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Review Article

Mucormycosis (Black Fungus) an Emerging Threat During 2nd Wave of COVID-19 Pandemic in India: A Review

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Abstract

COVID-19 treatment makes an immune system vulnerable to other infections such as Black fungus (Muceromycosis). India has been facing high rates of COVID-19 since April 2021 with a B.1.617 variant of the SARS- COV2 virus is a great concern. Mucormycosis is a rare type of fungal infection that occurs through exposure to fungi called mucormycetes. These fungi commonly occur in the environment particularly on leaves, soil, compost and animal dung and can entre the body through breathing, inhaling and exposed wounds in the skin. The oxygen supply by contaminated pipes and use of industrial oxygen along with dirty cylinders in the COVID-19 patients for a longer period of time has created a perfect environment for mucormycosis (Black fungus) infection.

Keywords: Mucormycosis, Black Fungus, COVID-19, SARS-COV2, variant, industrial oxygen, hospitalization.

INTRODUCTION

The emergence of the different infections during the COVID-19 pandemic made the health workers more vigillent, and one of the emerging infection is of Black fungus (Mucormycosis). It is a fungal infection caused by the fungi which belongs to the order Mucerales [1]. The species is the Mucor rhyzupus, Absidia and Cunnnighamella, genera are most often implicated. The Mcormycosis is also called as Zygomycosis. The main source of infection (reserviours) is soil, dumping places, walls of old buildings etc. Mucormycosis or "Zygomycosis are sometimes used interchangeably [2]. However zygomycota has been identified as polyphelitic and is not included in modern fungul classification systems and also zygomycosis includes Entomopthorales, mucormycosis exclude this group. The spors are the source of dispersal. This black fungus or mucormysis is caused by a group of moulds called mucormycetes and often affects the sinsuses, lungs, skin, and brain. In the context of covid-19, the condition commonly refered as the black fungus.

Types of mucormycosis. It is of different types depending on the organ infected:

a) **Rhinocereval (skin and brain):** This types of mycormycosis is an infection in the sinuses that can be spread to the brain. This type of infection is most common in people with uncontrolled diabetes and in the people who have had a kidney transplant
b) **Pulmornary (lungs) mucormycosis:** This is the most common type of infection in people with cancer and in people who have had a organ transplant or stem cell transplant.
c) **Cutaneous (Skin) mucormycosis:** This type of infection occurs when the fungi entre the body through the skin; it may be after surgery, burn, skin reputure or any other type of skin trauma. Such type of mucormycosis is found among people who have good immune system.
d) **Gastrointestinal mucrormycosis:** This mucormysis is more common among young children than adults especially premature and low birth wieight infants, less than 1 month of age, who have had antibiotics, surgery or medication that lowers the body's ability to fight germs and sickness
e) **Dissemmated mucromycosis:** It occurs when the infection spreads through the blood streams to affect another part of the body. The infection most commonly affects the brain, but also can affect other organs such as spleen, heart and skin [3].
f) **Signs and symptoms:** Mucormycosis frequently infects the sinuses, brain or lungs. Brain and oral cavity infection are most common type or forms of mucormycosis, besides fungus can also infect other areas of the body, such as skin, gastrointestinal

tract and other organ system [4]. Maxilla may be also affected in rare cases [5]. The rich blood vessels supply of maxillofacial areas usually prevents fungul infections, although more virulent fungi, such as those responsible for mucormycosis can often overcome this difficulty [5]. Infection ususally begans in the mouth or nose and enters the central nervous system via eyes [6]. The face swelled one sided, headache, congestion in the nose and sinus, leads to the "black lesions" acorss the nose or upper side of the mouth, fever and eye swelling can occur when a sinus or the brain is effected[7]. The eyes may appears to buldge, fever, cough, chest pain and difficult breathing, coughing up blood can occur when lungs are involved[7]. During the gastrointestinal tract infection, nausea tummy ache, vomiting and bleeding can occur. The affected skin may appears as a dusky reddish tender patch with a darkining centre due to tissue death [8]. Sometime ulcer is formed and it can be very painful.

The invasion of fungus into blood vessels result in the formation of blood clots and surrounding tissue death due to loss of blood supply[9].Dissimmated (wide spread) mucormycosis typically occurs in people who are already sick due to other medical complicaitons, therefore it can be difficult to know which symptoms are realted to fungal infection (mucormycosis). People with such infection in the brain can develop mental status change or coma.

Risk factors

Mucormycosis mostly occurs in such people which are less able to fight the infection (Predisposing factors)[8]. These includes organ transplant, AIDS, poorly controlled diabetes mellitus, iron overload, cancers such as lymphomas, kidney failure, long term corticosteroid and immunosuppressive therapy, cirrhosis and mal nutrition[10]. The people with low neutrophil count are also at risk of infection, other risk factor include tuberclosis (TB). The rising of iron due to deferoxamine treatment in kidney disease has also been reported to increase the risk of Mucormycosis [11]. The use of steroid commonly in the treatment of Covid -19 and reduce demage caused by the body's own immune system during coronavirus infection. These corticosteroid are immuno suppressant and increase blood sugar levels in both diabetics and non diabetics patients, and as a result both these effects may contribute to cases of mucormycosis [12].

Mechanisms

Most people are frequently exposed to Mucorales without developing the disease. It is generally spreaded by eating contiminated food, or by getting spores of moulds of the mucorales type in an open wound. It is not transmitted between people [13]. In people with poorly controlled diabetes, high sugar level provides suitable conditions for the development of filamentous sturctures that first attack to blood vessels and then penetrate them, as a result blocking them and causing tissue to die [14].

Diagnosis

The diagnosis of the disease requires the identification of the moulds in the affected tissue by biopsy and confirming it with fungal culture. As the causative fungi occur all around and culture all alone is not decisive. Tests may also include culture and direct detention of the fungus in Lung fluid, blood serum plasma and urine [15].

A). Imaging

The imaging i.e CT Scan of the lubgs and sinusis [16]. The signs of chest CT scan such as nodules, cavities, halo signs, pleural, effusions and wedge shaped shadows, showing invasion of blood vessels may suggest a fungal infection, but does not confirm mucormycosis. A reverse halo sign in a person with a blood cancer and low neutropil count is highly suggestive of mucormycosis[17]. CT scan images of mucormycosis can be useful to distinguish mucormycosis of the orbit and cellulitis of the orbit, but imaging may look identical to those of aspergillosis.

b) Cultural and Biopsy

For the confirmation of diagnosis biopsy samples can be cultured [18]. Culture from biopsy sample does not always give a result as the organism is very fragile.

C) Differntial Dignosis

Other filamentous fungi may however look similar. It may be difficult to differentiate from aspergillosis. Other possible diagnosis includes anthrax, cellulitis, bowel obstruction, clot in lungs, sinusitis, tuberculosis and fusariosis [19].

Treatment

In case of suspected mucormycosis patients, Amphotericin-B is initially given slowly into a vein, after that given daily for the next 14 days [20]. It is continued for sometime for longer duration. In 2015, without a randomized control trail, the FDA approved Isavuconazole as a treatment for mucormycosis [21]. Posaconazole is an alternative.

Surgical removal of fungus ball is also suggested. The disease must be monitored carefully for any sign of reemergence. Surgery can be very drastic and in some cases of disease involving the nasal cavity and the brain, removal of the infected brain tissue may be required. The removal of palate, eye structure or nasal cavity can be very disfuring [22]. Sometime more than one operation is required. Hyperbaric oxygen has been used as an adjuntive therapy, because higher oxygen pressure increase the ability of neutrophils to kill the fungus, but the efficency of this therapy is uncertain [23].

Prevention

The preventive measures includes wearing a mask in dusty area, avoid direct contact with water demaged buildings and protecting skin, feet and hands, where there is exposure to soil or manure such as work in the fields and gardening. In high risk groups such as organ transplant antifungal drugs may be given as preventive [24].

History

The first case of mucormycosis was possibly one described by Friedrich kuchenmiester in 1855[25]. Furbringer first described the disease in the lungs in 1876[76]. In 1884 Lichtheim established the development of disease in rabbits and described two species; Mucor corymbiafera and Mucor rhizopodiformis, later known as Lichtheimia and Rhizopus respectively. In 1943 its association with poorly controlled diabetes was reported in three cases with severe sinus, brain and eye involvement [26]. In 1953, Saksenarae vasiformis found to cause several cases was isolated from Indian forest soil and in 1979, P.C Misra examined soil from an Indian mango orchard from where they isolated Apopysomyces, later found to be a major cause of mucormycosis [26].

Arnold Paltauf coined the term Mycosis. Mucorina" in 1885 after describing the case with systemic system involving the sinus, brain and gastrointestinal tract, following which the term mucormycosis became popular [26].

This deisease has been reported in natural disasters and catastrophes; (2004) in Indian ocean tsunami and 2011 Missouri tornado [27]. A cluster of infections occurred in the wake of the 2011 Joplin tornado. By July 19, 2011 a total of 18 suspected cases of mucormycosis of the skin had been identified, of which 13 were confirmed.

In 2014 detail of a lethal mycormycosis outbreak which occurred in 2008 emerged after television and newspaper reports responded to article in a pediatric medical Journal [28]. A 2018 study found many freshly laundered hospital lineus deliverd to U.S transplant hospitals were contaminated with Mucorales [29]. Besides human mucormycosis cases have been described in cats, dogs, cows, horses, dolphin's bison and seals [30].

COVID-19 and Black fungus (Mucormycosis)

Covid-19 associated mucormycosis commonly referd to as back fungus is association of mucormysis an aggressive fungal infection with COVID-19. The prominent symptoms include swelling and blackning around eyes and brain a clinical manifestation sometime refered to as rhino-orbital cerebral (ROC) mucormycosis. This disease does not spread from person to person and is not contagious.

As India has facing high rates of COVID-19 since April 2021 and is struck with B.1.617 varient of coronavirus which is a agrat concern. Some scientist believe that severe COVID-9 could potentially weaken the body's immune response, this could lead to increased vulnerability of other infections, especially for the people who are immunocompromised. The particular concern in the present pandemic is an infection called mucormycosis commonly refered to as black fungus.

Status of Black fungus cases in India till 26th of May 2021

As the number of Covid patients infected with Mucormycosis spiked, the Health Ministry asked all states to decleare black fungus infection an epidemic.

India has reported 11,717 case of Mucorycosis (Black Fungus) till 26th of May 2021, with Gujarat, Maharashtra and Andra Pradesh having the highest number of cases. The disease has emerged as a new challenge in India's battle against COVID-19. Maharashtra has reported 2770 cases of Black fungs, where as Gujarat has logged 2,859 cases and Andra Pradesh 768 cases, Madhya Pradesh 752 cases, Telangana 744 cases, Uttar Pardesh 701 cases,Rajasthan 492 cases, Karnatka 481 cases, Bihar 215 cases, Tamil Nadu 236 cases are fome of the states which shows large no of Black fungus infections. Pain, redness around the eyes or nose, fever, headache, coughing, shortness of breath, bloody vomit and altered mental status are some of the symptoms of this disease. Experts are of the view that unsanitary conditions could increase the risk of developing infection. The pipes used for oxygen supply are contimmated, and use of industrial oxygen and dirty cylinders humidifiers are considered the cause of Mucormycosis, said Nishant Kumar, an ophthalmologist and Hinduja Hospital in Mumbai. The person with immune compromised system while using these pipes and oxygen for a lung period of time and as a result there infections get much more of an opportunity to get in.

As Covid -19 has been associated with a wide range of secondary bacterial and fungal infections, but experts says India's second COVID wave has created a perfect environment for mucormycosis. Low oxygen, diabetes, high iron level, immuno suppressions, as well as several other factors including prolonged hospitalization with mechanical ventilators creates an ideal milieu for contracting mucormycosis, researchers wrote in the Journal Diabetes and Metabolic syndrome: Clinical Research and Reviews. As a result individuals recovering from COVID-19 are at risk for mucoymycosis.

CONCLUSION

The patient's whoes immune system has been compromised when inhales Mucor spores may develop mucormycosis. This is rare, non contagions disease, but

it can be debilitating or fatal if not treated quickly. The frequency of mucormycosis infection has increased in the last decade, principally because of greater number of organ transplants. People who have received transplanted organs depend on immunosuppressant drugs to keep their bodies from rejecting the new organs, but in this state they are also predisposed to infection. People suffering from COVID-19 HIV/AIDS and other viral disease, congenital bone marrow disease, severe burns, cancer, untreated or irregularly treated diabetes have reduced immunity and are prone to developing mucormycosis. Covid - 19 patients who have received steroids are particularly at highe risk because steroids suppress the immune system.

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