SAGE Open Medical Case Reports
Volume 10: 1–5

DOI: 10.1177/2050313X221081386
journals.sagepub.com/home/sco
SAGE

A post-COVID-19 *Aspergillus fumigatus* posterior mediastinitis: Case report

Nadine El Hoyek[1], Jacques Ghorayeb[2], Iskandar Daou[3], Dany Jamal[4], Nathalie Mahfoud[5] and Georges Nawfal[3]

Abstract

Invasive aspergillosis is a life-threatening condition of the immunocompromised, with a low occurrence reported in the immunocompetent. Although usually made by invasive methods, its early diagnosis is the cornerstone of a better prognosis as it yields a timely management and thus a lower mortality risk. Mediastinal invasion by *Aspergillus* is, like any fungal mediastinitis, uncommon and usually results from a hematogeneous or a contiguous spread, a postoperative fungal infection, a complication of a descending necrotizing fasciitis, or from an esophageal perforation. We report a case of a diabetic patient with a previous history of hospitalization 2 months earlier for a COVID-19 infection, otherwise healthy, presenting with an unresolving dorsal pain. A malignancy was expected but further work-up showed *in fine* a posterior mediastinitis due to *Aspergillus fumigatus*. Thus, fungal etiologies are to be included as a differential while diagnosing a posterior mediastinitis even in a relatively immunocompetent patient and with no evident route of entry.

Keywords

Aspergillus fumigatus, COVID-19, pathology, posterior mediastinitis, radiology, surgery

Date received: 27 July 2021; accepted: 1 February 2022

Introduction

COVID-19 pandemic has spread throughout the world at an alarming pace since December 2019. It generated a spectrum of illness presentations, ranging from mild to severe, even fatal. It has been also associated with several complications throughout its course, mainly respiratory, sepsis, hypercoagulability, cardiac events, which can occur either in an acute setting or a delayed form.[1] Unlike influenza, which is known to be complicated by invasive aspergillosis (IA), there has not been to date a direct association between COVID-19 infection and IA, although some cases have been reported.[2] We report here a new case of COVID-19 complicated by IA of the posterior mediastinum.

Case presentation

A 70-year-old male non-hypertensive, non-smoker, well-controlled diabetic (HbA1c = 6.83%), presented for an unresolving back pain 2 months following a COVID-19-induced pneumonia. All routine blood investigations were normal except a slightly elevated white blood cell (WBC) (15,200/mm^3). No abnormal monoclonal gammopathy was detected on the serum protein electrophoresis for a suspected multiple myeloma. A contrast-enhanced chest–abdomen–pelvis computed tomography (CT) scanner showed mediastinal calcified lymph nodes and a dense infiltrative retroesophageal prevertebral lesion of the mediastinal adipose tissue from T2 till T8. The lung fields were clear except for some retractile subpleural fibrous bands (Figure 1).

While a stepwise increase in WBC and C-reactive protein (CRP) had been observed, a broad spectrum antibiotherapy was initiated. A dorsal MR was conducted 3 days later

[1]Department of Radiology, Hotel Dieu de France University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon
[2]Department of Orthopedic Surgery, Saint Joseph University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon
[3]Department of Radiology, Saint Joseph University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon
[4]Department of Intensive Care Unit, Saint Joseph University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon
[5]Department of Pathology, Saint Joseph University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, Lebanon

Corresponding Author:
Nadine El Hoyek, Department of Radiology, Hotel Dieu de France University Hospital, Faculty of Medicine, Saint Joseph University, Beirut, 17-5208, Lebanon.
Email: nadine.hoyek@yahoo.com

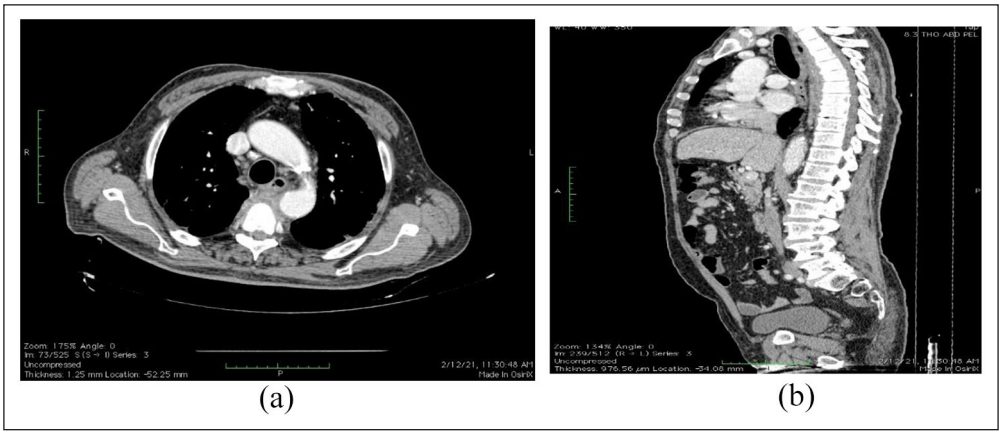

Figure 1. (a) CT axial mediastinal view showing subcentimeter and supracentimeter calcified lymph nodes at the paratracheal level. (b) CT sagittal view showing a dense infiltrative retroesophageal prevertebral lesion of the mediastinal adipose tissue extending from T2 till T8.

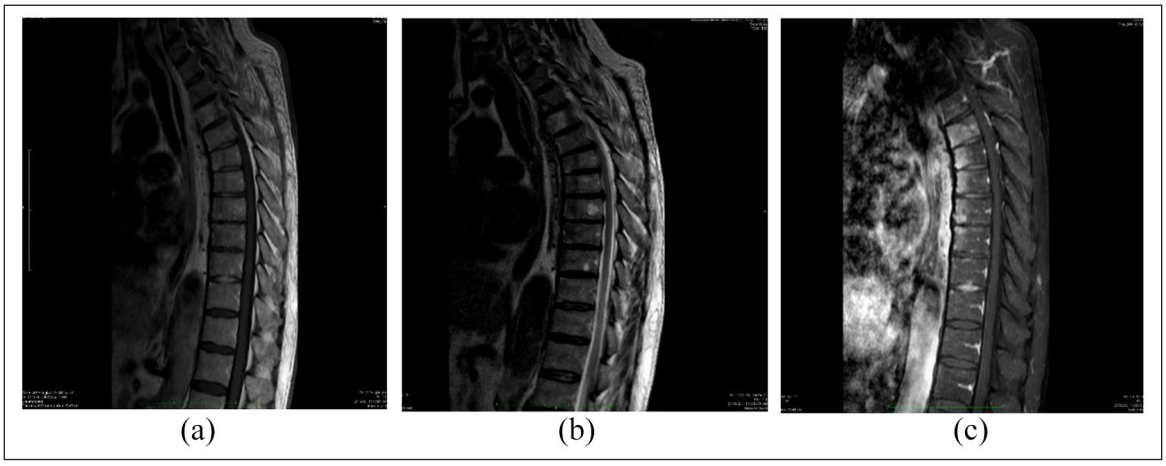

Figure 2. (a) T1-weighted sagittal images showing an intermediate signal expanding prevertebral lesion extending from the level of T2 till the level of T9. (b) T2-weighted sagittal images showing the high signal intensity of the lesion. (c) Post Gd-T1W-SPIR sagittal images showing contrast enhancement of the lesion.

showing an expanding prevertebral lesion from T2 till T9 (Figure 2).

Tuberculosis, HIV, and brucellosis testing along with blood culture came out negative. Serum galactomannan assay and reverse transcription polymerase chain reaction (RT-PCR) COVID-19 were also negative. A first percutaneous CT-guided biopsy of the prevertebral lesion was inconclusive. Rising WBC count and CRP were still reported. A control dorsal MR was carried out 10 days later, depicting a slight progression of the lesion without an intraspinal extension.

Empirical antifungal therapy with fluconazole 400 mg b.i.d. and amphotericin B 400 mg q.d. was initiated 2 days before a second CT-guided biopsy was performed. On light microscopy, necrotic lesions containing fungal organisms with acute-angle-branching hyphae were observed suggesting a mycotic infection. Culture showed growth of *Aspergillus fumigatus* (Figure 3).

At this stage, antifungal therapy was switched to voriconazole upon reception of culture, with a dosage of 400 mg b.i.d. for the first day reduced to 200 mg b.i.d. the day after for 14 consecutive days. An optimal treatment also required a surgical thoracotomy which was not executed due to the refusal of the patient's family members. While CRP levels decreased, the patient developed increasing levels of creatinine right after initiation of voriconazole and progressive oliguria, requiring hemodialysis sessions. Ten days after the last dorsal magnetic resonance imaging (MRI), the patient acutely developed paraplegia with an altered mental state mandating an intensive care unit (ICU) transfer. A head CT performed did not show any focal abnormality in the brain parenchyma with an adequate gray matter–white matter differentiation. In addition, lumbar puncture was normal with sterile cultures. A dorsal MR performed in an urgent setting showed a recent spinal cord compression at the level of T6 to T8 (Figure 4).

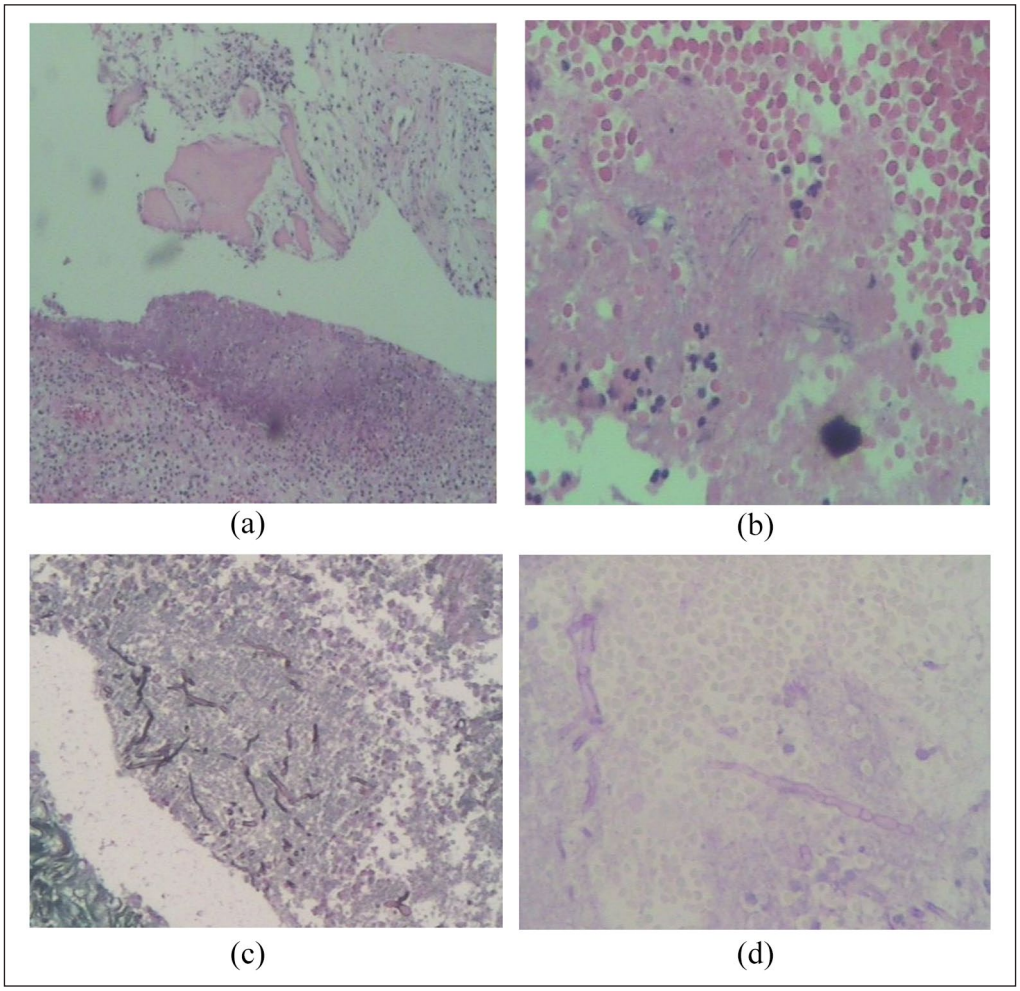

Figure 3. (a) Necrotic tissue. (b) Mycelial filaments within necrotic tissue. (c) and (d) Branched and septated hyphae in favor of *Aspergillus* infection.

Outcome and follow-up

Despite the antifungal treatment which was expectedly insufficient by itself without concomitant surgical intervention, the renal and neurological functions of the patient kept deteriorating, with him becoming comatose and intubated for the following 2 weeks before passing away.

Discussion

IA is a life-threatening infection that commonly targets individuals with chronic granulomatous disease, prolonged or profound neutropenia, solid organ or stem cell transplant, HIV/AIDS, chronic steroid, or tumor necrosis factor (TNF)-alpha antagonist use.[3–6] However, it has been, although rarely, encountered in healthy individuals.[7–9]

Mediastinal involvement with *Aspergillus* is by itself an extremely rare condition like any other fungus in the mediastinum, resulting from a direct spread from a contiguous pulmonary infection, a hematogeneous inoculation, a postoperative fungal infection, a complication of a descending necrotizing fasciitis, or from an esophageal perforation.[10–15] To our knowledge and based on the literature review, this is the first sporadic posterior mediastinitis to *Aspergillus fumigatus* following COVID-19 infection in a relatively immunocompetent patient.

Many IA cases have been described following a COVID-19 infection, most of them presenting as a COVID-19 *Aspergillus* pneumonia (CAPA).[16–18] The main risk factors reported are a severe illness requiring a long hospital stay, mechanical ventilation, an admission to ICU, corticosteroid therapy.[19,20] However, even though it needs larger registries to be confirmed and since the pandemic is still taking a toll on a worldwide scale, COVID-19 may be by itself an independent risk factor for subsequent *Aspergillus* infection.[17] Our patient, although he did not fulfill other classic host criteria for invasive fungal infection, had received during his COVID-19 hospitalization a 3-week corticosteroid therapy (dexamethasone 20 mg daily) which is his main predisposing risk factor for IA. Steroid therapy increases host immune vulnerability by impairing the frontline defense

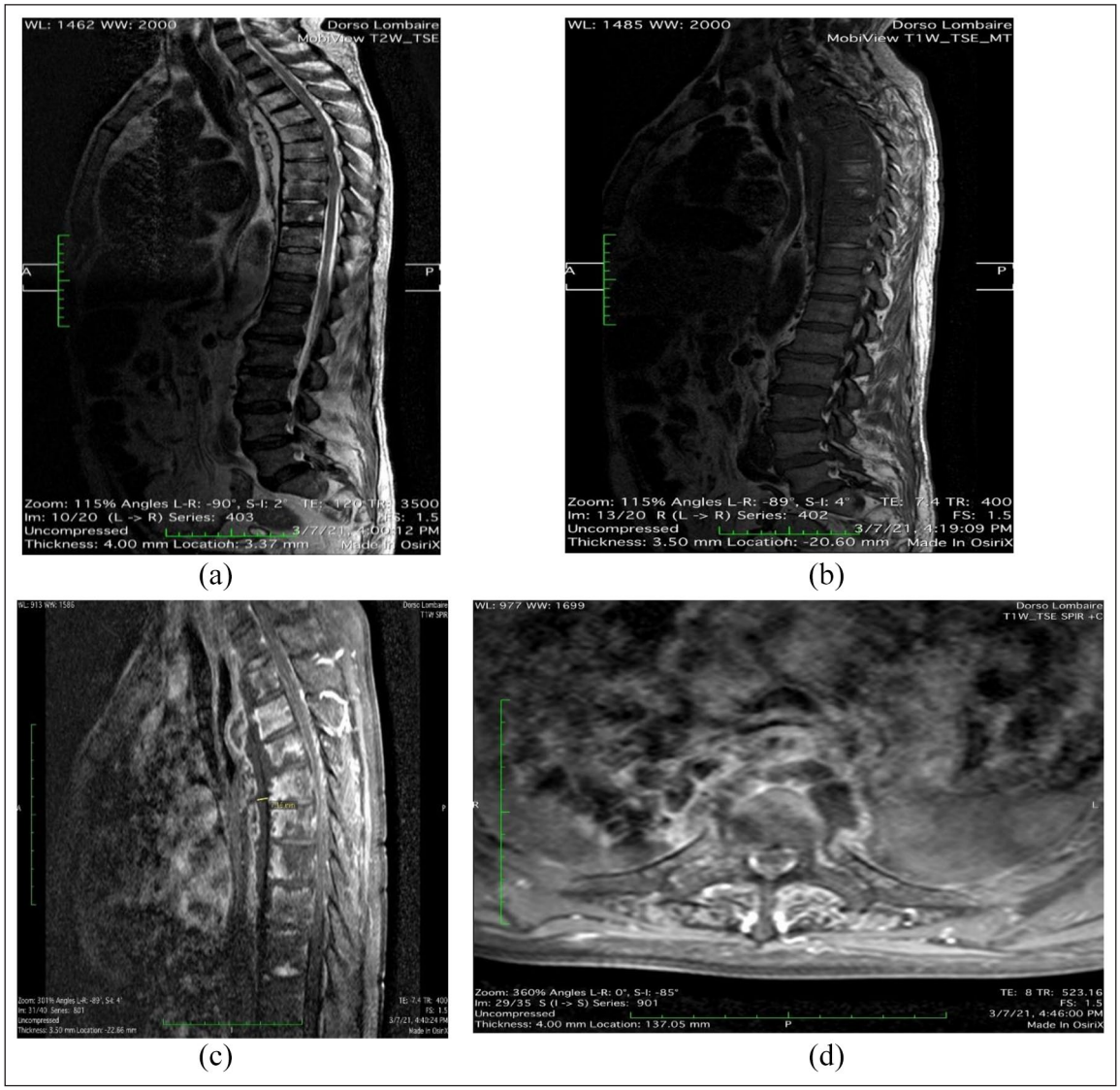

Figure 4. Progression of the peridural spread measuring 12 mm responsible for a recent spinal cord compression at the level of T6 to T8 with a high signal abnormality on T2-weighted images. The previously reported enhancement as well as the T2-signal abnormality of the vertebral bodies is significantly increased in addition to the prevertebral lesion thickness currently measuring 7.5 mm.

against mold infection.[21] His previous hospitalization for COVID-19 pneumonia lasted 2 weeks, did not mandate mechanical ventilation nor an admission to the ICU, and was not complicated by invasive pulmonary aspergillosis based on the findings of the SCAN.

We determined the immunocompetent status of our patient based on the medical history, the laboratory work-up, and the absence of underlying malignancy or chronic immunosuppressive drug use. His only predisposing factor was a 2-week dexamethasone course. No otherwise primary infection sites were detected (negative initial blood cultures, no surgical history of the mediastinum, no retropharyngeal or parapharyngeal abscess, and no esophageal perforation).

Since histopathological and culture are the mainstay for diagnosing *Aspergillus fumigatus* infection and knowing the fastidious nature of *Aspergillus*, a high index of suspicion and prompt diagnosis have to be attempted as they yield a better prognosis.[6,7,22]

Conclusion

IA should be suspected in case of clinical deterioration in patients with current or previous recent history of SARS-CoV-2. The virus itself might be a predisposing factor for IA in relatively immunocompetent patients. Prospective studies are needed to determine whether mycosis screening should be systematically performed in a post-COVID-19 complication presentation.

Acknowledgements

N.E.H. contributed to the writing of the whole manuscript. J.G. and D.J. participated in the clinical data collection and the inpatient

follow-up. G.N. and I.D. provided all the radiologic imaging. N.M. contributed to the writing of the histopathology section, in addition to providing original histopathology figures. All authors had full access to all of the data in the study. All authors critically revised the manuscript for important intellectual content and gave final approval for the version to be published.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Ethical considerations

We obtained the consent of the patient's family for the publication of his medical data. Patient privacy was fully protected, and personal information was handled such that the patient could not be identified.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ORCID iD

Nadine El Hoyek https://orcid.org/0000-0001-6110-3861

References

1. Chams N, Chams S, Badran R, et al. COVID-19: a multidisciplinary review. *Front Public Health* 2020; 8: 383.
2. Schein F, Munoz-Pons H, Mahinc C, et al. Fatal aspergillosis complicating severe SARS-CoV-2 infection: a case report. *J Mycol Med* 2020; 30(4): 101039.
3. Latgé J-P. Aspergillus fumigatus and aspergillosis. *Clin Microbiol Rev* 1999; 12(2): 310–350.
4. Baddley JW. Clinical risk factors for invasive aspergillosis. *Med Mycol* 2011; 49(Suppl. 1): S7–S12.
5. Segal BH and Walsh TJ. Current approaches to diagnosis and treatment of invasive aspergillosis. *Am J Respir Crit Care Med* 2006; 173(7): 707–717.
6. Chakrabarti A, Chatterjee SS, Das A, et al. Invasive aspergillosis in developing countries. *Med Mycol* 2011; 49(Suppl. 1): S35–S47.
7. Mohammed AP, Dhunputh P, Chiluka R, et al. An unusual case of invasive aspergillosis in an immunocompetent individual. *BMJ Case Rep* 2015; 2015: bcr2015210381.
8. Moreno-González G, Ricart de Mesones A, Tazi-Mezalek R, et al. Invasive pulmonary aspergillosis with disseminated infection in immunocompetent patient. *Can Respir J* 2016; 2016: 7984032.
9. Ranjan R, Mishra S and Ranjan S. Aspergillus vertebral osteomyelitis in an immunocompetent person. *Neurol India* 2010; 58(5): 806–808.
10. Wells WJ, Fox AH, Theodore PR, et al. Aspergillosis of the posterior mediastinum. *Ann Thorac Surg* 1994; 57: 1240–1243.
11. Atassi Ghassan SS and Al-Shamy Abdulrahman. Invasive aspergillosis of the neck and upper mediastinum with intraspinal extension: an unusual presentation. *Ann Saudi Med* 2002; 22(1–2): 84–86.
12. Lim JH, Kim JS, Yang CK, et al. Surgical treatment of mediastinal aspergilloma in a immunocompetent patient. *Korean J Thorac Cardiovasc Surg* 2014; 47(4): 431–433.
13. Hosseinikargar N, Basiri R, Asadzadeh M, et al. First report of invasive sspergillus rhinosinusitis in a critically ill COVID-19 patient affected by acute myeloid leukemia, northeastern Iran. *Clin Case Rep* 2021; 9(10): e04889.
14. Zarei F, Mirhendi H, Motamedi M, et al. Black *Aspergillus* species isolated from clinical and environmental samples in Iran. *J Med Microbiol* 2015; 64: 1454–1456.
15. Nourizadeh N, Adabizadeh A, Zarrinfar H, et al. Fungal biofilms in sinonasal polyposis: the role of fungal agents is notable? *J Oral Maxillofac Surg Med Pathol* 2019; 31(4): 295–298.
16. Borman AM, Palmer MD, Fraser M, et al. COVID-19-associated invasive aspergillosis: data from the UK national mycology reference laboratory. *J Clin Microbiol* 2020; 59(1): e02136.
17. Fekkar A, Poignon C, Blaize M, et al. Fungal infection during COVID-19: does *Aspergillus* mean secondary invasive aspergillosis? *Am J Respir Crit Care Med* 2020; 202(6): 902–903.
18. Song G, Liang G and Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. *Mycopathologia* 2020; 185(4): 599–606.
19. Apostolopoulou A, Esquer Garrigos Z, Vijayvargiya P, et al. Invasive pulmonary aspergillosis in patients with SARS-CoV-2 infection: a systematic review of the literature. *Diagnostics* 2020; 10: 807.
20. Ripa M, Galli L, Poli A, et al. Secondary infections in patients hospitalized with COVID-19: incidence and predictive factors. *Clin Microbiol Infect* 2021; 27(3): 451–457.
21. Lionakis MS and Kontoyiannis DP. Glucocorticoids and invasive fungal infections. *Lancet* 2003; 362(9398): 1828–1838.
22. Bajaj N, Chadha D, Hasija P, et al. Invasive aspergillosis presenting as an intracardiac mass in an immunocompetent host. *BMJ Case Rep* 2016; 2016: bcr2015213205.