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Case Series

Interesting presentations of mucormycosis in post-COVID patients

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ABSTRACT

Most documented cases of mucormycosis have been reported in patients with uncontrolled diabetes mellitus, neutropenia, or treatment with corticosteroids**.** Recently, with the second wave of COVID-19, the Indian subcontinent has witnessed a dramatic rise in mucormycosis infection in patients recovered from COVID-19. This association has been documented in various case reports/case series and institutional studies, and the mortality associated with this fungal infection is emerging as a cause of concern. Pulmonary mucormycosis is the second most common form after rhino-orbito-cerebral mucormycosis (ROCM), but most cases are diagnosed in autopsy specimens. Cutaneous, Gastro-intestinal and disseminated forms are relatively rare. This cases series comprises of 4 cases of mucormycosis in post-COVID patients with interesting presentations. We report two cases of combined pulmonary aspergillosis and pulmonary mucormycosis, one case of rhino-orbital-mucormycosis with lymph nodal involvement and one case of rhino-orbital mucormycosis with acute inflammatory demyelinating polyneuropathy (AIDP).

Keywords: ROCM, COVID-19, Pulmonary mucormycosis, Lymph node mucormycosis, AIDP

INTRODUCTION

Mucormycosis is an uncommon but a fatal fungal infection that usually affects patients with altered immunity. Mucormycosis is an angioinvasive disease caused by mold fungi of the genus *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella* and *Absidia* of order-mucorales, class-Zygomycetes.[1] The *Rhizopus Oryzae* is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the ROCM form.[2]

Globally, the prevalence of mucormycosis varied from 0.005 to 1.7 per million population, while its prevalence is nearly 80 times higher (0.14 per 1000) in India compared to developed countries, in a recent estimate of year 2019-2020.[3-5] India has highest cases of the mucormycosis in the world. Risk factors include diabetes mellitus, hematological malignancies, organ transplant, prolonged use of corticosteroids.[5-7] There has been a steep rise in studies of mucormycosis in people with COVID-19 especially from India. Rapidity of dissemination of mucormycosis is an extraordinary phenomenon and even a delay of 12 h in the diagnosis could be fatal, the reason being, 50% of cases of mucormycosis have been historically diagnosed only in the post-mortem autopsy series.[8]

Incidence of invasive pulmonary mucormycosis following COVID-19 is rare, with only two cases currently reported.[9] To our knowledge only one case of combined invasive aspergillosis and mucormycosis has been reported so far. Involvement of lymph nodes in mucormycosis is a rare finding. No case reports have been published till date describing lymph nodal involvement of mucormycosis in non-cancer patients.

We reported two cases of combined pulmonary aspergillosis and pulmonary mucormycosis, one case of rhino-orbito-mucormycosis with lymph nodal involvement and one case of rhino-orbital mucormycosis with AIDP.

CASE SERIES

Case 1

A 71-year-old male who is a known case of diabetes mellitus and hypertension presented with complaints of cough and breathlessness since 7 days. Patient had history of COVID-19 infection 1 month back and was treated with standard COVID-19 treatment protocol. He was unvaccinated. At the time of admission, patient was stable with saturation of 96% with 4 L face mask. On examination, bronchial breath sounds were heard over right middle zone and left upper zone. Patient baseline investigations was normal except for HbA1C of 8.4. Chest X-ray showed bilateral patchy infiltrates and cavitatory lesions. HRCT thorax revealed bilateral ground-glass opacities, consolidation with breakdown cavitation in right middle, left upper and lower lobes. The patient was started on empirical antibiotic treatment. ELISA for *Aspergillus galoctomannan* antigen was positive in blood and galactomannan index was raised (2.07). Microscopic examination of broncho-alveolar lavage (BAL) specimens under KOH mount revealed septate hyphae suggestive of aspergillosis, as well as broad aseptate hyphae suggestive of mucormycosis. Fungal culture showed *Aspergillus fumigatus* and *Aspergillus niger* growth. Patient was started on treatment according to protocol. On day 8, oxygen therapy was escalated in view of clinical deterioration and repeat CXR showed development of left pneumothorax. HRCT Thorax showed pyopneumothorax with loculated collection in left pleural cavity (Figure 1). Inter costal drainage (ICD) tube was inserted and patient is currently improving after 1 week of ICD insertion and is being planned for ICD removal and follow up on out-patient basis.

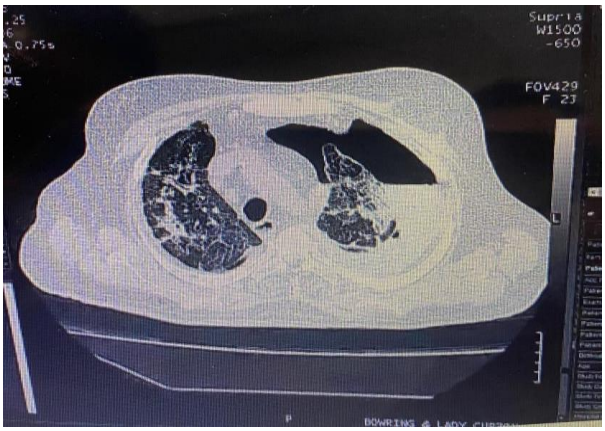

Figure 1: HRCT thorax showing bilateral consolidation with break down cavitation with left pyopneumothorax.

Case 2

A 53-year-old male who is a known case of diabetes mellitus presented with complaints of cough, blood-tinged sputum and breathlessness since 5 days with past history of admission for COVID-19 a month back and was treated with standard COVID-19 treatment protocol. Patient was unvaccinated. At the time of admission, patient was stable. On examination, bronchial breath sounds were heard over right middle zone. Baseline investigations revealed raised HbA1C of 8.8. CXR showed right patchy infiltrates and right middle lobe cavitatory lesions (Figure 2). HRCT thorax revealed thick walled cavitatory lesion in right middle lobe with surrounding ground glass opacities with features suggestive of atypical pneumonitis in resolving stage CORADS 5 and bilateral minimal pleural effusion. Sputum for culture sensitivity revealed coagulase negative *S. aureus* growth. KOH sputum revealed broad aseptate fungal hyphae suggestive of mucormycosis along with septate hyphae with dichotomous branching suggestive of aspergillosis. sputum geneXpert was negative for TB. However, ELISA for *Aspergillus galactomannan* assay in blood was positive (galactomannan index value 2.21). Patient was started on treatment according to protocol. Patient is currently improving and is stable.

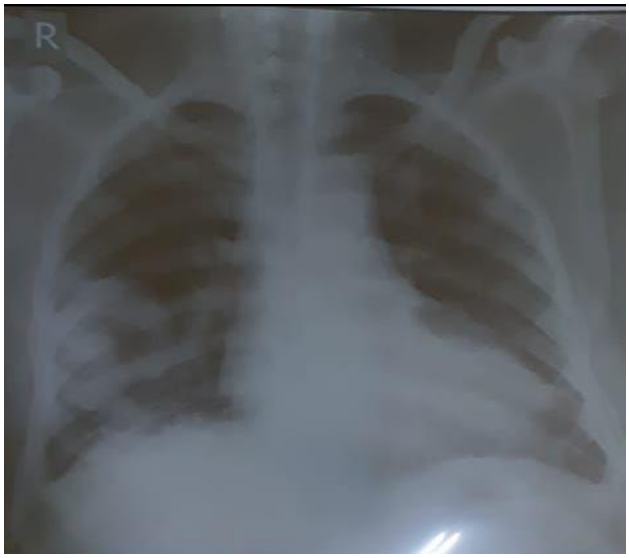

Figure 2: Chest X-ray showing right middle lobe cavitatory lesion.

Case 3

A 29-year-old male patient presented with complaints of swelling of left eye, blurring of vision, headache and excess lacrimation since 15 days. Patient had history of COVID-19 pneumonia 2 months ago and was hospitalized for 2 weeks and treated as per protocol. Patient was unvaccinated. He was a case of newly detected diabetes mellitus, post covid recovery since 1 month. On admission, patient had left LMN facial palsy. There were about 2-3 palpable upper cervical lymph nodes, following which USG neck was planned. USG Neck revealed few

lymph nodes in left upper, mid jugular and left submandibular region, largest measuring 5 cm. MRI para nasal sinus, revealed left ROMC. Surgical debridement and left orbital decompression were done. Blood investigations revealed elevated ESR-40 and CRP-87.44 HbA1c-13. CECT of neck confirmed the USG neck findings. FNAC lymph node showed aseptate fungal hyphae branching at right angles, PAS stain positive for fungal hyphae, epitheloid cell granuloma and giant cells (Figure 3), excision biopsy of lymph node confirmed the diagnosis of lymph node mucormycosis. Patient was diagnosed with invasive neck mucormycosis. Patient was started on treatment as per protocol and discharged.

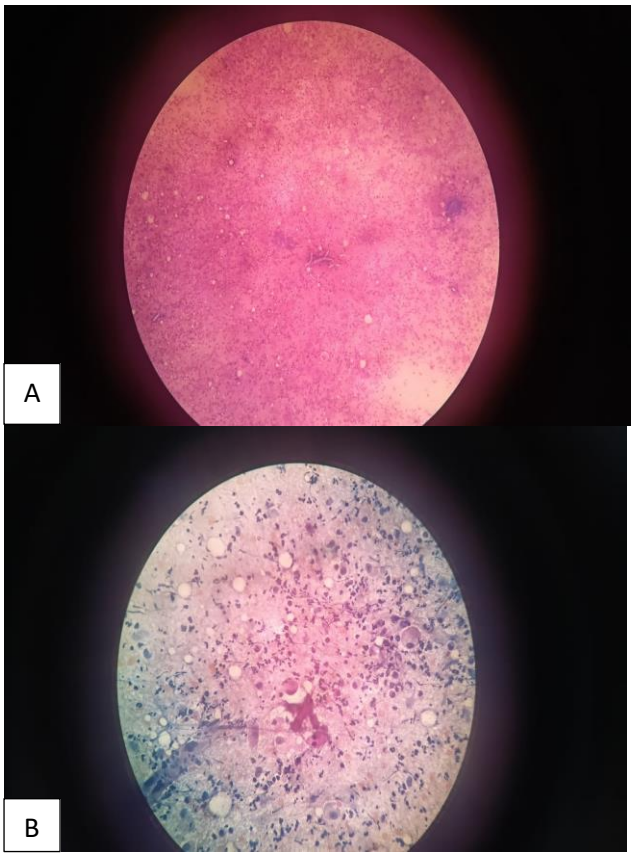

Figure 3 (A and B): Histopathology showed broad non-septate fungal hyphae with morphology suggestive of mucormycosis.

Case 4

A 59-year-old female presented with history of inability to walk since 2 weeks, facial pain since one week. Patient was a newly diagnosed diabetic with history of severe COVID pneumonia 3 weeks back for which she was treated at outside hospital ICU for 2 weeks. She was unvaccinated. After she was discharged from there, she was unable to walk or get up from bed without support. On examination, patient had normal vitals except for SpO_2 of 88 RA. CXR revealed fibrotic changes of bilateral mid and lower zones. Neurological examination revealed areflexic paraparesis with bilateral flexor plantars. Upper limb power was normal, sensory system intact. CBC showed raised total counts of 16600 per cubic millimetre. HbA1c was 11.8. KOH mount from nasal cavity showed broad aseptate fungal hyphae, with microscopic features suggestive of mucormycosis. MRI brain and PNS revealed invasive fungal sinusitis (stage III) with small vessel ischemic changes in brain. CSF analysis revealed albumin-cytological dissociation (protein 109.3, cell count-2, all lymphocytes) which was followed up by Nerve conduction study which was consistent with AIDP. Patient was planned for IV-Ig therapy, but attenders refused due to logistic reasons. On day 4 since admission to our hospital, patient developed sudden neck muscle weakness and inability to perform head raising, in view of impending respiratory failure, patient was shifted to ICU. However, patient aspirated and succumbed to illness the same night and could not be revived.

DISCUSSION

A complex interplay of factors, including pre-existing comorbidities, such as diabetes mellitus, previous respiratory pathology, use of immunosuppressive therapy, the risk of hospital-acquired infections, and systemic immune alterations of COVID-19 infection itself may lead to secondary infections, which are increasingly being recognized in view of their impact on morbidity and mortality.[11]

Definitive diagnosis of mucormycosis is made by the identification of causative fungal organisms by histopathological analysis of tissue specimens from patients with suspected signs and symptoms.[12] Since biopsy could not be obtained in 3 of our above cases except case 3, we report them as probable mucormycosis based on strong clinical suspicion, cytology, biochemical markers and fungal cultures.

Johnson et al reported a case of combined probable pulmonary aspergillosis and possible mucormycosis in a 79 year male patient with COVID-19 in the ICU.[13] Mucormycosis of lymphnodes is very rare. There has been only one case report of a pulmonary mucormycosis with lymphadenitis in a case of acute myeloid leukemia.[14] Another rare case presenting with earache, discharge and facial palsy with neck swelling with IJV thrombosis showed mucormycosis in lymphnodes on biopsy.[15] In our case we have reported a young male with new onset diabetes post covid with rhinoorbital mucormycosis with lymphnode involvement. This is probably the first case report of lymphnode mucormycosis detected in a non-cancer patient. Early recognition and treatment of the condition is key to favourable outcomes.

AIDP has been associated previously with other viruses. There have been case reports and systematic review by Josef Finsterer done on 220 cases of GBS in COVID suggested that COVID-GBS is not due to direct attack of the virus but rather due to an immunological reaction to the virus. It also shows that the number of reports about

COVID-GBS is increasing and that outcome is worse compared to non-COVID-GBS. Early diagnosis is warranted because if appropriate treatment is applied in due time overall outcome from infection may improve.[16]

CONCLUSION

Mucormycosis is very rare, but with the second wave of COVID, there is a sudden surge of cases. It was seen that none of the above cases were vaccinated against COVID-19. The universal risk factor, predisposing to the onset of mucormycosis in our study uncontrolled diabetes mellitus. Since mortality associated with mucormycosis is high despite surgical debridement and anti-fungal therapy, it is important to know the varied presentations of mucormycosis.

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REFERENCES

1. Eucker J, Sezer O, Graf B, Possinger K. Mucormycoses. Mycoses. 2001;44(7):253e60.
2. Sugar AM. In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. fifth ed. New York, USA: Churchill Livingstone. 2000.
3. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an Update. J Fungi. 2020;6(4):265.
4. Chander J, Kaur M, Singla N. Mucormycosis: battle with the deadly enemy over a five-year period in India. J. Fungi. 2018;4(2):46.
5. Prakash H, Chakrabarti A. Global epidemiology of mucormycosis. J Fungi. 2019;5:26.
6. International Diabetes Federation. Idf diabetes atlas, 2021. Available at: https://diabetesatlas.org/en/resources/. Accessed on 10 May 2021.
7. Jeong W, Keighley C, Wolfe R. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. Clin Microbiol Infect. 2019;25:26e34.
8. Maartens G, Wood MJ. The clinical presentation and diagnosis of invasive fungal infections. J Antimicrob Chemother. 1991;28(13e22):17e44.
9. Pasero D, Sanna S, Liperi C, Piredda D, Branca G, Casadio L et al. A challenging complication following SARS-CoV-2 infection: a case of pulmonary mucormycosis, Infection. 2021;49(5):1055-60.
10. Zurl C, Hoenigl M, Schulz E, Hatzl S, Gorkiewicz G, Krause R et al. Autopsy proven pulmonary mucormycosis due to Rhizopus microsporus in a critically ill COVID-19 patient with underlying hematological malignancy. J Fungi. 2021;7(2):88.
11. Chen N, Zhou M, Dong X. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507-13.
12. Ibrahim A, Kontoyiannis D. Update on mucormycosis pathogenesis. Curr Opin Infect Dis. 2013;26:508-15.
13. Johnson A, Ghazarian Z. Pulmonary aspergillosis and mucormycosis in a patient with COVID-19. Med Mycol Case Rep. 2021;32:64-7.
14. Fanci R, Pecile P, Di Lollo S, Dini C, Bosi A. Pulmonary mucormycosis with cervical lymph node involvement in a patient with acute myeloid leukaemia: a case report. Mycoses. 2008;51(4):354-6.
15. Kancharu FK, Viswam V, Sreeram P. Mucormycosis of Neck a Rare Presentation. Indian J Otolaryngol Head Neck Surg. 2020;1:37-41.
16. Finsterer J, Scorza FA. Guillain-Barre syndrome in 220 patients with COVID-19. Egypt J Neurol Psychiatry Neurosurg. 2021;57-55.

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