

SHORT COMMUNICATION

COVID-19 AND BLACK FUNGUS.

Gokulshankar S¹, Mohanty BK^{2*}

¹Faculty of Medicine, AIMST University, Malaysia

²Faculty of Medicine, Universiti Kuala Lumpur Royal College of Medicine Perak, Malaysia

Corresponding Author

Dr. Basanta Kumar Mohanty

UniKL Royal College of Medicine Perak, No. 3, Jalan Greentown, 30450 Ipoh, Malaysia.

Email: drbasantmohanty@gmail.com

Keywords: Mucorales, Mucormycosis, black fungus, COVID 19, SARS-CoV-2

Introduction

Opportunism in general is the practice of taking advantage of circumstances – sometimes when the opponent is weak. This opportunism is not only observed in human beings, but also in case of plethora of microorganisms that we are surrounded with externally as well as internally inside our body. These organisms take advantage of the opportunity and invade, multiply and mutate in side our body when our immune system is weak (immunosuppressed or immunocompromised) to cause life threatening diseases. Among these organisms, there are a group of fungi that do not affect healthy individuals but strike when there is an ‘opportunity’. Several predisposing conditions make a person susceptible to such opportunistic infections. Prolonged use of steroids or drugs that suppress the immune system, diseases like diabetes, cancer, and HIV are few such conditions which make a person vulnerable to such infections. The present pandemic COVID-19 caused by SARS-CoV 2 is another burning example which makes the patient’s immune system weak and crazy and the patient becomes susceptible to such opportunistic fungal infections if he is already immunocompromised.

There is a prefatory siren with the emergence of Mucormycosis¹ (caused by members of the order Mucorales) which is maiming COVID-19 patients now popularly termed as ‘**black fungus**’. Though, the term black fungus itself is a misnomer for infection caused by Mucorales, but is widely used today in newspapers, science articles and even in doctors’ circles and has become an accepted nomenclature. Media is always crazy about fancy names so ‘black fungus’ suits it perfectly with the catastrophe caused by the organism i.e. loss of eye sight to even death. The black fungus actually belongs to the group of dark pigment producing fungi (melanin or melanin-like) called the dematiaceous fungus². In case of Mucormycosis, the infected tissue blackens due to devitalized blood supply and gives this black appearance. This blackening effect has been erroneously led to the description of Mucorales as black fungus. But what draws attention is the sudden outbreak of this ‘otherwise rare’ disease Mucormycosis found to be in associated with COVID-19 patients especially the ones with underlying conditions like diabetes. The present surge of COVID-19 and emergence of this black fungus has already

created a havoc in India posing a great challenge to its otherwise overwhelmed health system and has been a notifiable disease. Malaysia being a country with significant diabetic population coupled with the current rapid increase in the nationwide COVID-19 cases need to take necessary precautions to prevent the emergence of these opportunistic infections among the vulnerable population.

Habitat and classification

Mucorales are ubiquitously present organism in the environment. It belongs to the Kingdom: Fungi, Phylum: Zygomycota, Order: Mucorales, It is commonly found as a saprophyte living in soil, plants, manure, and on dead and organic matter (rotten fruits and vegetables, etc). The spores of Mucorales are commonly prevalent in the air and could be possibly inhaled by any healthy person without any harm. But when the person has a lowered immunity, as in case of SARS-CoV-2, it can cause a life-threatening disease. The route of entry of this fungus is by inhalation of the spore, so it is advisable to keep the house mold-free. Wearing the mask can also prevent the inhalation of the spore of the fungus, but it is important that the masks are not used repeatedly and disposed of. Repeated use of masks can harbour the fungal spores. Mold and mildew thrive in a humid environment, so it is important to keep the home properly ventilated, carpets and screens dusted and kept free of humidity. Avoidance of construction sites and places that have high levels of dust pollution is mandatory.

Plausible reasons for sudden out break

- Though there are several possible reasons/hypotheses attributed for the rapid emergence of Mucormycosis in India, some points are worth consideration to make the necessary precautions to avoid such infections in Malaysia and the rest of the world.
- Prolonged use of steroids lowers the immunity and makes a person susceptible for

fungal infection. So, overuse and improper early initiation of steroids in covid treatment is not recommended. Steroids are to be used with utmost precaution and as per the guidelines. For instance, oral steroids are contraindicated with patients with normal oxygen saturation (SpO₂). Patients with mild to moderate infection and under self-quarantine should not take self-medication based on internet information without proper consultation of their physicians.

- COVID-19 patients who are recuperating and discharged from the hospitals should consult their doctors if any of the following symptoms appear – swelling around the nose or eyes, stuffy or bleeding nose, nasal blockage or coloured discharge, facial pain, pain near eyes, dental pain, loosening of teeth, blackening of the palate, etc. Patients who are on immune suppressive drugs and diabetics need to be extra cautious.
- Indiscriminate use of anti-microbials can kill the beneficial normal flora and make a person susceptible for opportunistic infection. So, self-therapy without proper medical supervision is not advisable.
- Overwhelming number of new COVID-19 cases can push the hospitals to extremities and thereby could have compromised the availability of hygienic ventilators, oxygen masks, humidifiers, etc. resulting in out breaks of Mucormycosis. Therefore, it is the responsibility of all to strictly follow the SOPs to reduce the burden on the health care system.
- The risk of Mucormycosis is significant in a population with high prevalence of diabetes and poorly controlled diabetes during SARS-CoV-2 infection. It is the responsibility of everyone to monitor the general health and wellbeing of the family members who are at high risk.
- The role zinc supplements used extensively for COVID-19 treatment needs to be studied for its co-relation to emergence of Mucormycosis. Some specialists also are of

opinion that extensive use of stream inhalation can also pave way for such opportunistic infections.

Diagnosis³

COVID-19 associated mucormycosis (CAM) is known to cause high morbidity and mortality if earlier diagnosis and management is not done.

First step is making the COVID-19 patients aware of the possible symptoms of Mucormycosis that is discussed earlier.

Suspected patients should immediately consult an ENT specialist, undergo appropriate radio-imaging study: MRI - PNS with brain contrast study for ROCM, plain CT thorax for pulmonary mucormycosis

Rhino-orbito-cerebral manifestation

Consult ENT surgeon/Ophthalmologist. A specialist is required for endoscopic collection of debrided tissue/biopsy. Usually, the collected samples are divided into two parts - one portion in sterile saline for microscopy & culture, other portion in formol saline for histopathology.

Pulmonary manifestation

- Collection of Broncho-alveolar lavage (BAL), Mini BAL, non-bronchoscopic lavage,
- Transbronchial biopsy
- CT guided biopsy from lung
- The samples need to be processed for microscopy & culture
- Chest X-ray and/ or HRCT – reverse halo sign, thick-walled cavity (need to differentiate from COVID-19 associated pulmonary aspergillosis), multiple nodules, pleural effusion
- Repeated negative galactomannan & beta-D-glucan test (for differential diagnosis from Aspergillosis).

Macroscopic and Microscopic appearance:

Colonies of Mucorales grow at room temperature (25-30°C) in Sabouraud or potato dextrose agar. The growth is so rapid that it quickly cover the surface of the agar. It has a fluffy or cotton candy

appearance. From the front, the colour of the colony is initially white and becomes grayish to brown in time (due to the development of sporangia).

Mucor is characterized by round, usually cylindrical or pear-shaped sporangia. The sporangia of *Mucor* consist of well-developed, subtending columellae. The hyphae may be simple or branched in appearance.

Treatment

Mucormycosis is a medical emergency and hence early diagnosis is the key in the management of the disease. Factors which are critical for eradication of mucormycosis are: early and rapid diagnosis, elimination of underlying predisposing conditions like immunosuppressive drugs, hyperglycaemia, metabolic acidosis, neutropenia and use of desferrioxamine, appropriate surgical debridement of infected tissue and appropriate antifungal therapy.^{4,5,6}

Due to difficulties in establishing an early definitive diagnosis, many patients will be treated empirically because of the presence of risk factors. Antifungal therapy: Intravenous amphotericin B is the drug of choice for initial treatment. The lipid formulations are preferred. The usual starting dose of liposomal amphotericin B is 5mg/kg/day. Some clinicians may go up to 10mg/kg/day. The treatment with amphotericin B should be continued for many weeks till the patient has shown signs of improvement. Then step down therapy can be done by using oral posaconazole or isavuconazole. The patients who do not respond to or cannot tolerate amphotericin B, the IV preparation of posaconazole or isavuconazole can be used as salvage therapy⁵.

The other agents which can be used as an adjunctive therapy are iron chelators like deferasirox and deferiprone. These agents do not act as siderophores and do not increase the risk of mucormycosis unlike that of deferoxamine, which can increase the risk of mucormycosis by enhancing growth and pathogenicity. Deferoxamine is a siderophore and increases iron

uptake by the fungus, which stimulates fungal growth leading to tissue invasion⁵.

Surgery: Aggressive surgical debridement of the affected tissues should be considered as soon as the diagnosis of mucormycosis is established.

Conclusion

Though the exact causes of the sudden outbreak of Mucormycosis is still a mystery. It is believed SARS CoV 2 virus can damage airway tissue and blood vessels, which could increase susceptibility of the victims to fungal infection. Further, Ferritin level goes up during COVID-19 infection and the extra iron available favours the growth of the fungus.^[6]

The only consolation amidst the major threat is the fact that the fungus is NOT contagious.

The spectrum of fungal infections that is seen currently is just a 'tip of the ice-berg'. In the present pandemic era, if the proper precautions and management of fungal infections are not done, there may be phenomenal increase of other fungal diseases like Aspergillosis^[7] and invasive Candidiasis just like Mucormycosis. It should be always remembered that in the epoch of immune suppression – Any fungus from A- Z (Aspergillus to Zycomycetes), can emerge into an opportunistic pathogen!

References

1. Revannavar SM, Supriya PS, Samaga L, Vineeth V K. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? *BMJ Case Reports CP*. 2021;14: e241663.
2. Rippon JW. *Medical mycology: The pathogenic fungi and the pathogenic Actinomycetes*. W.B. Saunders, Philadelphia. 1988.
3. Cornely OA, Alastruey-Izquierdo A, Arenz D, Chen SCA, Dannaoui E, Hochhegger B, et al. Mucormycosis ECMM MSG Global Guideline Writing Group. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. *Lancet Infect Dis*. 2019 ;19(12):405-421.
4. Garg D, Muthu V, Sehgal IS, Ramachandran R, Kaur H, Bhalla A, et al. Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature. *Mycopathologia*. 2021;186(2):289-298.
5. McCarthy M, Rosengart A, Schuetz AN, Kontoyiannis DP, Walsh TJ. *N Engl J Med*. 2014; 371(2):150-60.
6. Spellberg B, Edwards J Jr, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation, and management. *Clin Microbiol Rev*. 2005 ;18(3):556-69.
7. Arastehfar A, Carvalho A, van de Veerdonk FL, Jenks JD, Koehler P, Krause R, et al. COVID-19 Associated Pulmonary Aspergillosis (CAPA)-From Immunology to Treatment. *J Fungi (Basel)*. 2020; 24;6(2):91.