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INVASIVE PULMONARY ASPERGILLOSIS (IPA) IN RELATION WITH COVID-19: A REVIEW

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ABSTRACT

Invasive Pulmonary Aspergillosis (IPA) is the infection in humans caused due to the 20 species of Aspergillus out of 200 species. In that the majorly infectious species are Aspergillus flavus, A. fumigatus, A. niger and A. terreus. In COVID-19 the patients are suffering from the IPA those are having the allergic reaction (asthma), airway disease (cystic fibrosis) or immune deficiency patients. In COVID-19 the use of corticosteroids is high that's why the patients are get immunocompromised and they are having the chances to get infected by the IPA. The patients having the IPA found in COVID-19 as an asymptomatic, mild, moderate, severe and critical infection of COVID-19. In this review we studied some reports and taken the information from the various literature. The purpose of this review to provide brief information on the Introduction, Pathophysiology, who at risk, Symptoms, Treatment for Invasive Pulmonary Aspergillosis related to the COVID-19.

KEYWORDS: Invasive Pulmonary Aspergillosis, COVID-19, Aspergillus fumigatus.

1. INTRODUCTION

The fungal disease caused by the species aspergillus called as Aspergillosis. The Aspergillus fumigatus is the fungus that causes pulmonary aspergillosis and it is saprophytic and ubiquitous airborne fungus present in soil, heat moisture and organic matters. The patients

those are suffering from the allergic reaction (asthma), airway disease (cystic fibrosis), or immune deficiency are most likely to develop aspergillosis disease.[1]

The invasive pulmonary aspergillosis is an opportunistic infection in the immunocompromised patients. The patients those have prolonged neutropenia, hematopoietic stem cell transplant recipients, solid organ transplant recipients are under the risk of IPA.[2]

2. Ipa Relation with Covid-19

The pandemic disease COVID-19 emerged from Wuhan, China, in December 2019. There are several reports with COVID-19 associated pulmonary aspergillosis (CAPA) was recorded.[3] Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes the infection of lung causing pneumonia like lower respiratory infection and Acute Respiratory Distress Syndrome (ARDS) and the patients those are suffering from the respiratory tract infections are most likely to develop the pulmonary aspergillosis.[1,4,5]

The occurrence of pulmonary aspergillosis in relation with COVID-19 was reported by several studies. In local hospital of Jiangsu Province, China the Aspergillosis co-infection with COVID-19 patients shown by Zhu et al. from January 22 to February 2, 2020, in which 23.3% (60/243) patients were found. They found with pulmonary aspergillosis mostly in relation with COVID-19 patients and they were found as asymptomatic, mild, moderate, severe and critical infection. In this report there was no detailed symptoms were described. Additionally, in Belgium 20.6% (7/34) and in Netherland 19.6% (6/31) patients requires ICU admission for co-invasive pulmonary aspergillosis among COVID-19 patients was reported by studies. In France the incidence of pulmonary aspergillosis relation with COVID-19 patients was 33.3% (9/27) shown by Alanio et al. amongst mechanically ventilated patients.[6]

3. Pathophysiology

Approximately 20 species of Aspergillus can cause the human diseases out of 200 species. A fungal spore named conidia causes a primary infection via airborne inhalation and spores stored in lower respiratory tract. Majorly infection caused by various species like Aspergillus flavus, fumigatus, Aspergillus niger and Aspergillus terreus. Some rare species such as Aspergillus calidoustus and Aspergillus nidulans. Most common cause of Aspergillosis is Aspergillus fumigatus. A. fumigatus is a less prevalent than other species in the environment, that's why relative abundance of A. fumigatus partially explains success as pathogen. Air isolation count of A. niger and A. fumigatus is 56% and 0.3% respectively. Whereas A.

fumigatus (44%) was more dominant isolate compared to A. niger (17%) patients. Lower airways and alveoli can reach by smaller size, conidia of A. fumigatus (2.0-3.5 µm) and A. terreus (2.0-2.5 µm) rather than larger conidia of A. flavus (3-6 µm) and A. niger (4-5 µm). Invasive pulmonary aspergillosis caused by A. fumigatus and A. terreus it might be explained by conidial size. A. fumigatus have ability to grow germinate in high temperature because it is more thermotolerant than other Aspergillus species. That's why it is more proliferative in host. Inhaled Aspergillus spores are firstly defenced by mucociliary apparatus, anatomical and mechanical barriers in the airways. Whereas these defensive mucociliary cells and Alveolar macrophages, the first line of innate immunity, phagocytose and kill the conidia. Pro-inflammatory response activated by defensive mechanism to recruits neutrophils to kill Aspergillus hyphae that prevent intracellular killing by alveolar macrophages.[7,8]

4. Who At Risk

The patients those are suffering from the following disease condition are having the more chances to infect by the fungus Aspergillus.[1]

- Chronic Obstructive Pulmonary Disorder
- Bronchiectasis
- Cystic fibrosis
- Immunocompromised patients
- Patients with neutropenia
- Diabetes
- Asthmatic patients

5. SYMPTOMS

The following are the few symptoms to diagnose the Invasive Pulmonary Aspergillosis:

- Fever and chills
- A cough that brings up blood (haemoptysis)
- Shortness of breath
- Chest or joint pain
- Headaches or eye symptoms
- Skin lesions

6. TREATMENT[9,10]

A. Amphotericin B

Amphotericin B is one of the choices for IPA infection in COVID-19 infection. It was extracted from Streptomyces nodous species containing seven double bonds in fungal cell wall have a one component ergosterol when amphotericin B is attaches irreversibly to ergosterol result in disruption of cell membrane integrity and it leads to death. It is mostly used by intravenous route for systemic infection.

B. Posaconazole

Posaconazole is given by in biphasic colloidal dispersion form, if it taken with food then rate of absorption increases. It inhibits the enzyme 14 a demethylase that present in the biosynthesis pathway of sterol that lead to lanosterol to ergosterol. Ergosterol present in fungal cell wall due to the inhibition ergosterol level goes down and collection of methylated toxic radical which result in disorder of fungi cell wall membrane and its growth hampering, in lot of cases cell death occur.

C. Itraconazole and Voriconazole

Itraconazole could be a potent inhibitor and a substrate of CYP3A4, Voriconazole could be a potent inhibitor of CYP3A4, a moderate inhibitor of CYP2C19. Itraconazole is potent drug and its bind with the protein and metabolized by CYP3A4, it converts in active form hydroxyitraconazole, it inhibits cyp enzyme and pgp. It is given by the two ways i.e. Parentral route and oral route, orally well absorbed in the body if taken with the food. Voriconazole is developed for oral and parentral route. It metabolized in liver by the enzyme Cytochrome. It acts as a potent inhibitor of CYP3A4 and weak inhibitor of CYP2C9 and moderate inhibitor of CYP2C19.

D. Echinocandins (Caspofungin, Micafungin)

This class of drug inhibit the synthesis of 1,3 beta glucan, that enzyme plays role on cell synthesis. It shows specific toxic activity on fungi. The lack of glucan protein synthesis in mammalian tissue makes this an attractive target for antifungal activity.

CONCLUSION

Mostly the Aspergillus fumigatus is responsible for the Invasive Pulmonary Aspergillosis infection in COVID-19. In COVID-19 the use of the corticosteroids is more that's why the person get immunocompromised and therefore, the chances to get the fungal infection are

more. The Aspergillosis infection is severe and seen as an asymptomatic sometimes. For the treatment the various drugs are used like Amphotericin B, Posaconazole, Itraconazole, Voriconazole and Echinocandins.

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