The "black fungus" through a gray lens: Imaging COVID-19-associated mucormycosis

The COVID-19 pandemic has brought with it a multitude of parallel challenges on a global scale. Our understanding of the pathophysiology and treatment of COVID-19 continues to expand rapidly. In the midst of this pandemic, an ugly new epidemic has raised its head: that of an acute invasive rhino-orbito-cerebral infection by the “black fungus” mucor.

Mucor, a fungus belonging to the Mucorales genus, is found in a variety of ecological environments including soil, dust, decomposing vegetation, as well as excreta of animals like pigeons.[1] Despite this near ubiquitous existence, clinically significant human infections had been hitherto limited and never on such an unprecedented staggering scale, even in a country like India that already had a relatively high prevalence.[2] Many factors may be at play to create this perfect storm. The high prevalence of diabetes, unintended consequences of steroid administration, possible immune effects of the newer variants of the SARS-CoV-n2 virus and circumstantial evidence around the use of contaminated industrial oxygen may all have a role in this new scourge.[3,4]

Acute invasive fungal sinusitis (AIFS) in COVID-19-associated mucormycosis (CAM) has been known by many monikers including acute fulminant invasive fungal sinusitis and rhino-orbito-cerebral fungal sinusitis. Acute invasive fungal rhino-sinusitis may be the most appropriate basic descriptor since the middle turbinate is thought to be the epicenter of infection in most cases from where it tends to spread to the rest of the sinuses.[5] Unlike aspergilloma which has a tendency to form a fungal ball or mycetoma, mucor has angioinvasive properties that allow it to rapidly progress across tissue borders without respecting anatomical boundaries.[6] Spreading along neurovascular bundles appears to be the highway to hell for this pathogen, resulting in extensive tissue necrosis with consequent high mortality of 50–80% and a high morbidity in those who survive.[7]

Biopsy is essential to confirm the diagnosis.[8] However, imperative to the initial diagnosis and guidance of management is the use of radiological investigations such as MRI and CT. In general, CT is the most commonly used modality for imaging the paranasal sinuses and orbit. However, in mucormycosis, its use is limited as the bony destruction is often insignificant and the soft tissue changes are less apparent on CT.[5] Further, CT may entirely miss findings such as perineural spread along the trigeminal nerve and cavernous sinus involvement – both critical findings with ominous repercussions. The CT findings include a hypoattenuating (hypodense) opacification of the sinuses, usually unilateral, commonly the ethmoid, sphenoid, and maxillary sinuses.[9] This is unlike chronic fungal infections where the sinuses are hyperdense due to buildup of mineral rich fungal waste products.[5] CT continues to have a role, however, particularly in resource poor environments, for patients who are unstable and for complementary evaluation of bony changes.

MRI is an elegant imaging modality that is unsurpassed in its ability to demonstrate abnormalities of the soft tissue as well as bone marrow infiltration. Direct comparisons of MRI and CT in the detection and staging of AIFS have shown a superior sensitivity (86% vs 57–69%) with similar specificity (83% vs. 81%).[10] This disparity of improved sensitivity with similar specificity can be explained by the fact that both modalities look for the same specific hallmark of AIFS, i.e., direct visualization of extrasinus invasion as evidenced by abnormal perisinus soft tissue/edema and loss of perisinus fat planes, for which MRI is far superior. Once extrasinus involvement is present, the diagnosis of invasive sinusitis is apparent and then staging becomes the next objective. A recently proposed staging system allows for four levels of involvement – nasal cavity, paranasal sinuses and extrasinus involvement, orbital disease, and central nervous system involvement – and serves as a useful guide.[8] Many of these signs are subtle and often become apparent in the light of clinical findings. Gadolinium contrast administration is also necessary to allow delineation of subtle areas of invasion, recognition of necrosis, thrombosis of structures such as the cavernous sinus, and detection of meningitis.[10]

A methodical and systematic search of expected areas of spread for relevant findings is essential. A structured checklist for MRI assessment and reporting, which can be named the **REBOVasC checklist** may be useful so as to not miss critical findings in the radiological report [Table 1]. The checklist details six structures or compartments that can be involved in a roughly anterior to posterior direction of spread. An easy mnemonic to memorize the components of the REBOVasC checklist is “*REmember Basics Of Vicious CAM*.” A discussion between the treating team and the reading radiologist is always helpful in increasing the yield of findings and understanding their relevance. The article by Sreshta *et al*.[11] in this issue

Table 1: REBOVasC MRI checklist for structured reporting of CAM

Structure	Abnormalities
Rhinosinus	T2 heterogenous mucosal thickening, turbinate/ mucosal nonenhancement, fluid collections
Extrasinus	Facial subcutaneous soft tissue, pteryopalatine fossa, masticator spaces
Bone	Sinus walls, pterygoid processes, alveolar processes, sinus bordering orbit walls, skull base – destruction, subperiosteal abscesses
Orbital	Preseptal, postseptal inflammatory changes, optic nerve involvement (infarction, perineuritis), apex soft tissue, EOM nonenhancement, Globe
Vascular	Arterial: ICA steno-occlusion, ophthalmic artery occlusion, ECA occlusion, mycotic aneurysms Venous: Cavernous sinus – Direct invasion vs thrombosis/thrombophlebitis, Superior ophthalmic vein thrombosis
CNS	Ischemic changes – sterile infarcts (usually watershed, less commonly territorial), infarcts with secondary fungal invasion Direct invasion – abscesses/granulomas, meningitis, perineural spread via trigeminal nerve, contiguous brainstem involvement

EOM – Extraocular muscle, CNS – Central Nervous System of the Indian Journal of Ophthalmology is a timely and well-written comprehensive review of the imaging findings and patterns of this new plague. With better understanding of the pathophysiology of CAM, improved COVID-19 treatment protocols and increased vaccination coverage, it is hoped that the incidence of this deadly disease reduces. Till then, a multidisciplinary approach with clinicoradiological correlation is crucial in the diagnosis, staging, prognostication, and treatment of these patients with this devastating condition.

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Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_1506_21

Cite this article as: Nagesh CP. The "black fungus" through a gray lens: Imaging COVID-19-associated mucormycosis. Indian J Ophthalmol 2021;69:1648-9.

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