



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the Editor

Post COVID-19 mucormycosis in liver transplant recipients-Walking on a tight rope



ARTICLE INFO

Article history:

Available online 27 July 2021

Keywords:

Mucormycosis
Liver transplant
COVID-19

As India is recovering from second wave of SARS-CoV-2 pandemic, it is overwhelmed by the large number of mucormycosis cases in patients with COVID-19. Mucormycosis is a fatal invasive fungal infection commonly affecting immunocompromized host. It is caused by mold fungi belonging to order Mucorales. The *Rhizopus Oryzae* being the most common which is responsible for 60% of mucormycosis cases in humans [1,2]. Here we are sharing a case of mucormycosis infection in living donor related transplant recipient recovering from COVID-19.

A 47-year old liver transplant recipient female with type 2 diabetes mellitus, who underwent live donor related liver transplant 5 months before for non-alcoholic steatohepatitis related liver cirrhosis. In post-operative period she had acute cellular rejection which was managed with IV steroid pulse therapy. She also had cytomegalovirus viremia in post-transplant period and received ganciclovir. She developed fever and cough along with shortness of breath 4 weeks before. Her nasal and throat swab were taken which was positive for SARS-CoV-2. She was hospitalized in view of post liver transplant status and comorbidities. She also developed COVID-19 related pneumonia during hospitalization and received ICU care for few days. Her baseline immunosuppressive medications (Tacrolimus and Mycophenolate mofetil and wysolone) were stopped and intravenous methylprednisolone was started. She did not receive any specific antiviral therapy for SARS-CoV-2. During course of illness her bilirubin, AST and ALT started to rise. Possibility of drug induced hepatotoxicity was ruled out and methylprednisolone dose was increased due to possibility of rejection. After 2 weeks she started to complain of headache and nasal congestion. On examination there was perinasal swelling, erythema and tenderness. Contrast enhanced CT scan was suggestive of pansinusitis and orbital cellulitis. A diagnosis of mucormycosis was made and liposomal amphotericin was started. Her bilirubin progressively increased along with serum alkaline phosphatase, AST and ALT. Tacrolimus and mycophenolate were withhold in view of newly diagnosed mucormycosis. Her symptoms progressed and she also developed proptosis and blurred vision in right eye. In view of progressive rhino cerebral mucormycosis

Posaconazole was added and liposomal amphotericin B was continued. She was taken for urgent surgical debridement and right sided sinus cavity debridement, partial maxillectomy and right eye exenteration was done. Histopathological examination showed vasoinvasive and tissue invasive broad aseptate poorly branching hyphal forms suggestive of mucormycosis. Her condition didn't improve even after surgery and she succumbed on post-operative day 4.

Mucormycosis incidence has grown in transplant recipient population in past few decades. Mucormycosis is responsible for 2–8% cases of invasive fungal infection in this population, and prevalence varies according to the geographical area [3]. Dramatic upsurge of mucormycosis cases have been seen in India and other part of world during COVID-19 pandemic [2,4]. Diabetes mellitus (DM2), renal failure, and high dose steroids are the known risk factors for mucormycosis. Irrational use of steroids and high prevalence of DM2 might be reason of high number of mucormycosis cases being reported in India. Fatality in mucormycosis reach as up to 70% [5]. Early diagnosis, timely antifungal therapy and surgical debridement are key to prevent mortality. Antifungal therapy like amphotericin B or Posaconazole should be started without any delay. Management of mucormycosis in patients on immunosuppressive medications pose a difficult situation. While immunosuppressive medications increase the risk of uncontrolled fungal infection, withholding it may lead to rejection and graft loss as was seen in our case. Some studies recommend stopping the immunosuppression, while on the contrary one study showed that calcineurin inhibitors decrease the risk of mucormycosis [6,7]. Steroids are the mainstay of treatment in patients with severe COVID-19. Development of mucormycosis in transplant recipient with COVID-19 poses a management crisis and there are no clear recommendations for this subgroup of patients. There is high mortality despite the use of antifungals and surgical debridement as seen in our case [8]. Hence, formulation of treatment guideline for the subset of immunocompromised COVID-19 patients with mucormycosis is the need of hour.

<https://doi.org/10.1016/j.liver.2021.100033>

2666-9676/© 2021 The Author(s). Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Financial support

No grant or financial support was taken for this research.

Declaration of Competing Interest

All authors declare no conflicts of interest.

CRedit authorship contribution statement

Shekhar Singh Jadaun: Writing – original draft. **Sanjiv Saigal:** Funding acquisition, Writing – original draft. **Shweta A. Singh:** Writing – original draft. **Shaleen Agarwal:** Writing – original draft. **Subhash Gupta:** Writing – original draft.

Disclosure

None of the authors has any financial, professional or personal conflicts that are relevant to the manuscript.

References

- [1] Eucker J, Sezer O, Graf B, Possinger K. Mucormycoses. *Mycoses* 2001;44(7–8):253–60.
- [2] Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. *Diabetes Metab Syndr* 2021;15(4):102146.
- [3] Lantermier F, Sun HY, Ribaud P, Singh N, Kontoyiannis DP, Lortholary O. Mucormycosis in organ and stem cell transplant recipients. *Clin Infect Dis* 2012;54(11):1–8 Jun 1.
- [4] S. Mehta, A. Pandey Rhino-orbital mucormycosis associated with COVID-19. *Cureus*. 12(9):e10726.
- [5] Saeed N, Alsibae M, Tasleem S. Immunosuppression after liver transplantation in the face of rhino-orbito-cerebral mucormycosis: a treatment dilemma: 2306. *Off J Am Coll Gastroenterol ACG* 2017;112:S1261. Oct.
- [6] Almyroudis NG, Sutton DA, Linden P, Rinaldi MG, Fung J, Kusne S. Zygomycosis in solid organ transplant recipients in a tertiary transplant center and review of the literature. *Am J Transplant* 2006;6(10):2365–74.
- [7] Singh N, Aguado JM, Bonatti H, Forrest G, Gupta KL, Safdar N, et al. Zygomycosis in solid organ transplant recipients: a prospective, matched case-control study to assess risks for disease and outcome. *J Infect Dis* 2009;200(6):1002–11 Sep 15.
- [8] Meshram HS, Kute VB, Chauhan S, Desai S. Mucormycosis in post-COVID-19 renal transplant patients: a lethal complication in follow-up. *Transpl Infect Dis* 2021 [Internet] Jun 16 [cited 2021 Jul 14]; Available from: doi: 10.1111/tid.13663 <https://onlinelibrary.wiley.com/doi/10.1111/tid.13663>

Shekhar Singh Jadaun
Sanjiv Saigal*
Shweta A. Singh
Shaleen Agarwal
Sanjay Sachdeva
Subhash Gupta

Max Centre for Liver and Biliary Sciences, Max Super Specialty Hospital,
1 Press Enclave Road, Saket, Delhi 110017, India
Department of ENT, Max Super Specialty Hospital, Saket, Delhi, India

*Corresponding author.

E-mail addresses: drsanjivsaigal49@gmail.com (S. Saigal), sanjay.sachdeva@maxhealthcare.com (S. Sachdeva).

Received 23 July 2021

Accepted 24 July 2021

Available online 27 July 2021