2.5
osteonecrosis with osteomyelitis involving bilateral greater wing of sphenoid,	01	2.5
left zygomatic process of maxilla,	01	2.5
left pterygoid plate	01	2.5

maxillary sinus, 55% in bilateral frontal sinus, 52.5% in Sphenoid sinus, 15% in nasal cavity on both side, 12.5% on left and 7.5 % on right side of nasal cavity, 12.5% in bilateral ethmoid, 5% in right and left frontal sinus each (Table 3) (Fig. 2).The mucosal thickening appears polypoidal T2 and STIR hyperintense and T1 hyperintense and T2 hypointense foci within. On post contrast they demonstrate heterogenous enhancement. Out of 40 patients 2 had proptosis in left eye and 1 on each right and bilateral eyes (Table 4). A generalised edema(2.5%) was seen on maxillofacial region such as Clivus, Left preseptal soft tissue edema, Medial and lateral recti of right eye, Right optic nerve, Retromaxillary fat pad and muscle of mastications on right and left side, Retromaxillary fat pad and muscles of mastication on both side, mild soft tissue edema in left maxillo-facial region Pre-maxillary region, Leftoptic nerve, Medial rectus muscle, Right masticatory muscle, Periorbital edema on left side, Retroantral region on both sides (Table 5).The distribution of soft tissue swelling was as Left preseptal and maxillo facial region (7.5%), bilateral maxillofacial region, maxillofacial region on right side and right preseptal and maxillo facial region are 5.0% each, Retromaxillary, retroantral and masticatory space region, Intra and Extra coronal fat pad on right side and pre-maxillary and retroantral region are 2.5% each (Table 6). Other involvement like acute infract in left optic nerve (5%), left optic neuritis (5%), right optic neuritis (2.5%), deviated nasal septum with convexity towards right side (7.5%), left optic perineuritis (2.5%), osteonecrosis with osteomyelitis involving bilateral greater wing of sphenoid (2.5%), left zygomatic process of maxilla (2.5%), left pterygoid plate (2.5%) were also noted (Table 7).

Radiology plays an important in the diagnosis and management of Mucormycosis. Magnetic resonance imaging (MRI) consider as most definitive choice for diagnosis as well as to determine the extent of involvement. MRI provides a better assessment of devitalized tissues, vascular and perineural invasion, intracranial involvement and soft tissue resolution, as compared to other imaging modalities[9,10,11]. In the present study we have observed the anatomical involvement of maxillofacial region using MRI. This will help to know the pattern, severity and further management of disease.Depending upon the anatomical site, mucormycosis can be classified as rhino-orbito-cerebral mucormycosis (ROCM), pulmonary, cutaneous, gastrointestinal, disseminated and miscellaneous. Among all ROCM is the most common type mostly seen in imm-unocompromised patients[12,13,14]. The most common symptoms include headache, variable grade of fever, unilateral facial swelling. Blackened necrotic eschars of nasal mucosa and foul smelling are peculiar finding of the disease[15,16,17]. Reduced vision, orbital cellulitis, periorbital edema, proptosis, chemosis are all manifestations of orbital spread[18].

Herrera *et al.* stated that imaging findings of Mucormycosis can be opacification of the affected PNS and or mucosal thickening. On the T1 weighted images, most lesions were hypointense, whereas T2WI showed T2WI hyper intense lesions[19]. This can be correlated with our study. Safderet al. showed that on T2WI, a low signal intensity of fungal components may be detected with restricted diffusion on DWI[20]. A rim of soft-tissue thickness along the paranasal sinuses is the imaging characteristics of mucormycosis infection. Air-fluid concentration, sinus opacification and obliteration of the nasopharyngeal tissue planes are features of sinonasal mucormycosis infection. MR imaging shows, variable intensity within the sinuses on T1-and T2-weighted images. Fungal elements themselves may cause low signal intensity on T2 sequences. Slightly decreased T2 signal intensity with rhinocerebral mucormycosis can be due to the involved mucosa itself[20,21]. The “black turbinate sign” describes regions of non-enhancing soft tissue inside the affected nasal turbinate. This sign may help in identifying nasal mucormycosis at its early stages[22,23].

Patel *et al*. conducted a study in tertiary care centre, in which he reported rhino-orbital mucormycosis as the most common presentation (315/465, 67.7%) of mucormycosis. Diabetes mellitus was the most common predisposing factor (73.5%). AmphotericinB was the drug of choice (81.9%) and surgical treatment was performed in 62.2% of the participants. A combined medical and surgical management was associated with better survival. This study was done over a long duration of 1 year and 9 months and conducted at 12 centers[24]. Nithyanandam *et al*. in their study on the clinical features and treatment outcomes of rhino-orbital cerebral mucormycosis have reported that debridement of sinuses is necessary in all cases of rhino-orbital cerebral mucormycosis[25].

A prospective study conducted in Wales conducted a prospective study that showed that the use of corticosteroids in high-doses significantly increased the chances of COVID-19 patients developing aspergillosis (14.1%)[26,27]. Riche *et al*. stated that the risk of candidemia in critically ill COVID-19 patients receiving high-dose steroids have increased 10 times[28].

The present study shows the major involvement of maxillary sinus followed by other sinuses, nasal septum and surrounding structure. The prognosis of disease is good if it involves only maxillary sinus.It gets worse as it involves the other area such as orbit and brain. Thorough clinical examination, patient’s history, radiographic and pathological investigation helps in

early diagnosis of disease and hence appropriate management. A clinical findings such pain and swelling in maxillary sinus region, numbness over maxillofacial region, loosening of tooth, gingival swelling, draining sinus in association with maxillary teeth, blackish discoloration of hard palate, sudden blurring of vision, pain in eye, headache are the common complaint of the patient. Such complaint shouldn't be neglected in routine OPD.

CONCLUSION

The Rhino orbito cerebral Mucormycosis is the most common COVID 19 associated Mucormycosis. Immunocompromised patients are more prone for this disease.Early detection and aggressive management can save the life of the patient. Thorough surgical debridement is the line of treatment along with antifungal drugs such as Amphotericine B, Posoconazol were the drug of choice. In present study we just focus on the radiographic involvement of the disease. The large number of sample with clinical findings and post surgical follow up should be done for more definitive results.

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