

COVID 19 ASSOCIATED FUNGAL INFECTIONS ESPECIALLY MUCORMYCOSIS - A LETHAL ADDITION

Pathology

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ABSTRACT

Background :- Covid 19 continues to be a challenge to the health care system. Mucormycosis had risen to an alarming frequency in the second wave and has complicated the disease and its outcome.

Methods And Materials:- The present study consisted of 55 histopathologically confirmed cases of mucormycosis associated with COVID 19. Relevant clinical data were retrieved. Received specimens were examined grossly and processed for H and E stained sections.

Results:- Maximum patients were in the age group 41 to 60 years comprising 67.27% of cases. Mucormycosis was the leading fungal infection (87.27%) followed by a dual fungal infection (7.28%). Imaging studies and KOH mount could not detect fungus in 34.54% of the cases. Diabetes was found in 78.13% of patients of which many were on O2 support and received steroids therapy. Maxillectomy with partial palatotomy, mandibulectomy and enucleation of eyeball were performed in selected cases.

Conclusion - Histopathology is a reliable tool for the diagnosis of fungal infection. The present study found that diabetic patients who were on oxygen support and received steroid therapy were prone for mucormycosis. A high index of clinical suspicion is of paramount importance for timely management to reduce subsequent mortality and morbidity.

KEYWORDS

COVID19, fungal infection, Mucormycosis.

INTRODUCTION –

According to the CDC mucormycosis is a serious fungal infection caused by a group of molds called micromycetes.^[1] Mucormycosis had risen suddenly in the second wave as compared to the first wave in India. India had a whooping number of more than 47000 cases of mucormycosis from April to June 2021.^[2]

Mucormycosis is typically prevalent in preexisting co-morbidities and patients receiving steroids or immunomodulators for COVID 19 therapy.^{[3],[4],[5],[6],[7],[8]} We present our experience of 55 proved cases of COVID 19 associated fungal sinusitis.

RESULT –

Total 55 biopsy-confirmed cases of fungal sinusitis predominantly mucormycosis associated with COVID 19 were included in the study. Maximum cases were in the age group of 41 to 60 years comprising 67.27% of patients. Males outnumbered females consisting of 80% patients.

All patients were RTPCR positive COVID 19 infection. Post-COVID status was seen in 94.54% of cases. The predominant presentation was facial pain (74.5% of cases) followed by headache (67.2%), blackening of area, proptosis, eye swelling, orbital pain and swelling of the nose. Oxygen and steroids along with other supportive treatment were received by 83.64% of patients. Bilateral fungal sinusitis was found in 45% of cases, while only right or only left side involvement was seen in 31% and 24% of cases respectively. Single or twin co-morbidities were seen in 87.30% of cases. No co-morbidities were found in 12.70% of cases. Amongst it, diabetes mellitus was the dominant finding found in 78.13% of cases. Hypertension with diabetes, and RVD was found in 43.63%, 1.90% and 7.27% of patients respectively. Fungal sinusitis was not identified in 34.55% of cases. KOH mount showed fungus in 65.45% of cases comprising of mucormycosis, non-mucor fungal sinusitis and dual fungal infection in 54.55%, 9.09% and 1.82% of cases respectively. No fungus was identified in 34.55% of cases. Histopathology revealed mucormycosis in 87.27% of cases. The fungus was characterised by broad, hyaline, aseptate, ribbon-like hyphae with right-angle branching. Mixed or dual fungal infection of which one of the components as mucor was seen in 7.28% (4 cases) of cases. Overall mucormycosis was observed in 94.55% of cases. Amongst dual fungal infections, another component was aspergillus in three cases. In a single case of dual infection, non-mucor fungal species could not be identified. The culture was not done in that case. Aspergillus was found in 5.45% (3 cases) of patients. Necrosis with acute inflammation was

seen in 65.45% of cases. Granulomatous and mixed (acute inflammation and focal granulomas) were observed in 27.28% and 7.27% respectively. Fungal culture was done in 26 patients. Amongst it, 57.7% (15 cases) of cases did not show any growth. A positive culture was seen in 42.3% (11 cases) of cases. Amongst it, colonies of mucor were seen in 81.81% (9 cases) of cases and growth of aspergillus fungus was observed in two cases. Defacement surgery was indicated in eight patients. Maxillectomy was the most frequent surgery and was undertaken in six patients with additional palatotomy in three patients. Enucleation of eyeball and mandibulectomy were performed in a single case each. Out of 55 patients, 74.54% (41 cases) showed improvement. Defacement surgery with compromise in functional capacity was the outcome in 14.56% (8 cases) of cases. Mortality due to infection was noted in 10.90% (6 cases) of cases.

DISCUSSION -

Coronavirus causes severe acute respiratory distress syndrome and it is also associated with secondary bacterial and fungal infections.^[9] Mucormycosis had gone to an alarming frequency in India in the second wave as compared to the first wave. Maharashtra was the worst-hit state and it had yielded high morbidity and mortality.^[10]

Fungi gain entry into the nose and extend into paranasal sinuses. It rapidly progresses and has an angioinvasive tendency leading to vascular occlusion and subsequent infarction.

Maximum patients were in the age group 41 to 60 years comprising of 67.27% of cases.

Facial pain and headache due to fungal sinusitis were the commonest presenting symptoms which were in concordance with Ramaswami et al, Rajan M et al and Sharma S et al. The fungus penetrates deep into the soft tissue via angioinvasion and involves the bones of the walls of sinuses.

Interaction of SARS Cov2 virus with host immune system contributes to dysfunctional immune responses. This causes immune dysregulation with decreased counts of CD4+T and CD8+T cells.^{[11],[12],[13]} Hyperglycemia and ketosis are known to cause immune depletion and it is thought to cause depression of phagocytosis, chemotaxis and local inflammatory response.^{[14],[15]} Iron chelators like deferoxamine make the iron available required for the growth and virulence of the fungus.^[14] The present study had 73.13% of diabetic patients.

Observation of higher incidence of post-Covid mucormycosis in

diabetic patients is in concordance with Bhanuprasad et al, John et al, Sharma et al, Moorthy et al, Satish et al and Sarkar et al

Table No. 1 - Comparison Of Co- Morbidity (Diabetes Mellitus) With Other Studies

Authors (Year)	Sample size (n)	No. of Cases	%
Patel et al (2020)	465	342	73.5
Prakash et al (2019)	388	291	75
Bhanuprasad et al (2021)	164	159	97 (P <0.01)
Arunkumar et al (2021)	101	84	83.3
Martin et al (2021)	80	66	82.5
Ramaswami et al(2021)	70	49	70
John et al (2021)	41	38	93 (P <0.05)
Sharma et al (2021)	23	21	91.3
Moorthy et al (2021)	17	15	88.2
Satish et al (2021)	11	11	100
Sarkar et al (2021)	10	10	100
Mishra et al(2021)	10	8	80
Present Study	55	43	78.18

Oxygen therapy was received by 83.64% of patients in the present study which is comparable with a study of Bhanuprasad et al.

Steroid therapy is known to induce hyperglycemia. Steroid therapy was received by 83.64% of patients in the present study. Similar results were obtained by Bhanuprasad et al, Ramaswami et al, Sharma et al, Arunkumar et al, Sarkar et al.

Table No. 2 - Comparison Of Steroids With Other Studies -

Authors	Sample size	No. of cases	%
Bhanuprasad et al (2021)	164	117	71.6 (P<0.05)
Arunkumar et al (2021)	101	77	76.3
Martin et al (2021)	80	60	75
Ramaswami et al (2021)	70	49	70 (P <0.05)
John et al (2021)	41	36	88
Sharma et al (2021)	23	23	100
Moorthy et al (2021)	17	15	88.2
Sarkar et al (2021)	10	10	100
Mishra et al (2021)	10	6	60
Present Study	55	46	83.64

At the time of the initial visit, KOH mount from the site and paranasal sinuses were done in all patients. It had shown broad aseptate hyphae of mucor in 54.55% of cases. The non-mucor fungus was seen in 9.09% (5 cases) of cases. However 34.55% (19 cases) of cases did not demonstrate any fungus. This is due to an inherent property of fungus to invade deeper tissue through angioinvasion.

Histopathology revealed mucormycosis in 87.27% of cases. Mixed fungal infection of which one of the components as mucor was seen in 7.28% (4 cases) of cases. Overall mucormycosis was observed in 94.55% of cases. Amongst dual fungal infections, another component was aspergillus in 5.45% (three cases). In a single case of dual infection, non-mucor fungal species could not be identified. The culture was not done in that case. [Table no. 3]

Table No. 3 - Histopathology - Distribution Of Cases

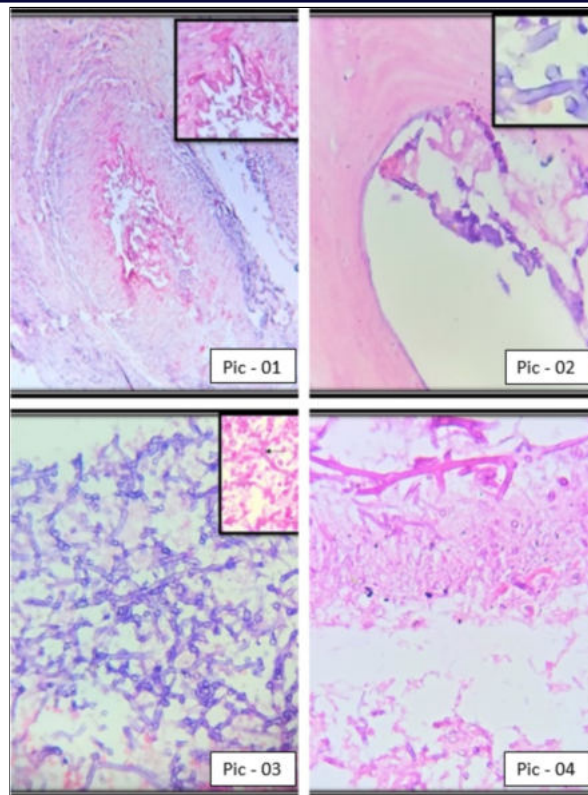
Histopathology	No. of cases	%
Mucor	48	87.27
Aspergillus	3	5.45
Dual	4	7.28
Total	55	100

Pic 01 – Photograph showing angioinvasion

Pic 02 – Photograph of bone marrow shows an invasion by Broad, aseptate, hyaline hyphae of mucor

Pic 03– Photograph shows bunches of broad, aseptate fungal hyphae with irregular right angled branching. Inset shows PAS positive Mucor.

Pic 04 - Photograph of dual fungal infection showing mucor and aspergillus



In the present study 14.56% (8 cases) patients landed in defacement surgery. Overall survival was seen in 89.10% of patients. Death ensued in 10.90% of patients which is far less than studies by Moorthy et al, Satish et al, Sarkar et al and Mishra et al.

CONCLUSION -

Histopathology is the most valuable and reliable tool for diagnosis as KOH preparation has limitations and culture is time-consuming.

The present study observed DM, steroid use as the risk factors and re-emphasizes the effective hyperglycemic control and judicious use of steroids. Awareness of warning symptoms, early diagnosis, strategic management by a multidisciplinary team is key to reduce mortality and defacement surgeries.

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