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CLINICOPATHOLOGICAL STUDY OF MUCORMYCOSIS

Pathology

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ABSTRACT

Introduction: Mucormycosis is an uncommon but fatal fungal infection occurring in compromised immune conditions mainly due to diabetic ketoacidosis, organ transplantation. In recent times of COVID pandemic, increased cases of mucormycosis were being reported. **Aim:** To study histopathological findings in mucormycosis and access predisposing factors for it. **Material and Methods:** This case series study was conducted from december 2020 to may 2021 in S. Nijalingappa medical collage, Pathology Department and Miskin laboratory, Bagalkot .We collected 98 cases of mucormycosis , did histopathological study of biopsy specimens in haematoxylin and eosin stained slides, collected case details regarding age, site, covid status of patient and associated co morbidities. **Results:** Out of 98 cases of mucormycosis reported, peak incidence is seen between 40 to 60 years of age, predominantly seen in males, 64.5% presented with post covid status, 42.5% associated with diabetes mellitus and predominant site involved was nasal cavity and sinuses. **Conclusion:** Mucormycosis being opportunistic infection is reported increasingly in covid-19 cases owing to low oxygen, high glucose, cytokine storm and compromised immunity.

KEYWORDS

Mucormycosis, COVID-19, Diabetes.

INTRODUCTION

Mucormycosis is a life-threatening fungal infection that usually occurs in immunocompromised patients.Fungi belongs to mucorales order, class-zygomycetes. Most species are of *Mucoraceae* family. Rhizopus oryzae is the most common type and responsible for nearly 60% of mucormycosis. Based on anatomical location Mucormycosis can present as rhino-orbital-cerebral form (ROCM), pulmonary, gastrointestinal, cutaneous,disseminated and uncommon presentation. ROCM is the most common form.

The term ROCM includes spectrum of disease from limited sinonasal disease to limited rhino-orbital disease and rhino-orbital-cerebral disease (CNS involvement). Mucormycosis infections show extensive angioinvasion with resultant vessel thrombosis and tissue necrosis (1). Earlier predisposing factors were mainly immunocompramised condition due to diabetic ketoacidosis, neutropenia, organ transplantation, increased serum levels of available iron(1). But in this COVID -19 pandemic period mucormycosis incidence has drastically increased owing to ideal environment for fungal growth of low oxygen, high glucose, acidic medium and decreased phagocytic activity of white blood cells(2).

Organisms of the class *Zygomycetes* were first noted to cause disease in humans in publications from the 1800's. Platauf is credited with the first description of zygomycosis in humans in his paper entitled Mycosis Mucorina (3). The names that have been given to these molds in the medical literature include *Zygomycota* and *Mucorales*. It is currently accepted that the broader subphylum *Mucoromycotina* has two orders, the *Mucorales* and the *Entomophthorales(4)*.

Histopathological study of mucormycosis shows nonpigmented (haylin), wide (5- to 20-µm), thin-walled, ribbon-like hyphae with few septations (pauciseptate) and right-angle branching, the hyphal elements will be found with abundant necrosis, hemorrhage, and blood vessel thrombosis.

Identification of fungal elements invading the blood vessel wall or inside their lumen is most important feature. Histopathology is rapid and cost-effective means of providing a definitive diagnosis of an invasive fungal infection(4). Grocott or Gomori methenamine silver [GMS] stain and Periodic acid Schiff (PAS) stain are special stains used to demonstrate fungal elements on histopathology slides.

METHODS:

This case series study was conducted from december 2020 to may 2021 in S. Nijalingappa medical collage, Pathology Department and Miskin laboratory, Bagalkot. Histopathological study of biopsy specimens received from sino-nasal cavity and orbit during study period was done and cases diagnosed mucormycosis were included in the study. Periodic acid schiff staining and Gomoris methanamine staining was done in required cases. Case details of all cases diagnosed mucormycosis were collected and analyzed associated co morbidities, location of mucormycosis and co infections. Excluded inadequate biopsies.

RESULT:

Total 98 cases are analysed in present study. Mucormycosis was seen predominantly in males (68%) than in females(32%). 86.7% of biopsies were obtained from sino-nasal cavity whereas 13.2% were from rhino-orbital region. Highest age group involved was 40-50 years (30 cases) followed by 50-60 years(24 cases), 60-70 years(20cases), 30-40 years(14cases), less than 20 years 7 cases and more than 70 years 3 case(Figure 1). Total 13 deaths were registered among cases included of which 7 cases belonged to 60-70 years age group.

In this study 35.50% cases of mucormycosis are positive for covid-19 and 64.5% cases are of post covid status. 42.50% cases are associated with diabetes mellitus (Includes pre existing as well as new-onset diabetic cases) and 1% associated with HIV. (Figure:2)

Co-infection of Actinomycosis, aspergillosis and Demetiaceous fungal infection with mucormycosis was noted in one case each respectively. One case showed mucormycosis, aspergillosis and demetiaceous fungal infection together (Figure:3,4,5).

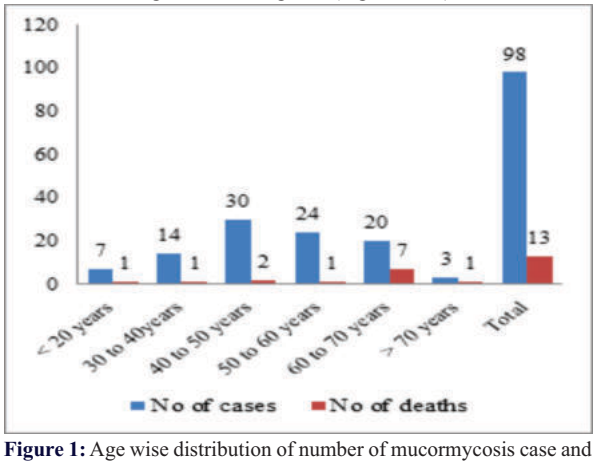

Figure 1: Age wise distribution of number of mucormycosis case and deaths due to it

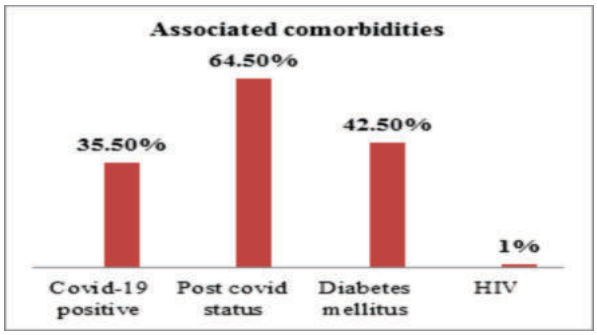

Figure 2: Comorbiditis associated with mucormycosis

DISCUSSION:

Mucorales genera are ubiquitous in the environment, inhaled spores causes disease in immunosuppressed patients. Primary host defence against mucormycosis is through macrophages that inhibit germination of spores and neutrophils that use the oxidative burst to kill proliferating hyphal elements, thus factors affecting these function of these cell types lead to mucormycosis. Earlier diabetic ketoacidosis,cancer chemotherapy , stem cell transplantation were major risk factors. These fungi thrive in presence of iron thus patients receiving iron-chelating agents such as deferoxamine are also at risk. With arrival of covid pandemic covid 19 disease became major risk factor for mucormycosis as new onset diabetes in covid patients, steroid therapy and long duration oxygen inhalation altogether creats an ideal environment for mucormycosis. In our study 35.50% cases of mucormycosis are positive for covid-19 and 64.5% cases are of post covid status i.e one to two months after being tested negative for covid 19 post therapy.

Studies on Mucormycosis in india prior to COVID 19 , prakash et al showed diabetic ketoacidosis in 18% and uncontrolled DM in 57%.(7). John et al study of 41 confirmed cases in people with covid-19 showed DM in 93% of cases , while 88% were receiving corticosteroids.(8) Our study showed DM including pre-existing as well as new onset in 42.5%.

Location of mucormycosis can be rhino-orbito cerebral(ROCM), pulmonary, cutaneous, gastrointestinal, disseminated or miscellaneous. Study of 465 cases of mucormycosis without covid-19 in india,patel et al showed rhino-orbital presentation in 67% followed by pulmonary in 13% and cutaneous type in 10.5%.(9) We also found cases with co infection of aspergillosis and demetaceous fungi. *Aspergillus* spp. are usually described as thin (3- to 12-µm), septate, acute-angle (45°) or dichotomous branching hyphae and Dematiaceous fungi are described as pigmented irregular hyphae and yeast-like structures both with septations.(4)

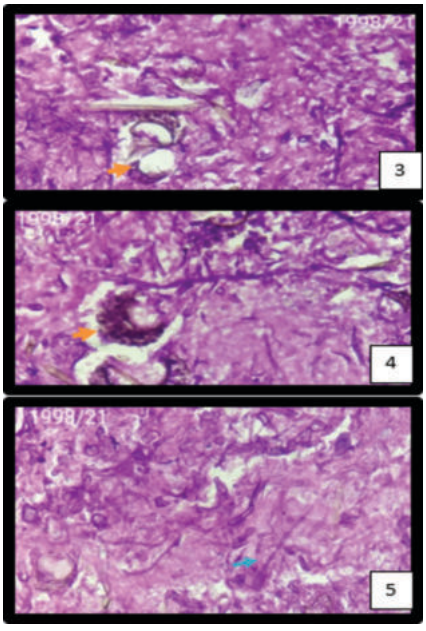

Figure 3,4,5:Histopathology of case with simultaneous mucormycosis, aspergillosis(▶) and demetaceous (▶) fungal infection.

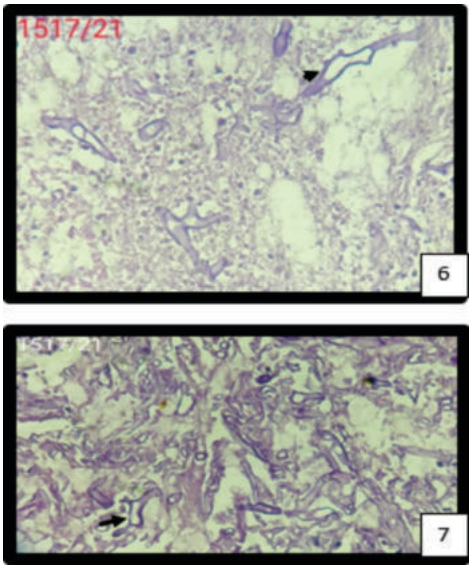

Figure:6,7 Shows Non septate, broad, hyaline hyphae with obtuse angle branching indicating mucormycosis.

CONCLUSIONS

Mucormycosis being opportunistic infection, is reported increasingly in covid-19 cases owing to low oxygen, high glucose (pre-existing diabetes, new-onset of hyperglycaemia, steroid induced hyperglycaemia), cytokine storm and compromised immunity. ROCM is most common type of mucormycosis in COVID-19. Covid-19 and Diabetes are individual high risk factors for Mucormycosis.

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