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An ophthalmologist's perspective on post COVID mucormycosis

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ABSTRACT

Background: Due to the surge of post COVID mucormycosis in India there has been a significant patient load seen in hospitals we have observed that mucor is not the only culprit and there has been other fungi like aspergillus and candida, who have led to increased morbidity and mortality.
Aim: To conduct a retrospective analysis on laboratory reports of specimens sent after surgical intervention of patients admitted with mucormycosis and to identify the weightage of different fungal infections in the post COVID era.
Materials and Methods: It is a hospital based retrospective review of mycology and histopathology reports of post COVID rhino orbital mucormycosis patients referred from ophthalmology, ear nose throat surgery, oral maxillofacial surgery, neurosurgery department of mahatma gandhi memorial medical college, Indore, Madhya Pradesh from 1 June to 7 July 2021.
Result: Out of 240 samples sent for histopathology examination, 1.6% samples showed mucormycosis with secondary aspergillosis while 98.33% samples showed primarily mucormycosis likewise 270 KOH mount reported around 8.51% mucormycosis with secondary aspergillosis, 4.81% reported primary aspergillosis, 72.15% reported primarily mucormycoses.
Conclusion: We acknowledge that aspergillus and candida has contributed significantly in post covid mycoses and that mucor is not the only culprit.

1. Introduction

Due to the surge of post COVID mucormycosis in India there has been a significant patient load seen in hospitals we have observed that mucor is not the only culprit and there has been other fungi like aspergillus and candida, who have led to increased morbidity and mortality.[1]

Fungi are ubiquitous eukaryotic organisms found in dead, decaying vegetative matter, soil and air Several fungi can cause devastating infections in humans which are not only vision threatening but also associated with high mortality, thus it becomes imperative to diagnose fungal disease at the earliest and initiate appropriate therapy.[2] This review aims to provide a comprehensive insight on laboratory diagnosis of post COVID rhino orbital cerebral mycosis.[3]

COVID-19 due to SARS-CoV-2 virus infection has been associated with a wide range of opportunistic fungal infections. Recently, several cases of Mucor mycosis in people who have recovered or had history of COVID-19 infection have been increasingly reported from India. Apart from mucor, aspergillus and candida have also been reported worldwide. The main cause identified in several studies in people with COVID-19 is hypoxia, uncontrolled blood glucose levels (new-onset hyperglycaemia), history of diabetes mellitus, irrational use of steroid, diabetic

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ketoacidosis, increased ferritin level, immunosuppression (?SARS-CoV-2 mediated), prolonged hospitalization, lack of hygiene and use of contaminated water in humidifiers of oxygen dependent patients.[4]

Despite the recognition that airborne Aspergillus fumigatus is increasingly recognized as an important cause of fungal super-infections among critically ill COVID-19 patients, the incidence of candidiasis has not been evaluated in this context.[5]

Mucor mycosis is a rare but a fatal fungal infection that usually affects immunocompromised patients.[6] Mucormycosis is predominantly an Angio invasive infection caused by mold fungi of the genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of Order-Mucorales, Class- Zygomycetes Mode of contamination occurs through the inhalation of fungal spores. The prevalence of mucormycosis is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019–2020. In other words, India is the diabetes capital of the world, until recently. DM is the most common risk factor associated with mucormycosis in India, although hematological malignancies and organ transplant are significant risk factors in Europe and the USA DM remains the leading risk factor associated with mucormycosis globally, with an overall mortality of 46%.[7] Long term use of corticosteroids and recently observed even a short course (cumulative dose > 600 mg) given during a month before, predisposes immunocompromised people to mucormycosis and aspergillosis.[2]

We are dealing with variety of fungal infections, characterized by the emergence of previously unknown human pathogens interacting with known pathogens, clinically difficult to identify due to new symptomatology. The spectrum of "at-risk" populations for invasive Aspergillus infections has increased in size due to the interplay of immunity and the virus. Fungal invading internal organs are difficult to distinguish from severe COVID-19 based on clinical or imaging findings, and a high index of suspicion is necessary to diagnose aspergillosis. If aspergillosis is a complication of COVID-19 infection in critically ill bed ridden patients, failure to diagnose the disease can lead to excess mortality. For this reason, it is imperative to establish the presence of fungus in tissue and to study the characterstics of fungal hyphae in depth and understand the nature of invasion.[8]

This review helps identify the causative agent in context of public health problem specially because these infections carry a high mortality rate.

2. Materials and Methods

It is a hospital based retrospective review of mycology and histopathology reports of post COVID rhino orbital mucormycosis patients referred from ophthalmology, ear nose throat department, oral maxillofacial department and neurosurgery department of mahatma Gandhi memorial medical college, Indore Madhya Pradesh from 1 June to 07 July 2021.

All patients with a clinical diagnosis of rhino orbital mucormycoses were included in this study Radiology imaging and clinical examination were the basis of intervention and the debrided/ resected specimen were sent to microbiology and histopathology for confirmatory diagnosis.

All the laboratory data collected on two separate spreadsheet one for histopathology and one for mycology (KOH mount) reports pattern of invasion, type of mycoses and secondary invasion by other fungus or bacteria were studied. In this study 510 subjects were included. All histopathology and mycology reports of tissue retrieved from mucormycosis suspect patients.

3. Result

1. Among all 240 histopathology reports, it was noted that mixed inflammatory cell infiltrate consists of neutrophils, eosinophils, macrophages and histiocytes along with areas of necrosis were present in all patients
2. Predominately vascular invasion was seen in exenterated eye balls and debrided tissue along with intravascular thrombosis
3. Out of 240 reports, only 57 were females rest 183 were males
4. 2 out of 12 exenterated eyeballs showed predominately neural tissue invasion
5. Giant cell reaction was seen in one patient
6. Microabcess was seen in 3 exenterated eye balls
7. Out of 240 samples, 4 samples (1.6%) showed pauci septate ribbon like hyphae branching at right angles with pseudohyphae suggestive of mucormycosis with secondary aspergillosis
8. Rest 236 samples (98.33%), showed wide angle branching with broad aseptate hyphae suggestive of mucormycosis microbiology report analysis :
9. Among all the 270 microbiology reports of KOH mount, 23 (8.51%) samples showed wide angle branching along with acute angle branching suggestive of mucormycosis with secondary aspergillosis.
10. Around 13 (4.81%) samples were reported only acute angle branching of hyphae suggestive of primary aspergillosis infection.
11. Around 39 (14.43%) samples reported no fungal elements.
12. Rest 195 sample (72.15%) showed only wide angle / right angle branching of hyphae suggestive of mucormycosis.
13. Out of 270 reports, 77 were females rest 193 were males.

Table 1: Histopathology analysis

Variable	Number	Frequency (%)
Total case analysed	240	-
Males	183	76.25
Females	57	23.75
Mucor	236	98.33
Aspergillus	00	-
Mucor with aspergillus	04	1.6
Candida	00	00
Antifungal therapy	151	
Surgery	170	

Table 2: Microbiology reports analysed

Variable	Number	Frequency
Total case analysed	270	
Male	193	71.48
Female	77	28.51
Aspergillus	13	4.81
Mucor	195	72.15
Mucor with aspergillus	23	8.51
No fungus detected	39	14.43
Antifungal therapy	251	
Surgery	170	

Table 3: Extension and location

Variable	Number	F requency
Nasal	327	64.11
Oral	54	10.58
Eye	19	3.72
Sinus	100	19.60
Lung	4	0.78
Brain	3	0.58
Bone	3	0.58

4. Discussion

Mucormycosis was considered a rare infection in healthy individuals but several reports from all over the world have documented that individuals who have successfully recoverd from COVID 19 infection, who are immunocompetent are suffering from this opportunistic fungal infection in the present scenario, sudden surge of fungal infection during the COVID 19 pandemic can be explained by SARS CoVi-2 mediated immunosuppression Mucor fungus primarily invades nose, sinuses, orbit, central nervous system, lung, retro orbital tissue, eye balls, skin, jaw bones, gum tissue and oral cavity but ROM is the commonest variety seen.[9] Giant cell invasion, thrombosis and eosinophilic necrosis of the underlying tissue is the pathological hallmark of mucormycosis. Microbiological identification of a fungal hyphae is based on diameter, presence or absence of septations, branching angle (right or acute angled branching), and pigmentation, presence or absence of pseudohyphae and spores.[10]

Limitations of this study include single tertiary referral center experience, and short-term follow-up. Future research studies are planned to update this experience with long-term follow-up and to stratify the patient according to the type of fungal infection and their outcome.

Previous studies have demonstrated a link between invasive Mucor infection and worse outcomes which needs amphotericin B as antifungal therapy. Voriconazole was suggested to have superiority over amphotericin B as a primary treatment for invasive Aspergillus infections with improved disease clearance.[11]

The majority of patients in the current study, received intravenous liposomal amphotericin B and kidney function test were done for each patient.

It has been observed that patients with limited disease extension, have the best outcome with minimal mortality and morbidity. This relatively better survival rate may be due to early diagnosis while close observation during the follow-up period after COVID-19 recovery, aggressive surgical debridement, and early use of antifungal medications.

5. Conclusion

We acknowledge that COVID-19 might be an independent risk factor for subsequent aspergillosis and mucormycosis or both. It was also observed that candidiasis was a result of mainly immunocompromised state or possible contamination. It is also possible that underlying diabetes mellitus, transiently deranged blood glucose profile, injudiscious use of steroid and long term hospitalisation with lack of hygiene can lead to multiple mixed mycoses. We also support the idea of identifying fungal infection clinically is very challenging, especially in the pandemic era and low resource setting. Co-ordinated efforts should therefore be made to further identify different fungal infections in specimens sent from resected tissue which can further guide the intensity of treatment.

6. Source of Funding

None.

7. Conflict of Interest

The authors declare no conflict of interest.

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