CASE REPORT

Covid-19 associated pulmonary aspergillosis with extensive cavitary pneumonia: A case report

Sadaf Hanif,[1] Madiha Iqbal,[2] Sher Muhammad Sethi[3]

Abstract

Covid-19 associated pulmonary aspergillosis (CAPA) is a new entity and is associated with high morbidity and mortality. Covid-19 is a pro-inflammatory and immunosuppressive disease, provoking fungal infections, especially by Aspergillus species.

We describe the case of a critically ill Covid-19 female patient, who was diagnosed with CAPA infection and acute respiratory distress syndrome (ARDS). She was given intravenous Remdesivir. Her chest X-ray a few days after admission showed multiple cavities. Her condition initially improved but deteriorated again, with worsening hypoxia and pneumothorax and multiple cavitary lesions on HRCT of the chest. Despite optimal treatment, she could not recover. Interestingly, she had no predisposing risk factor for pulmonary aspergillosis, such as chronic lung disease, diabetes or use of immunosuppressants such as Tocilizumab.

CAPA is an emerging entity with worsening hypoxia, and failure to improve can be an early sign. Early identification and treatment can improve survival and outcomes in Covid-19 patients.

Keywords: Covid-19, Aspergillosis, Thick-walled cavitation, CAPA.

DOI: 10.47391/JPMA.4793

Submission completion date: 14-09-2021
Acceptance date: 04-06-2022

Introduction

Coronavirus disease 2019 (Covid-19) is a viral disease caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2). With the ongoing pandemic, it is observed that patients with Covid-19 infections are at an increased risk of acquiring secondary bacterial and fungal infections.[1,2] Covid-19 associated pulmonary aspergillosis (CAPA) is a new entity and is associated with high morbidity and mortality. Covid-19 is a pro-inflammatory and immunosuppressive disease, provoking fungal infections, especially by Aspergillus species.[3] Pulmonary aspergillosis is reported in asymptomatic to severe and critical Covid-19 infections.[2] Aspergillus co-infection with coronavirus can be fatal, though early diagnosis and treatment can improve clinical outcomes.[3]

Here we report a unique case of Covid-19 infection that presented with extensive cavitary fungal pneumonia despite being on antifungal medications.

Case Report

A 57-year-old woman presented to the emergency department of the Aga Khan University Hospital, Karachi, in May 2021 with a history of fever and dyspnoea for 10 days. She denied any cough, haemoptysis, or chest pain. She had well-controlled hypertension. On arrival, she was afebrile, had a respiratory rate of 40 breaths per minute with oxygen saturation at 40% in ambient room air, heart rate was 116 beats/minute regular, and blood pressures of 116/86 mmHg. She was intubated because of hypoxic respiratory failure. She had a bilateral equal expansion of the chest with crepitation throughout the lung field, while other systemic examinations were unremarkable.

On admission, she had high white cell counts and beta D-glucan. The rest of the laboratory parameters are shown in Table-1. On arrival at the hospital, her PaO_2/FiO_2 ratio

Table-1: Laboratory parameters of the patient.

	Initial	On worsening	Normal reference range
Haemoglobin (g/dL)	15.9	11.2	11 - 14.5
White cells (per µL)	20,000	18,800	4,000 - 10,000
Platelets (per µL)	232	122	154 - 433
Creatinine	1.4	1.4	0.6 - 1
AST (U/L)	40	64	<35
ALT(U/L)	35	66	<35
Procalcitonin (ng/ml)	0.161	0.616	>2
Ferritin (ng/ml)	220		10 - 291
LDH	733		120 - 246
C-Reactive protein	13.6		0 - 14
D-dimer (mg/L FEU)	25.2	1.9	<0.5
Beta D-Glucan (pg/ml)	126	231	<80
Galactomannan		6.13	>0.7

AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase.

[1]Department of Internal Medicine and Critical Care, [2,3]Department of Internal Medicine, Aga Khan University Hospital, Karachi, Pakistan.
Correspondence: Sher Muhammad Sethi. Email: sher.sethi@gmail.com
ORCID ID. 0000-0001-7066-7124

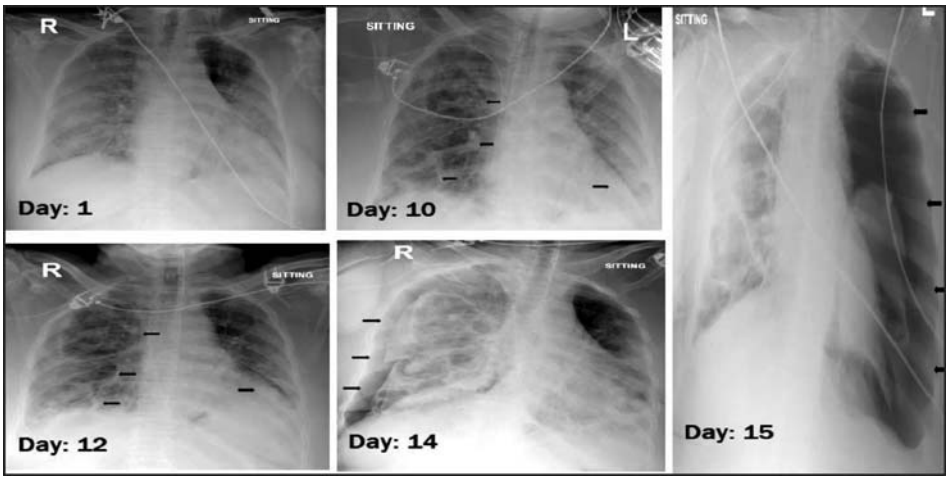

Figure-1: Initial chest X-ray of the patient on admission is shown as on Day 1; multiple cavitary lesion can be seen more on the right side on day 10, 12 and 14; left sided pneumothorax can be visualised in chest x-ray of day 15.

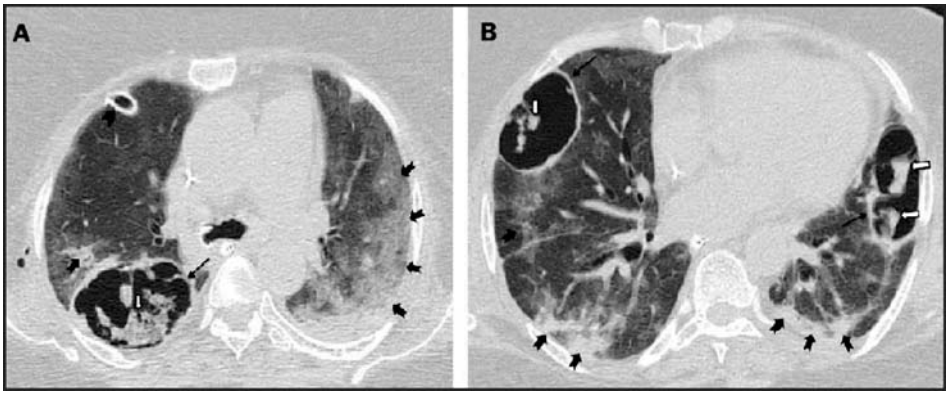

Figure-2: High resolution computed tomography of the chest shows multiple thick walled cavities in bilateral lung field (shown with white arrows); and extensive ground glass opacification are shown with black arrows.

was 103. The chest X-ray is shown in Figure-1. Nasopharyngeal swab for SARS-CoV-2 RT-PCR was positive. She was managed in the intensive care unit as Covid-19 associated ARDS. Sequential organ failure assessment (SOFA) score in the first 24 hours of ICU admission was 7. She was treated with intravenous steroids and Remdesivir (total 5 doses) and intermittent diuresis. As per ARDS net protocol, she was kept on high PEEP and low FiO2 settings. She was started on empirical antibiotics and three sessions of proning were done as recommended.

On the third day, her blood culture grew E.coli, and tracheal aspirate showed E.coli and aspergillus flavus. She was started on Voriconazole which was continued throughout the hospital stay. Repeat blood cultures were negative but tracheal aspirate on day 10 showed aspergillus flavus again and chryseobacterium indologenes. She clinically improved and her PEEP was gradually tapered. She was weaned and extubated to non-invasive ventilation on the 12th day of ICU stay. But, unfortunately, on day 15, she deteriorated with worsening hypoxia. She developed right-sided pneumothorax and was re-intubated after right-sided tube thoracotomy. HRCT of the chest revealed extensive ground-glass haziness and multiple bilateral cavitary lesions in the lung fields with central soft tissue components (Figure-2). Tracheal aspirate on day 16 was negative. On day 20, her beta D-glucan and galactomannan were high, and repeated tracheal aspirate showed Aspergillus flavus. She developed left-sided tension pneumothorax, and urgent left-sided tube thoracotomy was done. Over days, due to her deteriorating clinical condition, the patient's family decided to withdraw support. The patient succumbed to the illness and died.

Discussion

We report an interesting case of extensive fungal cavitary pneumonia in a patient with Covid-19 infection. There had been a debate that superimposed fungal infections are common with Covid-19 infection.[4] Van Arkel et al reported a high incidence of pulmonary aspergillosis in patients with Covid-19 infection.[5] In the past, aspergillus co-infection with viral pneumonia (influenza) has been described.[6] Interestingly, our patient presented with concomitant fungal infection and Covid-19 infection.

EORTC/MSG guidelines on CAPA are not validated in critically ill patients without any predisposing risk factors.[7] Koehler et al used an alternative algorithm on CAPA,[8] which was evaluated by Blot et al[9] and modified by Schauwvlieghe et al.[6] Our patient also fulfilled the criteria mentioned above. She was labelled as Covid-19 associated pulmonary aspergillosis. Despite initial treatment, her serum galactomannan was elevated and tracheal aspirate was positive for aspergillus flavus.

CAPA is a new entity and has gained global importance.[10] Chong et al reported a prevalence of 13.5%. The duration from illness to CAPA was between 8 to 16 days.[11]

Surprisingly, our patient presented with aspergillus infection and was treated and improved. Later, on day 15 she again developed worsening hypoxia and respiratory distress and was identified to have CAPA along with pneumothorax.

The severity of infection varies in CAPA from respiratory failure to ARDS. CAPA should be considered in patients with persistent hypoxic respiratory failure. The diagnosis is based on tracheal aspirate of aspergillus, galactomannan levels, and fungal cultures.[12] Radiological characteristics are difficult to differentiate between Covid-19 infection and invasive pulmonary aspergillosis. The presence of multiple pulmonary nodules or cavitation can point towards pulmonary aspergillosis.[13] Our patient also had extensive cavitary lesions identified on a CT scan of the chest. These cavitations were not present initially on chest X-ray. But on day 10 of her illness, she started to develop well-circumscribed cavitation on bilateral lung fields (Figure-1).

Antifungal treatment is recommended to be initiated. It helps to prevent the progression of the disease.[14] Covid-19 is an independent risk factor for fungal infections. The mortality with CAPA is high.[15] Voriconazole was given from the third day of her admission and her cultures were negative after a week. This indicates that she initially responded to the treatment. On worsening hypoxia, her cultures were re-sent (after five days) and again grew aspergillus. It could be due to resistance to Voriconazole or she might have developed re-infection with resistant aspergillus organism. This was not considered during her hospital stay. Despite proning and aggressive therapy, our patient succumbed to her illness.

We recommend that prospective and multi-centre studies be carried out in future to identify the risk factors and prevalence of CAPA with Covid-19 infections. Serum galactomannan and beta D-glucan can be important fungal markers in predicting the severity of the infection. Voriconazole is the mainstay treatment but should be vigilantly used because of the adverse effects. Resistance to Voriconazole can develop and should be considered in patients who have persistent aspergillus growth despite accurate dosage and duration.

Conclusion

In our patient, severe hypoxia with underlying pulmonary aspergillosis worsened despite optimal treatment and the patient could not improve. Detecting CAPA as soon as possible and treating the condition can improve the outcome and survival of critically ill Covid-19 patients.

Disclaimer: None.

Conflict of Interest: None to declare.

Funding Disclosure: None.

Consent for Publication: Patient's son gave consent for publication.

References

1. Lai CC, Wang CY, Hsueh PR. Co-infections among patients with Covid-19: The need for combination therapy with non-anti-SARS-CoV-2 agents? J Microbiol Immunol Infect. 2020; 53:505-12. doi: 10.1016/j.jmii.2020.05.013.
2. Zhu X, Ge Y, Wu T, Zhao K, Chen Y, Wu B, et al. Co-infection with respiratory pathogens among COVID-2019 cases. Virus Res. 2020; 285:198005. doi: 10.1016/j.virusres.2020.198005.
3. Lai CC, Yu WL. Covid-19 associated with pulmonary aspergillosis: A literature review. J Microbial Immunol Infect.2021; 54:46-53. doi: 10.1016/j.jmii.2020.09.004.
4. Nestler M, Godbout E, Lee K, Kim J, Noda AJ, Taylor P, et al. Fungal superinfection in patients with Covid-19: Role of antifungal stewardship? Am J Infect Control. 2021; 49:279-80. doi: 10.1016/j.ajic.2020.11.015.
5. Van Arkel ALE, Rijpstra TA, Belderbos HNA, van Wijngaarden P, Verweij PE, Bentvelsen RG. Covid-19-associated Pulmonary Aspergillosis. Am J Respir Crit Care Med. 2020; 202:132-5. doi: 10.1164/rccm.202004-1038LE.
6. Schauwvlieghe A, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Van Tienen C, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. Lancet Respir Med. 2018; 6:782-92. doi: 10.1016/S2213-2600(18)30274-1.
7. Donnelly JP, Chen SC, Kauffman CA, Steinbach WJ, Baddley JW, Verweij PE, et al. Revision and Update of the Consensus Definitions of Invasive Fungal Disease from the European Organisation for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. Clin Infect Dis. 2020; 71:1367-76. doi: 10.1093/cid/ciz1008.
8. Koehler P, Cornely OA, Bottiger BW, Dusse F, Eichenauer DA, Fuchs F, et al. Covid-19 associated pulmonary aspergillosis. Mycoses. 2020; 63:528-34. doi: 10.1111/myc.13096.
9. Blot SI, Taccone FS, Van den Abeele AM, Bulpa P, Meersseman W, Brusselaers N, et al. A clinical algorithm to diagnose invasive pulmonary aspergillosis in critically ill patients. Am J Respir Crit Care Med. 2012; 186:56-64. doi: 10.1164/rccm.201111-1978OC.
10. Mohamed A, Rogers TR, Talento AF. Covid-19 Associated Invasive Pulmonary Aspergillosis: Diagnostic and Therapeutic Challenges. J Fungi. 2020; 6:115. doi: 10.3390/jof6030115.
11. Chong WH, Neu KP. Incidence, diagnosis and outcomes of Covid-19-associated pulmonary aspergillosis (CAPA): a systematic review. J Hosp Infect. 2021; 113:115-29. doi: 10.1016/j.jhin.2021.04.012.
12. Abdalla S, Almaslamani MA, Hashim SM, Ibrahim AS, Omrani AS. Fatal Coronavirus Disease 2019-associated Pulmonary Aspergillosis; A Report of Two Cases and Review of the Literature. ID Cases. 2020; 22:e00935. doi: 10.1016/j.idcr.2020.e00935
13. White PL, Dhillon R, Cordey A, Hughes H, Faggian F, Soni S, et al. A national strategy to diagnose Covid-19 associated invasive fungal disease in the ICU. Clin Infect Dis. 2021; 73:e1634-44. doi: 10.1093/cid/ciaa1298.
14. Sharma A, Hofmeyr A, Bansal A, Thakkar D, Lam L, Harrington Z, et al. Covid-19 associated pulmonary aspergillosis (CAPA): An Australian case report. Med Mycol Case Rep. 2021; 31:6-10. doi: 10.1016/j.mmcr.2020.06.002.
15. Lahmer T, Kriescher S, Herner A, Rothe K, Spinner CD, Schneider J, et al. Invasive pulmonary aspergillosis in critically ill patients with severe COVID-19 pneumonia: Results from the prospective AspCovid-19 study. PloS One. 2021; 16:e0238825.