Original Research Article

A Retrospective correlative study of preoperative Radiological findings with intraoperative findings in post-covid-19 invasive rhino-orbital mucormycosis infection patients

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Abstract

Aim: To analyse combined computed tomography (CT) and magnetic resonance imaging (MRI) characteristics of invasive rhino-orbital mucormycosis (IROM) in post-COVID-19 infection patients and their correlation with intraoperative findings for accurate diagnosis and delineation of the extent of involvement of the disease.**Material and method:** In this study, we have selected 50 patients diagnosed to have post covid 19 invasive rhino-orbital mucormycosis who underwent combined plain CT/MRI with contrast preoperatively and endoscopic debridement of mucormycosis. A correlation of intraoperative findings with preoperative radiological findings of the extent of invasion was studied in a retrospective manner.**Results:** A good correlation was found between preoperative radiological findings in plain CT Paranasal sinuses, contrast MRI fat suppressed T2 images and intraop findings of endoscopic debridement of fungal sinusitis except for a few cases of frontal sinus pathology and pterygopalatine fossa involvement.**Conclusion:** Conjunctive use of plain CT, which depicts bone destruction and other reactive bony changes along with contrast MRI, which reveals characteristic findings of soft-tissue thickening of the involved sinuses with extension of disease to the orbits, cavernous sinus and intracranial structures are useful for accurate diagnosis and early recognition of the disease and its extension. Preoperative plain CT and MRI with contrast helps to initiate appropriate and timely treatment, which is vital to prevent a fatal outcome.

Keywords: post covid , mucormycosis , plain CT scan, contrast MRI scan.

Introduction

In the second wave of the coronavirus disease (COVID-19) pandemic, INDIA is witnessing a devastating outbreak of Mucormycosis, an opportunistic fungal infection. Prior to pandemic, it is relatively a rare infection seen in immunocompromised individuals with poorly controlled diabetes mellitus, haematological diseases and following transplantation or chemotherapy. With the rampant use of steroids, oxygen, and/or prolonged intensive care admission in treating moderate to severe COVID-19 inflammatory syndromes in patients had lead to development of mucormycosis [1].The immunocompromised state leads to inevitable fulminant progression of invasive fungal disease and sometimes leads to death. Henceforth, the government of India has asked the states to notify every case under the "Epidemic Diseases Act'[2].Prognosis depends on the immunological status of the patient. It generally carries high morbidity. Limited involvement survival rates are between 50% and 80%[3]. If further spread occurs to other vital structures i.e., brain, neurovascular structures then mortality is greater than 80%. For appropriate early management prompt diagnosis is always required which needs the support of imaging techniques. The present correlative study states the role of how far the imaging studies are helpful in precise management of the disease for a better prognosis of patient.

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Material and Methods

In this retrospective study, 50 patients with Invasive Rhino orbital mucormycosis infection proven at biopsy, culture, or KOH staining in the immediate period or within 6 months of COVID-19 infection, who underwent CT and MRI evaluation and endoscopic debridement of mucormycosis were included from 1st April 2021 to 1st August 2021.

Inclusion Criteria: All the patients of age group 20 to 70 years diagnosed to have invasive fungal sinusitis on CT PNS and MRI with contrast, fat suppressed, T2 flair images and confirmed by biopsy .

Exclusion Criteria:

1. Patients with active covid 19 status and poor response to treatment
2. Patients with uncontrolled diabetes status
3. Patients with a glomerular filtration rate (GFR) of <40 and co-morbidities like ILD, CLD, uncontrolled diabetes etc.
4. Patients with claustrophobia and MRI incompatible implants

The parameters used for correlation in plain CT /contrast MRI of Paranasal sinuses, orbits and brain findings are fungal invasion of unilateral or bilateral paranasal sinuses,associated thinning/erosions of sinus walls, bony nasal septum, , medial wall, orbital involvement ,destruction of the hard palate, maxillary alveolar arch, and

greater/lesser palatine foramina, Cavernous sinus involvement and intracranial involvement.

Methods of Collection of Data: 1. The cases selected for the study were subjected to detailed history taking and examination. 2. A routine haemogram (HB,BT,CT,TC,DC) and urine examination (Albumin, sugar, microscopy) done. 3. All the patients in active stage of the covid 19 disease were treated. 4. Each patient underwent a plain computed tomography and MRI contrast of nose ,paranasal sinuses,orbits and brain and endoscopic debridement of mucormycosis.

Results

The retrospective observational analysis of 50 patients showed the affected age group in the range of 20 to 70 years with men (28, 56%) affected more than women (22, 44%).

In our study we included patients above 20 yrs of age. Majority of the study sample i.e. (22 out of 50 i.e.44%) were found to be in the age group of 51 to 60 years (5th decade).Out of the 50 patients, 41 (82%) patients were diabetic with 42 (84%) patients having other co-morbidities, such as hypertension (17, 34%), cardiac (3, 6%), renal (6, 12%), liver (1, 2%) diseases as well as cancer (1, 2%). Eight (16%) patients did not have any comorbidities. Onset of symptoms was from 2 weeks to 5 months after the beginning of the COVID-19 illness.Forty-two (84%) patients had received steroids. Tocilizumab was given to two (4%) patients and remdesivir to 27 (54%) patients. Thirty-one (62%) patients required oxygen (ranging from oxygen by mask to invasive ventilation therapy) during treatment of their COVID-19 illness.

Table 1: Gender Frequency Table.

Gender	Frequency	Percent
Females	22	44
Males	28	56
Total	50	100

Table 2: Age wise distribution of the study sample.

Age (Years)	No. of Patients	Percentage
20-30	1	2%
31-40	4	8%
41-50	8	16%
51-60	22	44%
61-70	15	30%
Total	50	100

Table 3: Frequency of comorbid diseases in covid 19 patients with invasive rhino orbital mucormycosis .

Co morbid disease	Number of patients	Percentage
1. Diabetes Mellitus	42	84%
2. Cardiac Diseases	18	36%
3. Renal Diseases	7	14%
4. Liver Diseases	1	2%
4 Malignancies	1	2%

Table 4: Treatment received for covid 19

Treatment received for covid 19	Number of patients	Percentage
1. Steroids	42	84%
2. Oxygen by mask/invasive ventilation therapy	31	62%
3. Inj Remdesivir	27	54%
4. Inj Tocilizumab	2	4%

CT scan of Paranasal sinus of 50 patients showed involvement of the bilateral paranasal sinuses in 31 (62%) patients, with predominant right-sided involvement in 16 (32%) and predominant left-sided involvement in 15 (30%) patients. There was predominant involvement of the maxillary sinuses in 26 (52%) and ethmoid sinuses in 19 (38%). Predominant sphenoid sinus involvement was seen in six (12%) patients. Frontal sinus involvement seen in 2(4%) patients . Extension of the disease to the orbit was seen in 35 (70%) patients in which right-sided involvement was seen in 18 (36%) patients and left-sided involvement was seen in 17 patients (34%). Bilateral orbital involvement was seen in two patients (4%). Cavernous sinus involvement was evident in 5 patients (10%). Involvement of the extrasinus hardpalate 10(20%) patients, skull base 2 (4%).

MRI showed T2 isointense to mildly hypointense soft tissue thickening with heterogeneous (predominantly no enhancement in the necrotic components) contrast enhancement as the chief finding for diagnosing the presence of fungal elements. On the MRI, loss of contrast enhancement seen in 25(50%) patients, periantral fat stranding in 15(30%) patients, intraorbital involvement in 35(70%) patients, intracranial involvement in 5(10%) patients.

Table 5: Distribution of cases according to the Degree of invasion of paranasal sinuses in plain CT.

Disease extent	No of Patients	Percentages
Maxillary sinuses	26	52%
Anterior and Posterior ethmoids	19	38%
Sphenoid sinus	6	12%
Frontal sinus	2	4%
Orbital involvement	30	60%
Extrasinus involvement	10	20%

Table 6: Distribution of cases according to the extent of invasion in MRI with Contrast.

MRI findings	No of patients	Percentage
Loss of contrast enhancement	25	50%
Periantral fat stranding(extra sinus)	15	30%
Frontal sinsus	4	8%
Intraorbital involvement	32	68%
Intracranial involvement	5	10%

Table 7: Distribution of cases according to the Intraoperative extent of disease.

Intraoperative Findings	No of patients	Percentage
Maxillary sinuses	24	48%
Anterior and Posterior ethmoids	15	30%
Sphenoid sinus	8	16%
Frontal sinus	6	12%
Orbital involvement	30	60%
Extra sinus involvement	14	28%
Intracranial involvement	5	10%

Endoscopic debridement of fungal sinusitis done in all 50 cases. Intraoperative findings showed involvement of the maxillary sinuses in 24 (48%) and ethmoid sinuses in 15 (30%). Predominant sphenoid sinus involvement was seen in 8 (16%) patients. Frontal sinus involvement seen in 6(12%) patients . Extension of the disease to the orbit was seen in 30 (60%). Extrasinus involvement i.e involvement of pterygopalatine fossa and premaxillay soft tissue is seen in 14 (28%) patients. Intracranial involvement is seen in 5(10%) patients intraoperatively. A good correlation was found between CT Paranasal sinuses, contrast MRI fat suppressed T2 images and intraop findings of endoscopic debridement of fungal sinusitis except for a few cases of frontal sinus pathology and pterygopalatine fossa involvement .

Discussion

Mucormycosis also known as zygomycosis and phycomycosis was first described by Paulltauf in 1885[4] is an acute, fulminant, and often lethal opportunistic infection typically affecting diabetic or immunocompromised patients[1], the common causative organisms include Absidia, Mucor, and Rhizopus. They are ubiquitous fungi occurring in soil, air, skin, body orifices, manure, spoiled food, dust and decaying vegetation and diverse organic material[5,6,12]. Inoculation occurs by inhalation, when spores reach the nasal cavity and/or nasopharynx, the fungus may then spread to the paranasal sinuses and subsequently to the orbit, meninges, and brain by direct extension[7]. Given the opportunity, fungal spores can invade (which are often not phagocytised due to poor immune response). They germinate, forming angioinvasive hyphae that cause infarction of the involved tissue, giving in a “dry” gangrene appearance. Based on organ involvement it is classified into rhino-orbital cerebral, pulmonary, cutaneous, gastrointestinal, or disseminated fungal disease.Honavar SG proposed a four staged system to determine the anatomical extent and severity of rhino orbital cerebral mucormycosis(ROCM). It includes signs and symptoms, imaging and nasal endoscopy. Stage 1 - disease limited to nasal mucosa, Stage 2 - disease extending to paranasal sinuses, Stage 3 - disease involving the orbit, Stage 4 - involvement of central nervous system.

Presentation and Spread of rhino orbital cerebral mucormycosis (ROCM) : Clinically, presenting symptoms are nonspecific including headache, low-grade fever, facial swelling, and orbital or paranasal sinus syndrome, black lesions on nasal bridge or palate or buccal mucosa, fever, Lethargy, seizures, slurred speech, partial paralysis. This fungal infection of the nasal cavity and paranasal sinuses further spreads to cause necrotizing vasculitis that extends rapidly into deep face, orbits, cranial cavity, and brain through skull base partitions and foramina[2]. Orbital involvement results from spread through the nasolacrimal duct and medial orbital wall. Such invasion is facilitated by the thinness of the lamina papyracea, congenital dehiscence and the perforations of the medial wall by arteries and veins[8,9].Its angioinvasive nature results in vascular occlusion, thrombosis, and infarction, as well as dissemination to the central nervous system from the primary focus[5,10,11].Spread to the brain may occur via the orbital apex, orbital vessels, or via the cribriform plate [12].Imaging studies –Both Contrast-enhanced MRI or CT scan helps in knowing the extent of the disease so that appropriate surgical approach can be planned. CT shows varying degree of sinus opacification with most having a tumefactive nature[6], this emphysematous soft tissue in nasal structures is a specific sign of early disease. Unilateral nasal cavity soft tissue mucosal thickening is the most consistent early CT finding of fungal invasion. Severe thickening of the nasal mucosa along the turbinates, nasal walls and septum is seen in most cases. These radiological findings are consistent with the endoscopic and surgical findings of significant mucosal edema and inflammation areas of tissue ischemia. This corresponds with a described early finding of disease on MRI termed black turbinate sign and this lack of contrast enhancement in nasal cavity due to mucosal necrosis occurs in patients with mucormycosis because of its angioinvasive nature. Bone erosion, extrasinus extension and obliteration of periantral fat are highly suggestive of invasive nature and advanced stage of fungal infection.MRI contrast study plays a vital role which reveals mucosal enhancement within the sinuses and non-enhancement of the nasal turbinates (black turbinate sign)[13].It demonstrates variable signal intensity depending on the sinus contents, due to iron and manganese in the fungal elements[14] and it is highly suggestive of invasive fungal rhinosinusitis. Perineural extension and inflammation of extraocular muscles can be well appreciated. Involvement of infratemporal fossa, pterygopalatine fossa and masticator space can be seen. Enhancing lesions at orbital apex, foramen rotundum and cavernous sinus with narrowing of internal carotid artery probably suggest angioinvasion. Necrotizing cellulitis changes were commonly seen in the involvement of facial muscles and premaxillary fat. Altered signal intensity changes involving skull base marrow are suggestive of infiltration. Relatively, MRI provides better evaluation of soft tissue and intracranial involvement, skull base invasion, perineural spread and vascular obstruction. Antifungal therapy and Surgical debridement: Mucormycosis is difficult to treat. Early recognition, diagnosis and prompt administration of appropriate antifungals, reversal of immunosuppression and surgical debridement is done. It may sometimes require both intravenous amphotericin B antifungal therapy and surgical excision, thus necessitating a multidisciplinary team approach in a facility setting for improving outcomes for patients with mucormycosis. In the early stages, immediate induction of intravenous liposomal Amphotericin B is advocated 5-10mg/kg with strict metabolic control. In cases with compromised renal function IV Isavuconazole 200mg thrice a day on day 1-2, 200mg once a day from day 3; or IV Posaconazole 300mg twice a day on day 1, 300mg once a day from day 2 are recommended. Prepare the patient and prioritise surgery. Based on the extent of involvement,

early and aggressive debridement of entire necrotic tissue in the nasal vault and paranasal sinuses is done which includes turbinectomy, palatal resection, medial orbital wall resection with clean margins. If involvement of orbit is aggressive, orbital exenteration is required. Induction therapy with intravenous liposomal amphotericin B 5-10mg/kg body weight for a minimum of 4weeks, followed by step down treatment with oral Isavuconazole 200mg thrice a day on day 1-2, 200mg once a day from day 3; or IV Posaconazole 300mg twice a day on day 1, 300mg once a day from day 2 for 3-6months or for a minimum of 6weeks following clinical regression and radiological regression or stabilization is recommended.

Untreated cases can rapidly progress and can be aggressive[15,16] . Complications associated with wider intracranial extension can be potentially fatal[17-19].Because of its lethal nature, it must be recognized early and treated aggressively, the support of imaging techniques is always needed to know about the involvement and invasion into surrounding structures so that appropriate surgical approach can be planned.

Conclusion

In summary, it is of utmost importance not to delay, miss, or misdiagnose fungal infections associated with COVID-19. Using a combined CT/MRI protocol, it is possible to depict the entire extent of disease, which may present with minor symptoms, such as a swollen eye. This can ultimately save the life of a patient and help tailor invasive treatments. Patients with COVID-19 develop over expression of inflammatory cytokines and an impaired cell-mediated immune response with decreased CD4-T and CD8-T cell counts and thus are susceptible to fungal infection. The disease itself accompanied with the immunocompromised state and extensive use of steroids in patients leads to a higher incidence of fungal infections. Preoperative combined CT/MRI protocol is the most important tool in the early diagnosis of invasive and non-invasive fungal rhinosinusitis.

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