Case Report: Splenic Mucormycosis; A Post-Covid Sequelae

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Abstract

Introduction: Mucormycosis is an invasive disease associated with high mortality ranging from 25-62%. There is an increase in the incidence of mucormycosis in post COVID-19 infection patients.

Case presentation: A 55 year old male presented to the emergency department with complain of pain abdomen and with a past medical history of renal transplantation and recent COVID-19 infection. On CT abdomen evaluation he was found to have hypodense spleen suggestive of splenic abscess.

Investigations and Treatment: Splenectomy was done, which on microbiological examination revealed mucormycosis. The patient was treated with amphotericin B for 3 weeks followed by posaconazole for another 2 weeks.

Discussion: Mucormycosis, although a rare infection, has been classically linked to organ transplantation which can also be considered as a possible reason for immunosuppression in this case. Transplant physicians must be aware that patients with COVID-19 are at risk of developing unusual opportunistic infections.

Introduction

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, has heavily hit all the countries in the world.[1] The disease has imposed one of the major challenge in management due to significant rate of intensive care unit admissions.[2] Bacterial and fungal infections are now well-known complications of COVID-19.[3] Although the risk of fungal infection with candida, aspergillus and pneumocystitis jiroveci in setting of COVID-19 is well recognized, the unexplored emergence of mucormycosis in patients with COVID-19 is a new challenge.[4]

Mucormycosis is an angioinvasive infection caused by a group of saprophytic aerobic fungi called mucormycetes. The fungi belongs to the subphylum *Mucoromycotina* in the order Mucorales.[5]

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The major risk factors predisposing individuals to the disease are uncontrolled diabetes mellitus or acidic metabolic disorders, solid organ transplantation, prolonged or profound neutropenia, hematologic malignancies, prolonged use of corticosteroids and hemodialysis. The risk is high for people living with HIV, and those using immunomodulating drugs, including the use of anti-fungal voriconazole.[6]

Rhizopus oryzae is the most common organism accounting for approximately 70% of all cases of mucormycosis.[7] Rhinocerebral and pulmonary mucormycosis are the most common forms with cutaneous, gastrointestinal and dissemated forms being less common. Isolated splenic mucormycosis has been very rarely reported so far.[8]

All Mucorales grow rapidly on most fungal media such as Sabouraud dextrose agar (SDA) incubated at 25–30 °C. Isolation of *Mucorales* from a sterile site or repeated positive cultures of the fungi from a non-sterile site are considered significant in a high-risk patient with predisposing factors for acquisition of mucormycosis.[9] The disease requires prompt diagnosis and early treatment which usually consist of liposomal amphotericin B and surgery.[6]

Case presentation

On November 2021, a 55 year old male patient with known history of renal transplantation 2 months back and post-covid status, presented to the emergency department of Nepal Mediciti Hospital, Saibu, Lalitpur, with a complaint of pain abdomen for over 20 days. The pain was left sided over left upper and lower quadrant. On examination, the patient was conscious oriented alert, not on respiratory distress and pallor and cyanosis were not present. Abdomen was soft, non-tender on palpation. There was no organomegaly. Other systemic examinations were unremarkable.

Investigations

Investigations revealed haemoglobin of 9.3 gm/dL, total leucocyte count of 13900 cells/mm^3 with the absolute neutrophil count being 84.30%, RBC 2.85 million/mm^3 and platelet 360000 cells/mm^3. HRCT of lungs revealed patchy consolidation in left upper, right middle and lower lobes. Minimal ground glass opacity was observed in right upper and middle lobes with moderate left pleural effusion with fissural extension. CT abdomen showed hypodense lesion in spleen abutting the posterior abdominal wall with loss of fat plane. Diagnosis of splenic abscess was established and he was planned for splenectomy.

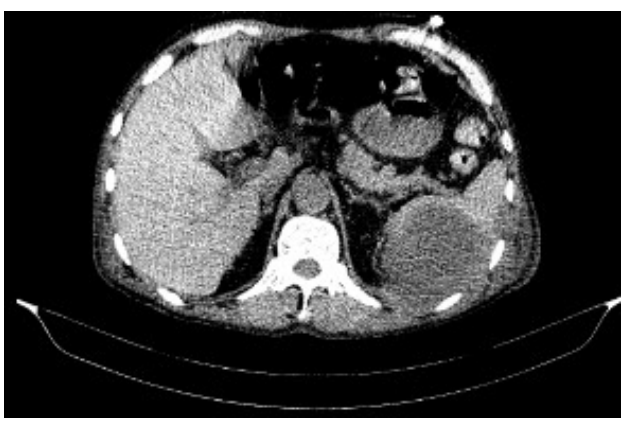

Fig.1; CT scan- transverse view of abdominal cavity

Treatment

Splenectomy was done. Spleen was inflamed, with adhesion at hilum and filled with 100 mL dirty colored fluid. Diaphragm was intact with no obvious connection with the pus cavity.

Culture from the splenic pus collection was sent for microbiological analysis. For a rapid presumptive diagnosis, direct examination of the sample was done via KOH wet mount which revealed the presence of broad, aseptate, filamentous, ribbon-like hyphae with wide-angle branching.

The sample was then inoculated in blood agar, chocolate agar and MacConkey agar and incubated at 37^{0}C for 24-48 hours to examine the presence of any bacterial growth, and in SDA and incubated in BOD at 25^{0}C for fungal growth analysis. Cottony, white mycelia with grey to black top were observed in 24 hours of incubation in SDA and blood agar after 24 hours. Lactophenol cotton blue mount (LPCB) was prepared from the colonies which showed broad, hyaline, aseptate hyphae with presence of rhizoid, stolons and both solitary and tufted ovoid sporangiophores suggesting the growth of *Rhizopus oryzae* (Fig.3).

Amphotericin B was started for 3 weeks followed by posaconazole for another 2 weeks.

Fig.2; Broad, non-septate, ribbon-like hyphae in KOH wet mount

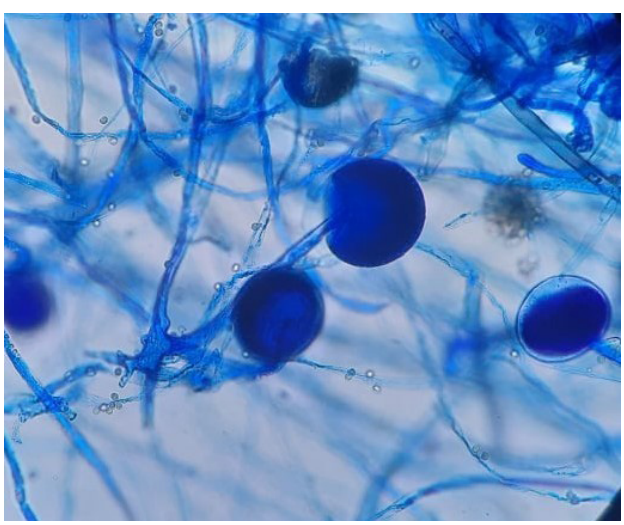

Fig.3; LPCB mount showing branched sporangiophores with sporangium and rhizoid

Outcome and follow up

Patient was followed up on 4th week. On follow up, recollection of fluid was observed in the peritoneal cavity via ultrasound. The fluid was sent for microbiological analysis which did not reveal any fungal growth. However, due to angioinvasive nature and possibility of recurrence of *Mucorales*, patient was further advised for 1 week of amphotericin B. On further follow up, the recollected fluid was still persistent and showed growth of *Rhizopus oryzae*. The patient is currently under oral posaconazole.

Discussion

Several immucompromised conditions contribute to the emergence of mucormycosis after Covid-19 out of which chronic immunosuppression and uncontrolled diabetes are most commonly discussed.[10,11] Although a rare infection, the disease has been classically linked to solid organ transplantation which can also be considered as a possible reason for immunosuppression in this case.

Mucormycosis can involve respiratory tract ranging from nasal cavity to lungs, orbit, gartrointestinal tract, heart, kidney, spleen, joint and bones and even mediastinum with rhinocerebral and pulmonary forms being most common.[8] Rhinocerebral mucormycosis has been frequently found to be associated with uncontrolled diabetes whereas pulmonary involvement is often observed in patients having neutropenia, bone marrow and organ transplant, and hematological malignancies, while GIT gets involved more in malnourished individuals.[10] Post covid mucormycosis in patients with chronic renal impairment was reported by Roushdy *et al*[12] in Egypt and Arana *et al*[13] in Spain. Cases of splenic mucormycosis were reported by Meshram *et al*[11] among two renal transplant recipients who had acquired severe COVID-19 infection in India.

The diagnosis is made through the demonstration and microscopic analysis of the causative agent in the smear of aspirated fluid or biopsied sample of the involved organ. Currently, liposomal amphotericin B, posaconazole, isavuconazole, and itraconazole, are the main therapeutic options available. Aggressive treatment involving use of amphotericin B and surgical debridement or removal of the involved organs or tissues is the mainstay of treatment.[14,15]

Mucromycosis has high mortality rate with survival rate only up to 36%.[14] With ROCM (rhino-orbital-cerebral mucormycosis) remaining the most common form during this pandemic, isolated splenic mucormycosis is an unsual occurrence. This, therefore, emphasizes the need of meticulous approach in screening mucormycosis in COVID-19 patients with high risk factors including solid organ transplant. The lack of clinical suspicion and the difficulty in isolating the fungus could lead to a delay in diagnosis and treatment initiation. A multidisciplinary approach to transplant patients with post–COVID-19 sequelae is required to avoid any undesirable consequences.

List of Abbreviations

COVID-19	Coronavirus Disease 2019
HIV	Human Immunodeficiency Virus
SDA	Sabauraud's Dextrose Agar
BOD	Biological Oxygen Demand
LPCB	Lactophenol Cotton Blue
GIT	Gastrointestinal Tract
ROCM	Rhino-orbital-cerebral mucormycosis

References

1. Bardi T, Pintado V, Gomez-Rojo M, Escudero-Sanchez R, Azzam Lopez A, Diez-Remesal Y, et al. Nosocomial infections associated to COVID-19 in the intensive care unit: clinical characteristics and outcome. *Eur J Clin Microbiol Infect Dis.* 2021; 40: 495–502.
2. Song G, Liang G, Liu W. Fungal Co-infections Associated with Global COVID-19 Pandemic: A Clinical and Diagnostic Perspective from China. *Mycopathologia*. 2020; 31: 1–8.
3. Romereo IF, Bastian Mr, Pollan BP, Maseda E, Rodrigeuz JC, SARS-CoV-2 Working Group. Isolation of Aspergillus spp. in respiratory samples of patients with COVID-19 in a Spanish Tertiary Care. *Mycoses*. 2020; 10.1111/myc.13155.
4. Kumari A, Rao NP, Patnaik U, Malik V, Tevatia MS, Thakur S, et al. Management outcomes of mucormycosis in COVID-19 patients: A preliminary report from a tertiary care hospital. *Med J Armed Forces India*. 2021; 77: S289–95.
5. Alqhamdi S, Idress B, Alharbi A, Aljurais N. Case report: Disseminated pulmonary mucormycosis involving spleen in diabetic patient with aggressive surgical approach. *Int J Surg Case Rep.* 2019; 54: 42-6.
6. World Health Organization. Coronavirus Disease (COVID-19)/ Mucormycosis. Available from https://www.who.int/india/emergencies/coronavirus-disease-(covid-19)/mucormycosis
7. Ibrahim AS, Spellberg B, Walsh TJ, Kontoyiannis DP. Pathogenesis of Mucormycosis. *Clin Infect Dis.* 2012; 54: S16-22.
8. Sharma SK, Balasubramanian P, Radotra B, Singhal M. Isolated splenic mucormycosis in a case of aplastic anaemia. *BMJ Case Reports.* 2018; bcr-2017-223243.
9. Skiada A, Lass-Floerl C, Klimko N, Ibrahim A, Roilides E, Petrikkos G. Challenges in the diagnosis and treatment of mucormycosis. *Medical Mycology.* 2018; 56: S93–101.
10. Meshram HS, Kumar D, Kute VB. Rare and Unusual Follow-up Sequelae of Coronavirus Disease 2019: Splenic Mucormycosis in a Renal Transplant Recipient. *Transplant Proc.* 2021; 000: 1-3.
11. Meshram HS, Kute VB, Chauhan S, Desai S. Mucormycosis in post-COVID-19 renal transplant patients: A lethal complication in follow-up. *Transplant Infectious Disease.* 2021; 23: e13663.
12. Roushdy T, Hamid E. A case series of post COVID-19 mucormycosis—a neurological prospective. *Egypt J Neurol Psychiatr Neurosurg.* 2021; 57: 100.
13. Arana C, Cuevas Ramírez RE, Xipell M, Casals J, Moreno A, Herrera S, et al. Mucormycosis associated with COVID-19 in two kidney transplant patients. *Transpl Infect Dis.* 2021; 13: e13652.
14. Gupta V, Singh SK, Kakkar N, Jain S, Kalra N, Sakia UN. Splenic and renal mucormycosis in a healthy host: successful management by aggressive treatment. *Top Gastroenterol.* 2010; 31: 57-8.
15. Cornely OA, Alastruey-Izquierdo A, 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. *Lancet Infect Dis.* 2019; 19: e405–21.