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PATTERNS AND CLINICAL BURDEN OF FUNGAL INFECTIONS IN COVID-19 PATIENTS: 6 MONTHS OF A STUDY CONDUCTED IN WESTERN INDIA

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Abstract
Invasive fungal infections have become a major complication in COVID-19 patients, particularly in India. The proposed prospective study aims to determine the prevalence, risk factors, and range of fungal infections, such as mucormycosis and aspergillosis, in 232 COVID-19 positive patients at a NABL accredited laboratory in Western India. The results indicate that diabetes mellitus, the use of corticosteroids, and hyperglycemia have a high likelihood of causing fungal infections mainly in the nose areas, sinuses, and rhino-orbit areas of patients with COVID-19. The diagnosis was easy and timely with the use of the laboratory screening through the use of the KOH mounts and cultures. The prompt treatment is vital since these infections progress fast and are deadly and the importance of close clinical handling by administration of antifungal agents like lyophilized Amphotericin B is highlighted.

Keywords: COVID-19; mucormycosis; diabetes; corticosteroid therapy

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-caused Coronavirus Disease 2019 (COVID-19) has been linked to a variety of opportunistic bacterial and fungal diseases. The predominant fungal pathogens causing co-infection in persons with COVID-19 have been identified as Aspergillosis and Candida [1-3]. Several instances of mucormycosis in patients with COVID 19 have recently been documented across the globe, particularly in India. An ideal environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins), and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated [4-6].

Paltauf initially identified phycomycosis or zygomycosis in 1885, and Baker, an American pathologist, created the term Mucormycosis in 1957 to characterise a severe Rhizopus infection. Mucormycosis is a rare but deadly fungal illness that generally affects those who have weakened immune systems [7, 8]. Mold fungus of the genera Rhizopus, Mucor, Rhizomucor, Cunninghamella, and Absidia of the Order Mucorales, Class Zygomycetes, cause mucormycosis, an angioinvasive

illness. The Rhizopus Oryzae is the most prevalent kind, accounting for about 60% of human mucormycosis infections and 90% of the Rhino-orbital-cerebral (ROCM) variant. The inhalation of fungus spores is the mode of contamination [9-11].

According to a recent projection for the year 2019-2020, the prevalence of mucormycosis ranged from 0.005 to 1.7 per million people worldwide, with India's prevalence approximately 80 times higher (0.14 per 1000) than affluent nations. In other words, India has the world's highest rate of mucormycosis [12, 13]. Mucormycosis has a significant death rate. Intracranial involvement of mucormycosis elevates the fatality rate to as high as 90 percent. Furthermore, the quickness with which mucormycosis spreads is an exceptional phenomena, and even a 12-hour delay in diagnosis may be lethal, which is why 50 percent of mucormycosis patients have traditionally been detected only in post-mortem autopsy series [14-17]. A case series of 232 individuals with COVID-19 infection and mucormycosis is presented here.

Material and Methods

Case presentation

The study was conducted over a period of 6 months on 232 patients in Metropolis Helthcare Rajkot,Gujarat, A well-established NABL Accredited lab. Various samples (Figure 1) were collected to find out presence of fungal infection in these post covid patient with varied symptoms [18].

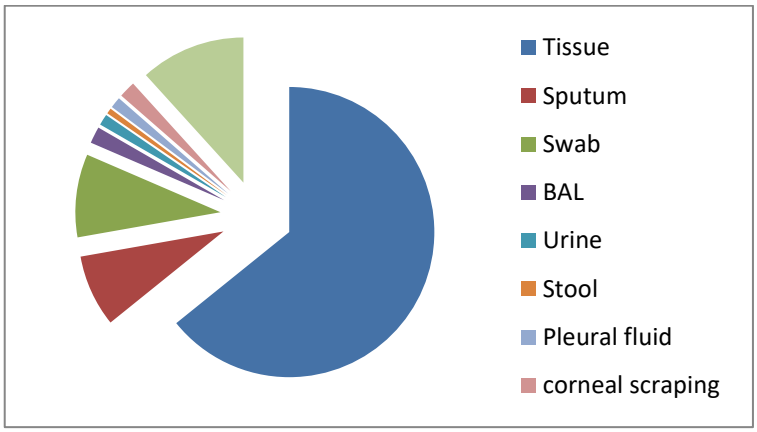

Figure-1: Various symptoms in post covid patient

The patient with the diagnosis of mucormycosis was identified with a positive KOH mount and associated clinical features suggestive of fungal infection. All the samples were first examined directly in low power and high power , KOH mount for the presence of any fungal element (Figure 2).

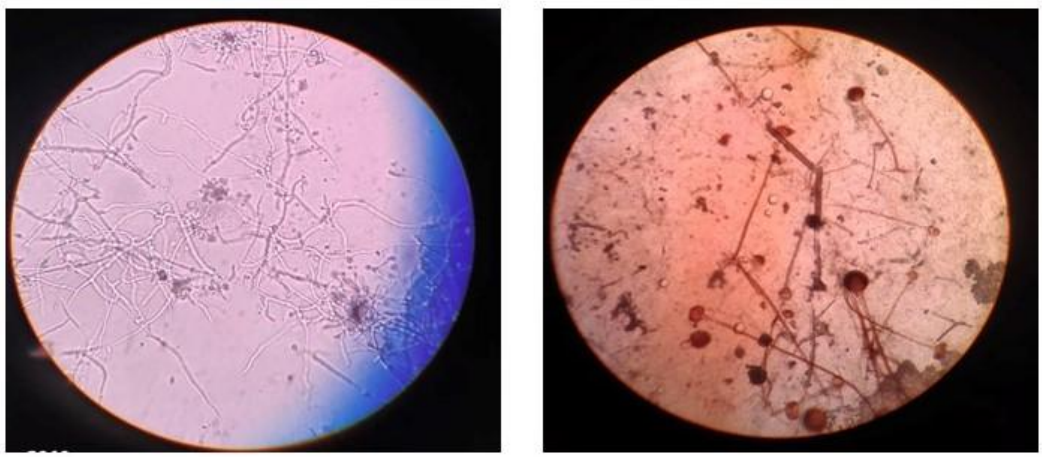

Figure 2: Direct smear with 10% KOH

After KOH examination the samples were steaked on Seborauds Dextrose Agar & Rose bengal agar for fungal growth in two sepaarate sets at 25ºC and 37ºC. The tubes were kept for atleast 7 days for growth. Presence of white fluffy growth covering the whole plate or tubes wre typical of Mucor spp.as they commomnly known as lid lifters.the growth were confirmed with Lactophenol cotton Blue stain as shown in Figure 3 [19, 20].

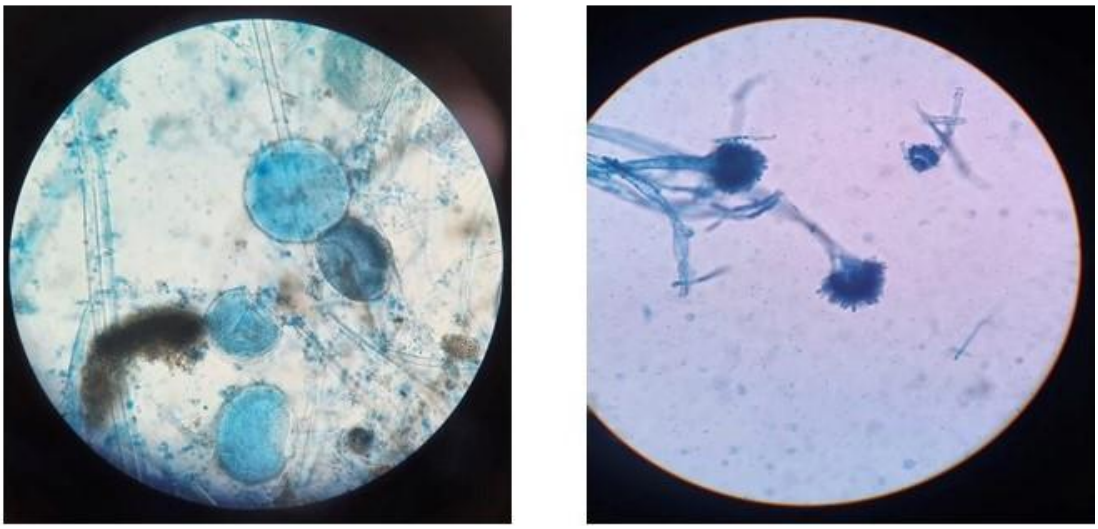

Figure 3: Lactophenol cotton blue staining of the cultured fungi shows hyphae with nodal rhizoids and short sporangiophores with round black sporangia

Result

A total of 231 cases of mucormycosis including confirmed (56.70%) and suspected (43.29%) in people with confirmed (RT-PCR diagnosis) COVID-19 were retrieved.

Out of 131 confirmed cases of mucormycosis while 14 of them having mixed infection of Aspergillus and mucor spp. 21 were having Aspergillus spp. Infection alone while 2 of them were found to be infected with Candida spp. Commonest organ involved with mucormycosis was nose and sinus (57.14%), followed by rhino-orbital (22.07%) and Pulmonary type (20.77%).

Discussion

Although mucormycosis is exceedingly uncommon in healthy people, it is caused by a number of immunocompromised diseases. This includes uncontrolled diabetes with or without DKA, haematological and other cancers, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, deferoxamine therapy, severe burns, AIDS, intravenous drug abusers, malnutrition, and open wounds after trauma [21, 22]. Mucormycosis may affect the nose, sinuses, orbit, CNS, lungs (pulmonary), gastrointestinal tract (GIT), skin, jaw bones, joints, heart, kidney, and mediastinum (invasive kind), but ROCM is the most prevalent variant observed in clinical practise across the globe. It's worth noting that the phrase "rhino-orbital-cerebral illness" encompasses the complete range of diseases ranging from restricted sino-nasal disease (tissue invasion), limited rhinoorbital disease (progression to orbits), and rhino-orbital-cerebral disease (CNS involvement) [23-25]. Due to the underlying illness, the region of participation may vary. For example, ROCM is commonly associated with uncontrolled diabetes and DKA, lung involvement is frequently seen in patients with neutropenia, bone marrow and organ transplantation, and haematological malignancies, and GIT involvement is more common in malnourished people [26, 27]. Mucormycosis is characterised by giant cell invasion, thrombosis, and eosinophilic necrosis of the underlying tissue. It is distinguished from other fungal diseases by microbiological identification of the hyphae based on width, presence or absence of septa, branching angle (right or acute branching), and coloration [28, 29].

The Smith and Krichner criteria for the clinical diagnosis of mucormycosis, published in 1950, are still regarded the gold standard and include the following [30, 31]:
I Blood-tinged nasal discharge and facial pain on the same side, (ii) Soft peri-orbital or peri-nasal swelling with discoloration and induration, (iv) Ptosis of the eyelid, proptosis of the eyeball, and complete ophthalmoplegia, and (v) Ptosis of the eyelid, proptosis of the eyeball, and complete ophthalmoplegia (v) Multiple cranial nerve palsies that are unrelated to lesions that have been recorded
Patel et al (15) found that rhinoorbital presentation was the most prevalent (67.7%), followed by pulmonary (13.3%) and cutaneous types in a study of 465 patients with mucormycosis without COVID-19 in India (10.5 percent) [32, 33]. In Indians, predisposing factors for mucormycosis include diabetes (73.5%), malignancy (9.0%), and organ transplantation (7.7 percent). According to a prospective Indian research conducted before to the COVID-19 pandemic, the presence of DM increases the risk of developing ROCM by 7.5-fold (Odds ratio 7.55, P = 0.001) [34, 35].
In a recent systematic study done by John et al from April 9, 2021 to April 9, 2021, DM was recorded in 93 percent of verified mucormycosis cases in patients with COVID-19, with 88 percent getting corticosteroids [36, 37]. These results are comparable with those of a larger case series of 231 mucormycosis patients in Covid-19, in which 80 percent of cases had a clinical history of DM and more than two-thirds (76.3 percent) received corticosteroids during their hospital stay. In persons with COVID-19, these data point to an unholy trifecta of mucormycosis, diabetes, and steroid use [38-40].

Conclusion

Patient infected with COVID -19, given steroid herapy having history of DM are more likely to develop fungal infection. Most commonly mucormycosis followed by Aspergillosis. Some of the patients also developed mixed infection. Screening can easily be done by KOH mount and confirmed by culture. Early diagnosis and treatment is utmost priorty as LAMB (Lyophilized Amphotericin B) is the drug of choice which is expensive as well as toxic too. If ignored patient may need complete exenteration of the organ involved.

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