

Case Report

Computed Tomographic Findings of Invasive Mucormycosis in COVID-19 Patients on Steroid Therapy at A Tertiary Care Centre — A Case Series

Srijak Bhattacharyya¹ Raj Saha¹, Prasun Das¹, Swadha Priya Basu², Subhargha Mandal³, Tanuka Mandal⁴

Background : As India continues to cope with the existing rise in COVID-19 infections, Mucormycosis has emerged as a formidable complication in COVID infected Diabetics on Steroid Therapy.

Case presentation : We describe the imaging findings in 6 cases of invasive Mucormycosis in Sero-positive COVID-19 patients on Steroid Therapy (5 of whom were also diabetic). 4 cases had predominantly varying involvement of the paranasal sinuses with extension into the orbital compartment and 2 were also associated with pulmonary involvement.

Conclusions : Mucormycosis leads to aggressive Necrosis of the Para-nasal sinuses extending to the brain as well as the orbit. Pulmonary Necrosis is also common owing to its angioinvasive nature. Delay in treatment is often fatal so prompt treatment must be initiated even before histological confirmation using the knowledge of risk factors and characteristic radiological imaging appearances.

[J Indian Med Assoc 2021; 119(12): 81-4]

Key words : COVID-19, Mucormycosis, Bird's Nest Sign.

Mucormycosis is a fungal infection caused by members of Zygomycetes, order Mucorales. It is seen in patients debilitated by Immune or Metabolic Disorder¹. Phagocytes are the main defence mechanism against Mucormycosis² by preventing the multiplication of fungal spores. They are inhibited by corticosteroids. Angio invasiveness with Vessel Thrombosis and Tissue necrosis is characteristic of Mucormycosis³. Diabetes Mellitus, especially if uncontrolled along with use of corticosteroids in the treatment of COVID-19 infection are one of the main risk factors⁴. Neutropenia, intravenous drug use, malnutrition, solid organ or stem cell transplantation and severe skin damages due to burns and surgical suture sites are the other notable risk factors⁵. COVID-19 had wreaked havoc on the World since the first detected case on December, 2019. Of late the situation has been complicated with a rise in the number of co-infections notably Mucormycosis especially in India. High mortality rate of over 50% has been recorded in patients suffering from mucormycosis⁶. Recently, Chest Computed Tomography (Axial and coronal

Editor's Comment :

- COVID-19 patients on long term steroid therapy, diabetic or immunosuppressed to coexisting ailment are susceptible to infection by Mucormycosis.
- NCCT PNS is a useful tool for early detection of mucor infection during follow up of such patients who complain of nasal discharge, blockage, facial pain, epistaxis.
- Obliteration of retroantral fat is a reliable sign for involvement of PNS.
- Concomitant HRCT of the chest may also be done to look for pulmonary involvement, classically the Bird's nest sign.
- Although confirmed by histopathology, early imaging diagnosis can aid in prompt treatment and reduce mortality.

sections) has given a highly accurate and non-invasive modality of accurately imaging and early treatment of invasive mould Pneumonia in immunocompromised patients⁷. Based on clinical details, radiology findings and histopathology- the final diagnosis of Mucormycosis was made. We have come across 6 cases of Invasive Mucormycosis following COVID-19 infection with varying involvement of Lung parenchyma, Paranasal air sinuses and Orbits. In order to confirm the diagnosis, histopathological evaluation of the nasal specimen of all 6 cases was done on Potassium Hydroxide (KOH) wet mount.

CASE SERIES

The six patients suffering from Invasive Mucormycosis, all of whom had history of seropositive COVID-19 in recent past were reviewed by us retrospectively during their admission and treatment

Nil Ratan Sircar Medical College and Hospital, Kolkata 700014

¹MBBS, Postgraduate Trainee, Department of Radiodiagnosis

²MBBS, Dip (Card), MD (Radiodiagnosis), Professor & Head, Department of Radiodiagnosis and Corresponding Author

³MBBS, Postgraduate Trainee, Department of Pathology

⁴MD (General Medicine), Senior Resident, R G Kar Medical College and Hospital, Kolkata 700004

Received on : 01/12/2021

Accepted on : 08/12/2021

under the Department of Otorhinolaryngology. Their medical records, clinical data and demographics were reviewed along with Radiological and Histopathological findings. All the patients were previously treated or currently undergoing treatment for COVID-19 at our hospital and they subsequently developed symptoms namely facial pain, nasal blockage with or without discharge, Epistaxis, Chemosis and Swelling of the eye and even loss vision in one patient. The mean age of the subjects were 54.1 years (range 42-73 years). 5 of the 6 patients were Diabetic. All 6 patients had received steroids for at least 10 days. Remdesivir had also been administered to 5 patients. All the patients bar one had other co-morbidities like Hypertension, Chronic Kidney Disease (CKD) and Chronic Obstructive Pulmonary Disease (COPD). In 2 patients had severe COVID-19 infection while the rest had moderate disease based on past CT severity score. CT scan of the Paranasal Sinus (PNS) and Thorax revealed thickening of the mucosa of the paranasal sinuses with adjacent bone erosion and even extension into the orbit in some cases. A few cases also revealed a central cavity with irregular intersecting lines surrounded by consolidation referred to classically as a BIRD'S NEST sign.

DISCUSSION

Mucormycosis is an invasive fungal infection first described by Paulltauf A in 1885⁸. Even though it can involve different organs the most common type is the Rhino Cerebral Form⁹. In our case series we observed 6 patients with recent history of proven moderate to severe

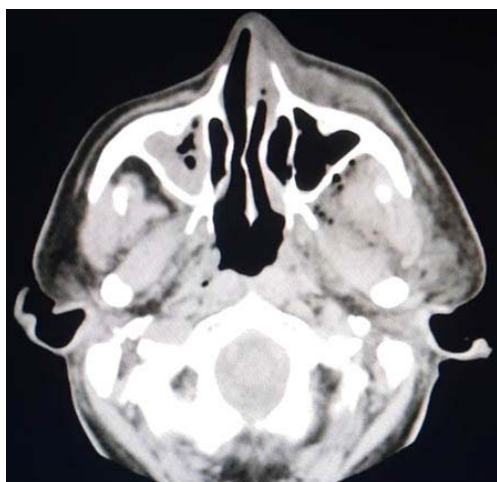


Fig 1 — Axial section of NCCT PNS shows obliteration of the left retro antral fat plane with mucosal thickening in adjacent maxillary antrum. There is also partial obliteration of the retro antral fat plane on the right with near complete opacification of the maxillary sinus

COVID-19 infections, 5 of them were diabetic with one having coexisting kidney disease and another suffering from Chronic Obstructive Pulmonary Disease (COPD). All of them had received systemic steroid therapy for atleast 10 days. In the Computed Tomography scan of the head and paranasal sinuses, obliteration of the left retro antral fat plane with mucosal thickening of the adjacent maxillary antrum was seen. Along with it partial obliteration of the retro antral fat lane with nearly complete opacification of the maxillary sinus was noted. (Fig 1) This raised the suspicion that the pathology responsible was something other than simple sinusitis. In another patient, absolute opacification of the maxillary sinus along with the anterior ethmoidal air cells that had a central collection of air without any air-fluid level was noted. Corresponding Osteomeatal Unit (OMU) was blocked. There was a small defect involving the inferomedial and posterior-lateral wall of maxillary sinus on the same side. In one of the cases we found mucosal thickening in bilateral sphenoid and maxillary sinus and left ethmoidal sinus. Irregular outlined soft tissue density lesion seen at inferomedial aspect of left orbit and left side of mid cheek anterior to left maxillary antrum (Fig 2). The lesion is communicated within left anterior ethmoid sinus through small bony erosions. Inflammatory changes noted in left retromaxillary region. Both maxillary ostia

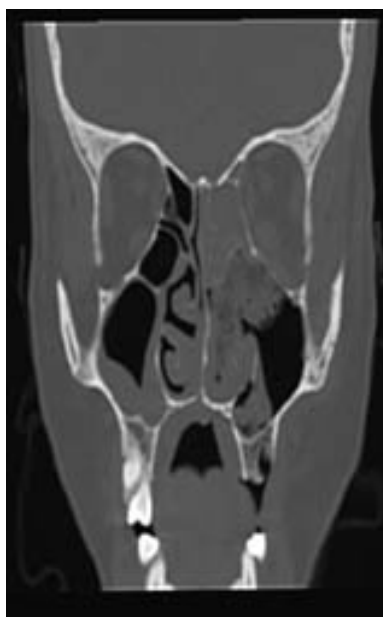


Fig 2 — Coronal NCCT PNS shows mucosal thickening of the left maxillary sinus. Invasion into the adjacent nasal cavity. Mucosal thickening also noted on the right side. Erosion of the medial wall of the maxillary antrum noted with thinning of the inferior and medial walls of the orbit

are blocked associated with left sided proptosis. In 2 of our cases we also did HRCT thorax to look for pulmonary involvement. In one case we found a few thick-walled cavitating lesion with few residual Fibrotic Opacities (Fig 5). In another, we found a cavity surrounded by a dense area of consolidation with few intersecting irregular areas of stranding within it resembling the classical reverse halo sign or Bird's nest sign (Fig 3). Gamba *et al* had showed in their study previously that mucosal thickening without air fluid level on CT scan is a sign of early disease activity¹⁰ while Silverman *et al* in their study had described that the presence of orbital, facial and retro antral fat stranding is a sign of aggressive disease activity¹¹. A similar case was

Serial Number	1	2	3	4	5	6
Age (Years)	54	49	52	42	73	55
Sex	Female	Male	Male	Female	Male	Male
Co-morbidities	DM HTH	DM COPD	DM HTN	NONE	DM HTN CKD	DM HTN
Addiction	None	Smoker	None	None	None	None
Severity of COVID-19	Moderate	Severe	Moderate	Moderate	Severe	Moderate
Steroids	Yes	Yes	Yes	Yes	Yes	Yes
Presentation	Facial Pain and Nose Block	Epistaxis, Loss of Vision	Swelling of the Left Eye	Left Eye Pain and Chemosis	Chemosis With Loss of Vision in Right Eye	Facial Pain and Nasal Discharge
HPE and Fungal Smear (Broad Aseptate Hyphae)	Yes	Yes	Yes	Yes	Yes	Yes
CT Findings	Yes	Yes	Yes	Yes	Yes	Yes
DM - Diabetes Mellitus, HTN - Hypertension, HTH - Hypothyroidism, CKD – Chronic Kidney Disease, COPD – Chronic Obstructive Pulmonary Disease						



Fig 3

reported by Sethi HS *et al*, who had peripheral ground glass opacities in both the lungs (a typical radiological sign found in patients suffering from COVID-19) along with mucosal thickening in right ethmoidal and both the maxillary sinuses with small defect in the infero-medial and postero-lateral wall of the maxillary sinus in the right. This was associated with slight soft tissue thickening of the orbit on the right side infiltrating into the inferior rectus muscle and blocking the osteo-meatal complex¹². In the study done by Mandeep garg *et al*¹³, they found that the most frequent CT findings were consolidation and cavitation, while the 'reverse halo' was seen in two patients. All the patients were operated on at the Department of Otorhinolaryngology and the surgical specimens were sent for Histopathology to the

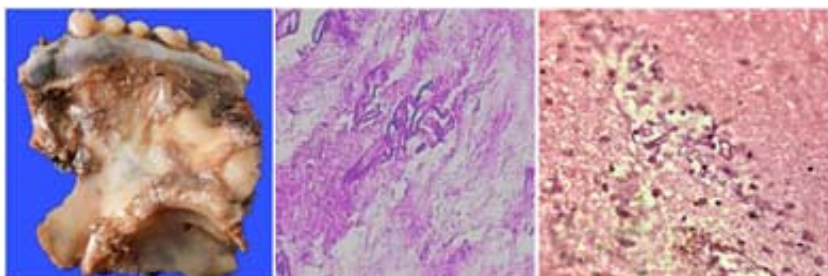


Fig 4

Department of Pathology. In one of our cases on gross specimen we found part of maxilla with necrotic material and congestion throughout the specimen. On H & E stain we found wide areas of Necrosis and some fungal elements. PAS stain confirmed Mucormycosis by showing broad branching PAS positive fungal hyphae.

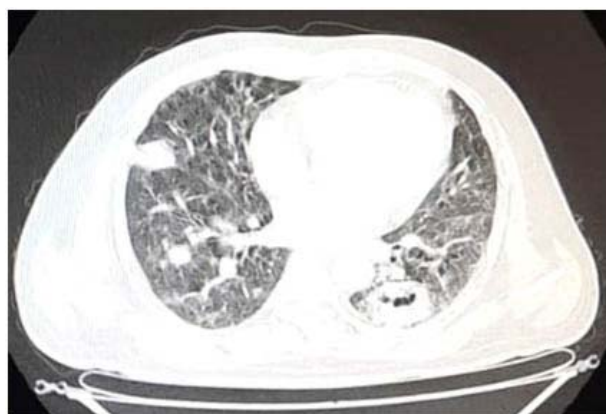


Fig 5 — Axial HRCT thorax shows a thick-walled cavitating lesion in the left lower lobe with few nodular opacities seen in the right lower lobe. Patchy Fibrotic opacities were seen throughout the lung (notpictured)

Sunil V Jagtap *et al*, in case report described an immunocompromised patient on ART for last 10 years, who was suffering from Maxillary Mucormycosis after being infected with COVID-19 and receiving steroids. The PAS and Grocott's Methanamine silver stain done on the tissue sent from the necrotic area of the nasal cavity showed fungal hyphae of Mucormycosis (Fig 4).

CONCLUSION

We propose that, patients with moderate to severe COVID-19 infection with compromised immunity due to Diabetes, Chronic Lung and Kidney Disease and prolonged Systemic Steroid Therapy are susceptible to mucormycosis because of impairment of barrier defense, dysfunction of phagocytes and lymphocytes. Early diagnosis can be made from imaging features seen on CECT, PNS and HRCT thorax which can aid treating clinicians for prompt treatment of secondary fungal infections and substantially reduce morbidity and mortality.

REFERENCES

- Rippon J — Medical Mycology. Philadelphia, PA: WB Saunders. 982: 615-37.
- Waldorf AR, Ruderman N, Diamond RD — Specific susceptibility to mucormycosis in murine diabetes and bronchoalveolar macrophage defense mechanisms against *Rhizopus*. *J Clin Invest* 1984; **74(1)**: 150-60.
- Bouchara JP, Oumeziane NA, Lissitzky JC, Larcher G, Tronchin G, Chabasse D — Attachment of spores of the human pathogenic fungus *Rhizopus oryzae* to extracellular matrix components. *Eur J Cell Biol* 1996; **70(1)**: 76-83.
- Dyer O — Covid-19: India sees record deaths as "black fungus" spreads fear. *BMJ* 2021; 373.
- Berdai MA, Labib S, Harandou M — Rhinocerebral mucormycosis complicating ketoacidosis diabetes. *Presse Med* 2016; **45**: 145-6.
- Centers for Disease Control and Prevention — Mucormycosis statistics. <https://www.cdc.gov/fungal/diseases/mucormycosis/statistics.html>
- Caillot D, Mannone L, Cuisenier B, Couaillier JF — Role of early diagnosis and aggressive surgery in the management of invasive pulmonary aspergillosis in neutropenic patients. *Clin Microbiol Infect* 2001; **7 (Suppl. 2)**: 54-61
- Diego A, Herrera ABD — Imaging findings of rhinocerebral mucormycosis. *Skull Base Off J North Am Skull Base Soc* 2009; **19**: 117-25.
- Petrikos G, Skiada A, Lortholary O, Roilides E, Walsh TJ, Kontoyiannis DP — Epidemiology and clinical manifestations of mucormycosis. *Clin Infect Dis* 2012; **54**: S23-34
- Gamba JL, Woodruff WW, Djang WT, Yeates AE — Craniofacial mucormycosis: assessment with CT. *Radiology* 1986; **160**: 207-12.
- Silverman CS, Mancuso AA — Periantral soft-tissue infiltration and its relevance to the early detection of invasive fungal sinusitis: CT and MR findings. *Am J Neuroradiol* 1998; **19**: 321-5.
- Sethi HS, Sen KK, Mohanty SS — COVID-19-associated rhino-orbital mucormycosis (CAROM) — a case report. *Egypt J Radiol Nucl Med* 2021; **52**: 165.
- Garg M, Prabhakar N, Muthu V, Farookh S, Kaur H, Suri V, Agarwal R — CT Findings of COVID-19-associated Pulmonary Mucormycosis: A Case Series and Literature Review. *Radiology* 2021; **31**: 211583.
- Jagtap — IP Archives of Cytology and Histopathology Research 2021; **6(2)**: 135-9.