CASE REPORT

Black fungus: A rising consternation among COVID patients presenting to a tertiary care hospital in Islamabad-Pakistan Institute of Medical Sciences

Manza Maqsood Khan, Syed Ansab Hasnain, Altaf Hussain, Malik Jawad Faisal

Abstract

For almost one and a half year the world is facing the pandemic called COVID-19, which is an acute respiratory distress syndrome caused by coronavirus 2 (SARS-CoV2). This disease has already engulfed many lives and has not been tamed so far. Physicians all over the world still, trying to get a hold of this global health issue, are faced with another life-threatening challenge associated with COVID-19, called black fungus-Mucormycosis. Within a span of few weeks, we have encountered three cases of black fungus in our institute which has stirred a serious concern among physicians in Pakistan.

Keywords: Mucormycosis, Black fungus, COVID-19, Pandemic.

DOI: https://doi.org/10.47391/JPMA.4225

Introduction

For almost one-and-a-half-years, the world is facing the dreadful pandemic called Corona Virus Disease-19 (COVID-19). It is caused by an acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2). It has been creating havoc all over the globe, taking almost 3.6 million lives according to WHO statistics.[1] In Pakistan there have been 928,588 confirmed cases with 81,540 in Federal Capital (Islamabad) according to Ministry of Health, government of Pakistan.[2] Fortunately, due to vigorous measures taken by the government, the mortality in Pakistan has been controlled in comparison to our neighbouring countries like India and Iran.

The world had not recovered from this deadly virus when the healthcare professionals met with another challenge — a fungal infection in COVID-19 recovered patients. With diffuse lower respiratory tract infection causing alveolar destruction[3], patients inflicted with the disease also present with decreased immune cells that cause immunosuppression.[4] The fungal infections encountered in COVID-19 patients are Mucor, Aspergillus and Candida.[5,6] In Pakistan, very few cases of Mucormycosis have been reported in recovered COVID-19 patients. Mucormycosis is also known as "Black fungus" which belongs to the family of genera Mucorales. It is an angio-invasive infection that mostly involves nose, eye and brain, often seen in diabetic and immunocompromised patients. These patients present with orbital swelling, blurring of vision/double vision, breathing difficulty and blackish discoloration of oral or nasal mucosa. The infection is aggressive, significantly increasing the mortality and morbidity of COVID-19 patients. We encountered three such cases in April 2021, within a span of three weeks.

Department of Head and Neck, Pakistan Institute of Medical Sciences, Islamabad, Pakistan.

Correspondence: Manza Maqsood Khan. Email: manzakhan93@yahoo.com

Case Studies

Case 1: A 48-years old diabetic female, mother of three, presented to us in the ENT outpatient department of Pakistan Institute of Medical Sciences, Islamabad, with right orbital swelling, facial swelling and blurring of vision, after she was recovering from COVID-19 contracted two weeks back. She had recently attended a funeral at her hometown and thereafter started having respiratory symptoms, for which she was taken to a local hospital where she tested positive for COVID-19. She was hospitalised for two weeks as she was unable to maintain oxygen saturation. During her hospital course, supportive treatment was given which included IV fluids, anti-pyretics, hypoglycaemics and IV steroids (0.5-1mg/kg/day of methyl prednisolone). As her oxygen saturation remained 92% with less than 5liter of O_2 and her lab parameters including CRP, ESR, Serum Ferritin and D-dimers never exceeded the cut off value, so tocilizumab was not prescribed. She recovered uneventfully from the infection and was discharged. Inspite of general weakness she remained well for a week, but soon she started developing orbital swelling, accompanied by deterioration of vision and headache which was located mainly over the forehead and infra-orbital region. Her complete workup including haematologic investigation and cross-sectional imaging was done. CT scan showed right sided proptosis and demonstration of right abnormal soft tissue fullness and stranding in pre-septal space of right orbit, mild oedema of extra-ocular muscles and involvement of paranasal sinuses with erosion of medial and lateral walls of maxillary sinus and lamina papyracea. The history, examination and radiological findings lead to a provisional diagnosis of an extensive

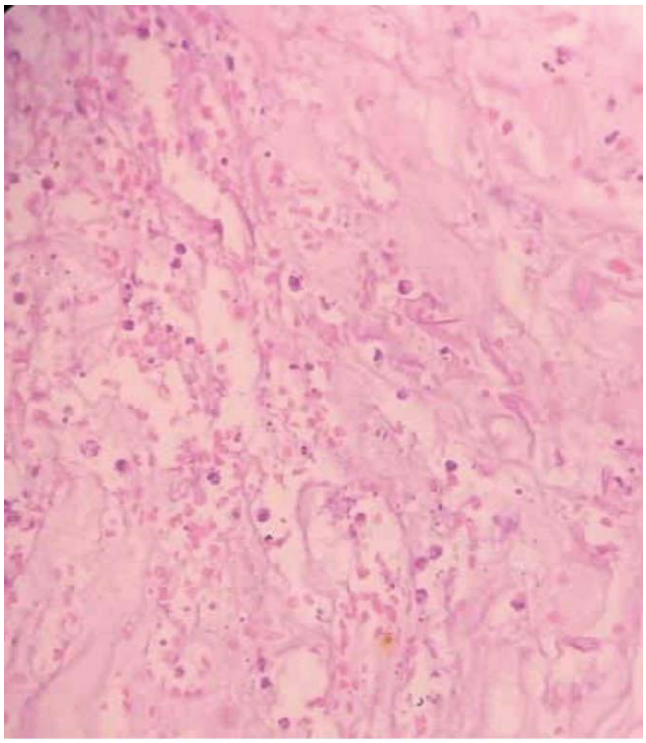

Figure-1: Fungal Hyphae seen in H&E staining.

fungal disease. After anaesthesia and medical assessment, the patient was subjected to endoscopic clearance of the lesion accompanied with enucleation of the right eye. The tissue retrieved was sent for histopathological examination. Microscopic examination showed broad based aseptate hyphae, favouring mucormycosis (Figure-1). After complete treatment which took 6 weeks including surgery, administration of IV amphotericin B (with strictly monitored renal function tests) and prosthetic rehabilitation, the patient was discharged and is on regular follow-up with complete otolaryngological examination and cross-sectional imaging as required.

Case 2: A similar scenario was encountered with a 55-years old female suffering from chronic kidney disease with poorly controlled diabetes mellitus. She was admitted to the Nephrology department for her renal disease where she contracted the infection. She was shifted to the COVID isolation unit where she received tocilizumab in a dose of 6mg/kg IV as she had sustained respiratory rate of greater than 30 breaths per minute and had chronic kidney disease. She also received other supportive care including IV fluids, anti-pyretic with strict renal function monitoring and frequent nephrological consultations. She remained admitted for three weeks and was then sent home. After 5 days of discharge, she developed nasal obstruction for which she visited the ENT clinic. On examination there was black discolouration of

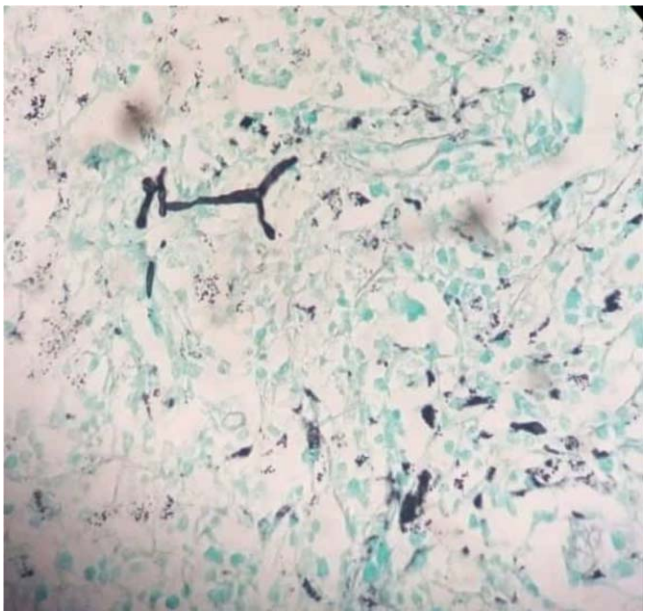

Figure-2: Methenamine silver-stained smear showing broad, irregular, and nonseptate hyphae of mucormycosis.

nasal mucosa more over the right lateral wall. Scrapings from the nasal cavity were taken and sent for fungal culture sensitivity and histopathological examination. Microscopic examination revealed broad based hyphae with few fruiting head which was in coherence with mucormycosis (Figure-2). The patient was counselled about the nature of the disease and was offered surgery, but she refused due to domestic issues. However, she was instructed to return to the ENT clinic as soon as possible, as ultimately, she would need surgical intervention.

Case 3: The third case was an eighteen years old female diagnosed with aplastic anaemia. She was admitted to the medical ward of Pakistan Institute of Medical Sciences with right eye swelling and blackish discoloration of the nasal bridge. On inquiring about any COVID-19 infection she revealed that she was diagnosed with COVID-19 three weeks back, but she was not hospitalised. The only symptom she had was fever for which she kept taking over the counter anti-pyretics. On examination, the nasal cavity was full of black slough and crusts especially along the inferior turbinates. CT scan was done which showed extensive disease involving right eye and all the sinuses except the sphenoids. There was also non-enhancement of right cavernous sinus noted with slight prominence of right superior ophthalmic vein suggesting cavernous sinuses thrombosis. Microscopic examination of scrapings from the nose showed broad based hyphae with irregular, thin, non-parallel cell wall lacking septae favouring mucormycosis as shown in Figure-3. Extensive debridement was needed for this patient but could not be

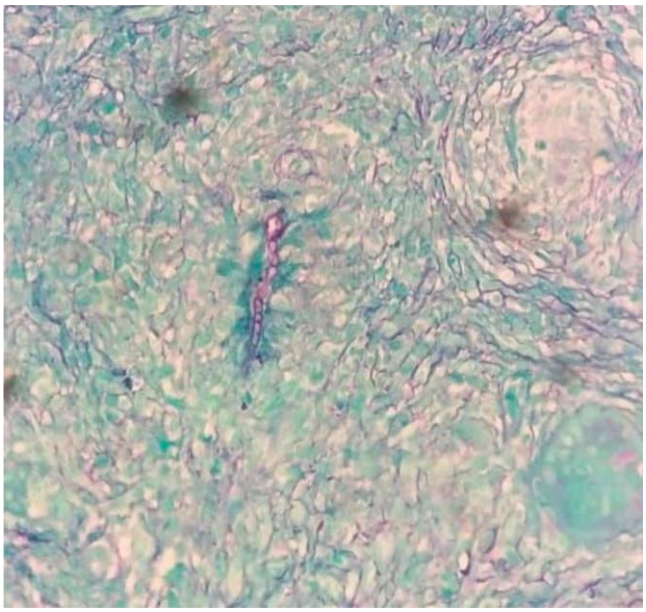

Figure-3: Periodic Acid Schiff (PAS) stain demarcating fungal element.

done as the patient was not fit for General Anaesthesia. Currently the patient is on IV antifungals and being optimised for General Anaesthesia.

Discussion

Mucormycosis is an aggressive disease and is mostly associated with high morbidity and mortality due to which it often becomes a challenge for physicians to deal with.[7] It is most commonly found in critically ill patients with underlying morbidities as uncontrolled diabetes mellitus.[8,9] The golden rule in the management of this disease is early diagnosis, aggressive surgical clearance, addressing the underlying chronic disease process and intravenous antifungals.[10]

Mucormycosis following COVID-19 has been mostly seen in India, where the health-care system has been unable to cope with the onslaught.[11] In addition to the overwhelming and uncontrollable second wave of COVID-19 in India, the country is also dealing with an outbreak of mucormycosis.[12] With an overall case fatality rate of 50%, mucormycosis has emerged as a public health concern especially among COVID-19 patients[13] and several hypotheses have been proposed regarding the possible aetiology of the disease. COVID-19 is known to adversely affect the immunity of the patients and also increases the production of cytokines causing inflammation.[14] Decreased immunity may lead to mucormycosis, as the condition is favourable for opportunistic fungi. The other reason might be the blind use of corticosteroids in COVID-19 patients as this not only affects blood sugar level but also decreases the immunity and makes them more susceptible to mucormycosis.[15] Over the past few weeks, we have seen three cases of black fungus in quick succession in our tertiary care setup which raised some serious concerns. All the above-mentioned cases were seen in patients who recently recovered from the COVID-19 infection and the symptoms appeared within two weeks of recovery. Two of the above-mentioned cases were of poorly controlled diabetes mellitus which made them prone to fungal infection and supposedly the main reasons behind them was the use of corticosteroids during their hospital stay that caused increased blood glucose level and acidic pH, leading to defective motility and killing of fungi by neutrophils.[12] Our third patient in the series was a known case of aplastic anaemia. A possible explanation of fungal infection in this patient most certainly is profound neutropenia which weakens body's immune system. Neutropenia may be present primarily due to haematologic disorder like leukaemias or secondarily due to myeloablative treatment used for underlying haematological malignancy.[16] There are many studies that report increased incidence of fungal infections in haematological disorders.[17,18]

Conclusion

COVID-19 not only decreases the defence system of the body by increasing the inflammatory cytokines but also weakens the cell mediated immune system by decreasing CD4 and CD8 cells thus making patients more susceptible to fungal infection. Moreover, immunocompromised state of the patients like prolonged neutropenia, increased use of steroids and poor glycaemic control play additional role in pathophysiology of the disease. Due to relentless nature of this fungal infection, it is very important to diagnose it early and use aggressive approach in the management from the very beginning.

Consent Form: All the three patients consented to have their reports published for enhancing science.

Disclaimer: None to declare.

Conflict of Interest: One of the co-authors of this manuscript also signed the IRB. There is no conflict of interest in it.

Funding Sources: None to declare.

References

1. WHO Coronavirus (COVID-19) Dashboard. [Online] [Cited 2021 May 11]. Available from: URL: http://www.covid19.who.int/
2. COVID-19 Dashboard. [Online] [Cited 2021 March 27]. Available from: URL: http://www.covid.gov.pk/
3. Tay MZ, Poh CM, Renia L, MacAry PA , Ng LFP. The trinity of COVID-19: immunity, inflammation and intervention. Nat Rev Immunol. 2020; 20:363-74.

4. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. J Infect. 2020; 80:388-93.
5. Sahoo JP, Mishra AP, Pradhan P, Samal KC. Misfortunes Never Come Alone- The New "Black Fungus" Accompanying COVID-19 Wave. Biotica Res Today. 2021; 3:318-20.
6. Song G, Liang G, Liu W. Fungal Co-infection Associated with Global COVID-19 Pandemic: A Clinical and Diagnostic Perspective from China. Mycopathologia. 2020; 185:599-606.
7. Cornely OA, Izquierdo AA, Arenz D, Chen SCA, Dannaoui E , Hochhegger B, et al. 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. 2019; 19:e405-21.
8. Pillsbury HC, Fisher ND. Rhinocerebral Mucormycosis. Arch Otolaryngol. 1977; 103:600-4.
9. Lehrer RI, Howard DH, Sypherd PS, Edwards JE, Segal GP. Mucormycosis. Ann Int Med. 1980; 93:93-108.
10. Spellberg B, Edwards J Jr, Ibrahim A. Novel perspectives on mucormycosis: pathophysiology, presentation and management. Clin Microbiol Rev. 2005; 18: 556-69.
11. Dyer O. Covid-19: India sees record deaths as "black fungus" spreads fear. BMJ. 2021; 373: n128.
12. Bhatia M. The rise of mucormycosis in COVID-19 patients in India. Expert Review of Anti-infective Therapy. 2021;19:12-25.
13. WHO [Online] 2021 [Cited 2021 August 21]. Available from: URL: http://www.who.int/india/emergencies/coronavirus-disease-(covid-19)/mucormycosis
14. Yazdanpanah F, Hamblin MR, Rezaei N. The immune system and COVID-19: Friend or Foe? Life Sci. 2020; 256: 117900.
15. Alekseyev K, Didenko L, Chaudhry B. Rhinocerebral Mucormycosis and COVID-19 Pneumonia. J Med Cases. 2021; 12:85-9.
16. Pagano L, Offidani M, Fianchi L, Nosari A, Candoni A, Picardi M, et al. Mucormycosis in hematologic patients. Haematologica. 2004; 89:207-14.
17. Tedder M, Soratt JA, Anstadt MP, Hedge SS, Lowe JE. Pulmonary mucormycosis: results of medical and surgical therapy. Ann thorac Surg. 1994; 57:1044-50.
18. Kontoyiannis DP, Wessel VC, Bodey GP, Rolston KV. Zygoycosis in the 1990s in a tertiary-care cancer center. Clin Infect Dis. 2000; 30:851-60.