Review Article

Imaging Features of Rhinocerebral Mucormycosis: A Review

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ABSTRACT

Mucormycosis is a distinct angioinvasive infection caused by filamentous fungi belonging to the Mucorales order of the Zygomycetes class. Mucormycosis has surpassed candidiasis and aspergillosis as the third most prevalent invasive mycosis in patients undergoing hematological and allogeneic stem cell transplantation. Mucormycosis is still a concern in patients with diabetes mellitus in the Western world. Furthermore, this disease is becoming more widely recognized in newly developed countries, such as India, in people who have uncontrolled diabetes or in cases of trauma. Data on radiologic features on this type of mycosis are scant. This review aims to throw light on imaging features of mucormycosis which help in early diagnosis and prompt treatment of the disease.

Key words: Advanced Imaging, Conventional Imaging, Diagnosis, Fungal Infection, Mucormycosis, Post-COVID complications

INTRODUCTION

Mucormycosis is a fungal infection caused by fungi in the Mucoraceae family that is sometimes lethal.[1] Rhizopus, mucor, and *Absidia* species are the most common pathogens in this family. Phycomycosis or zygomycosis was first described in 1885 by Paltauf and later coined as Mucormycosis in 1957 by Baker.[2] *Rhizopus oryzae* is the most common type and responsible for nearly 60% of mucormycosis cases in humans. Mucoracea can be found in soil, decomposing vegetation, and other forms of organic materials. Mucormycosis is a polymorphic disease that manifests itself in a variety of ways.[3]

Rhinocerebral, pulmonary, cutaneous, cardiac, gastrointestinal, and disseminated are the different types. The most prevalent form of mucormycosis, rhinocerebral mucormycosis (RCM), is usually a fatal fulminant infection. RCM is further classified as rhino-maxillary and rhino-orbito-cerebral mucormycosis.[4]

Several cases of mucormycosis in patients with COVID-19 have recently been reported all over the world, particularly in India. An optimal condition of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, and steroid-induced hyperglycemia), acidic medium (metabolic acidosis and diabetic ketoacidosis [DKA]), high iron levels (increased ferritins), and decreased phagocytic activity of white blood cells due to immunosuppression (SARS-CoV-2 mediated, steroid mediated, or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators appears to be allowing Mucorales spores to germinate in persons with COVID-19. It has also been reported from otherwise normal individuals.[5] RCM may result in severe intracranial ischemic and hemorrhagic lesions.[6]

According to the World Health Organization, the global incidence rate of mucormycosis ranges from 0.005 to 1.7 per million people. Mucormycosis prevalence in India is estimated to be 140 per million people, which is nearly 80 times higher than in developed countries.[7]

Early diagnosis and treatment are mandatory for a successful management of this infection.[8] Both computed tomography (CT) and magnetic resonance imaging (MRI) play an essential role in the diagnosis of RCM. While CT is better for identifying bone erosion, MRI is better for soft-tissue evaluation, intraorbital extension, and intracranial and vascular invasion. Specific CT and MRI procedures such as CT angiography or enhanced magnetic resonance (MR) angiography, as well as more advanced MRI sequences such as gadolinium three-dimensional black blood imaging, can help determine the extent of vascular invasion.[6] In this pictorial review, we describe conventional imaging, specific CT, cone-beam CT (CBCT), and MRI signs of RCM, mainly focusing on its life-threatening complications due to vascular involvement.

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IMAGING TECHNIQUES

Imaging modalities are valuable tools which are complementary to clinical evaluation in assessing the extent of disease and diagnosis of complications. Early changes of RCM can be noted on panoramic radiograph. CT, CBCT, and MRI play an essential role in the diagnostic process of RCM.

IMAGING FINDINGS

Panoramic Radiograph

Previous literature showed the presence of a non-healing socket of the lower right second molar with evidence of a small area of bone destruction and generalized horizontal bone loss indicating adult periodontitis, discontinuity in rhinomaxillary area with moth-eaten appearance in maxillary anterior region extending from maxillary second molar to left maxillary left first molar region with haziness in bilateral maxillary sinus, haziness of the left maxillary sinus with erosion of maxillary sinus walls.[9-11]

CT

According to literature, the ethmoid sinus is found to be the most common sinus involved. Multiple sinuses were affected in majority of the cases. Maxillary, ethmoid, and sphenoid were the most commonly involved sinuses. Bilateral involvement of sinus was less common than unilateral involvement. The sinuses involved in mucormycosis are detailed paranasal sinuses infection. Unilateral involvement of the ethmoid and sphenoid sinuses is the most common finding in RCM. Unenhanced CT detects RCM as a homogenous opacification of the sinus cavity with well-defined, considerably hyperdense foci within the inflammatory reaction, most likely due to calcium phosphate and calcium sulfate deposits in necrotic regions of mycetoma.[12]

Bone erosion may be evident on unenhanced CT reconstruction of bone algorithm; however, outside the sinuses the disease progression can occur through the vascular and perineural spread with an intact bony wall, thus causing minimal bone erosion.[6]

The extent of orbital and cranial involvement can be determined by CT. Without an air-fluid level, CT shows opacification of the paranasal sinuses, thickening of the sinus mucosa, and bone destruction. There may also be soft-tissue edema, proptosis, and swelling of the extraocular muscles.[10]

Soft-tissue infiltration of the deep face characterized by obliteration of the normal fat planes in the infratemporal fossa, pterygopalatine fossa, and pterygomaxillary fissure is another early sign. On CT, there are three forms of contrast enhancement, the most common of which is mild enhancement. Other variants have low-density opacification and no post-contrast enhancement, as well as a heterogeneously enhancing intrasinus abscess-like appearance with varying enhancing and non-enhancing regions. The presence of retroantral, facial, and orbital fat stranding and hypodense soft-tissue proliferation in patients with non-enhancing opacification of the sinuses reflects the infection's aggressive nature.[12]

The surrounding walls of the involved sinuses were found to be normal (60%) in a previous study, with infection spreading across uninvolved bone into the perisinus fat. Bone involvement was detected in 40% of the patients, with bone rarefaction, erosions, and permeative deterioration involving the sinus walls and neighboring bony structures. On CT, non-specific inflammatory turbinate hypertrophy and inflammatory fluid in the nasal cavity indicate nasal cavity involvement. Involvement of the nasal septum is also noted.[12]

Subtle sinus mucosal thickening or thickening of the extraocular muscles is the most prevalent findings on CT scanning of the head or sinuses. Despite clinical evidence of progressive disease, it is also common to find no abnormalities in the bones of the sinuses. However, when present, the finding of bony erosion of the sinuses is strongly suggestive of the diagnosis in the appropriate clinical context (e.g., patient in DKA with proptosis).[13]

Chronic post-treatment bone findings

Following treatment and improved blood glucose management, a chronic persistent form of bone involvement was detected in the surrounding bones of the affected sinuses in some cases of acute mucormycosis. On follow-up imaging, the affected bones revealed varied widening, sclerosis, erosions, and uneven lytic destruction.[13]

CBCT

It was noted that there was a breach in continuity in the nasal and maxillary areas, as well as haziness and obliteration of both maxillary sinuses, along with moth-eaten appearance of bone.[10]

Discontinuity was also seen in the maxillary sinus walls on both sides, affecting the nasal concha and septum, as well as bilateral obliteration of the maxillary sinus. Furthermore, there were osteolytic lesions involving the alveolar bone of maxilla, extending from the second molar to the left maxillary first molar region, along with perforation of the palate and involvement of the maxillary sinus.[14]

A case of mucormycosis involving maxilla reported to the Outpatient Department of Oral Medicine and Radiology, Institute of Dental Sciences, Bareilly, Uttar Pradesh, with CBCT images showing mixed radiolucent radiopaque pathology with destruction of buccal and lingual cortical plates of right and left side [Figures 1 and 2].

MRI

MRI is currently the preferred method for establishing a diagnosis of cavernous sinus thrombosis.[15] MRI with MR venogram demonstrates that the involved cavernous sinus has no venous flow, and carotid CT angiography or MR angiography can show narrowing or occlusion of the ICA's intercavernous section.

On T1W images of MRI, the lesions were all isointense or slightly hypointense. Rhinocerebral lesions appear on T2W imaging as

1. T2 isointense to mildly hypointense soft-tissue lesions in seven cases (37%)

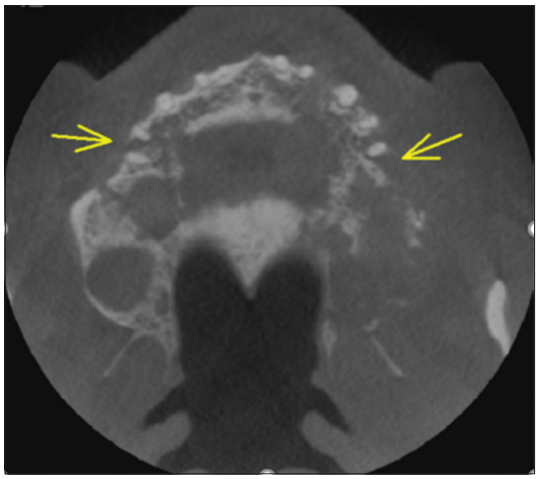

Figure 1: Axial computed tomography image showing mixed radiolucent radiopaque pathology with destruction of buccal and lingual cortical plates of the right and left sides

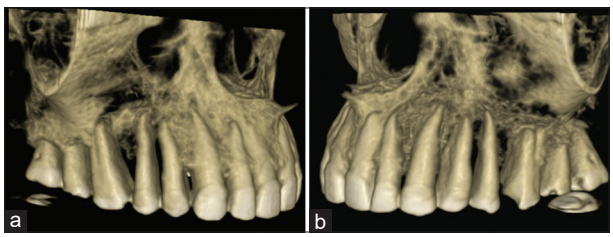

Figure 2: (a and b) Three-dimensional cone-beam computed tomography images showing perforation of buccal and lingual cortical plates of the right and left maxilla of the same case

2. Six cases (32%) of T2 heterogeneous soft-tissue lesions
3. In six cases (32%), T2 hyperintense mucosal thickening and intrasinus T2 hyperintense fluid were seen.

In two cases, including the sphenoid sinus, which was markedly T2 hypointense, bulky non-enhancing extrasinus soft tissue was found in the adjacent cavernous sinus. Bulky hypointense soft tissue was found in the pterygopalatine fossa in one such occurrence involving the maxillary sinus. In four cases (29%), post-contrast scans revealed patterns of enhancement that included intense homogeneous enhancement. In 36% of cases, there was heterogeneous enhancement with varying enhancing and non-enhancing regions, and in 5 cases (36%), there was complete central non-enhancement of the lesion with or without a thin irregular rim of peripheral enhancement. Fat-suppressed post-gadolinium pictures revealed the best enhancement of the lesions and pattern of extension of infection.[6] Only two patients had the black turbinate sign reported by Safder *et al*. as a characteristic of early nasal mucormycosis.[16]

Extrasinus extension

The orbit (76%) and face (57%) are the most prevalent extrasinus sites, followed by the orbital apex, masticator space, pterygopalatine fossa, bone, skull base, cavernous sinus, brain, and internal carotid artery. Most of the patients (25, 58%) seemed to have advanced disease (stages 3) on presentation, according to the classification Rupa *et al*.[12]

CONCLUSION

The early diagnosis and treatment of mucormycosis is very important in terms of prognosis. Imaging aids in determining the extent of disease, detecting complications such as internal carotid artery thrombosis, and is indispensable for surgical planning. Radiographic imaging is aids in establishing the extent of sinus, orbital, or intracranial progression of mucormycosis and determining the efficacy of treatment. The precise anatomical location of infection is critical for determining treatment options and overall prognosis. However, imaging modalities such as MRI reveal only non-specific characteristics such as mucosal thickening in the early stages of the disease, potentially delaying diagnosis. As a result, a high clinical suspicion is required for early detection of this illness.

REFERENCES

1. Kolekar JS. Rhinocerebral mucormycosis: A retrospective study. Ind J Otolaryngol Head Neck Surg 2015;67:93-6.
2. Kerezoudis P, Watts CR, Bydon M, Dababneh AS, Deyo CN, Frye JM, *et al*. Diagnosis and treatment of isolated cerebral mucormycosis: Patient-level data meta-analysis and mayo clinic experience. World Neurosurg 2019;123:425-34.
3. Gomes MZ, Lewis RE, Kontoyiannis DP. Mucormycosis caused by unusual mucormycetes, non-*Rhizopus*,-*Mucor*, and-*Lichtheimia* species. Clin Microbiol Rev 2011;24:411-45.
4. Spellberg B, Edwards J Jr., Ibrahim A. Novel perspectives on mucormycosis: Pathophysiology, presentation, and management. Clin Microbiol Rev 2005;18:556-69.
5. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr Clin Res Rev 2021;15:1-7.
6. Mazzai L, Anglani M, Giraudo C, Martucci M, Cester G, Causin F. Imaging features of rhinocerebral mucormycosis: From onset to vascular complications. Acta Radiol 2021:2021:284185120988828.
7. Yoon HJ, Choi HY, Kim YK, Song YJ, Ki MR. Prevalence of fungal infections using national health insurance data from 2009-2013, South Korea. Epidemiol Health 2014;36:1-10.
8. Skiada A, Lanternier F, Groll AH, Pagano L, Zimmerli S, Herbrecht R. Diagnosis and treatment of mucormycosis in patients with hematological malignancies: Guidelines from the 3rd European conference on infections in leukemia (ECIL 3). Haematologica 2013;98:1-4.
9. Bakathir AA. Mucormycosis of the jaw after dental extractions: Two case reports. Sultan Qaboos Univ Med J 2006;6:77-82.
10. Pandilwar PK, Khan K, Shah K, Sanap M, Unnikrishnan KS, Nerurkar S. Mucormycosis: A rare entity with rising clinical presentation in immunocompromised hosts. Int J Surg Case Rep 2020;77:57-61.
11. Shastry SP, Murthy PS, Jyotsna T, Kumar NN. Cone beam computed tomography: A diagnostic aid in rhinomaxillary mucormycosis following tooth extraction in patient with diabetes mellitus. J Indian Acad Oral Med Radiol 2020;32:60-4.
12. Therakathu J, Prabhu S, Irodi A, Sudhakar SV, Yadav VK, Rupa V.

Imaging features of rhinocerebral mucormycosis: A study of 43 patients. Egypt J Radiol Nuclear Med 2018;49:447-52.
13. Ganesh R, Manikumar S, Vasanthi T. Rhinocerebral mucormycosis in an adolescent with Type 1 diabetes mellitus: Case report. Ann Trop Paediatr 2008;28:297-300.
14. Pagare J, Johaley S. Diagnostic role of CBCT in fulminating mucormycosis of maxilla. Int J Res Rev 2019;6:575-9.
15. Mbarek C, Zribi S, Khamassi K, Hariga I, Ouni H, Ben Amor M, *et al*. Rhinocerebral mucormycosis: Five cases and a literature review. B-ENT 2011;7:189-93.
16. Chikley A, Ben-Ami R, Kontoyiannis DP. Mucorm of the central nervous system. J Fung 2019;5:1-20.