

CASE REPORT

Open Access



Endocarditis caused by *Aspergillus fumigatus* in a patient 9 months after COVID-19 infection recovery: a case report and review of the literature

Zeynab Yassin¹, Shokoufeh Hajsadeghi² , Mohsen Taghavi Shavazi³ , Mahsa Fattahi⁴ ,
Koohyar Ahmadzadeh⁵ , Armita Farid⁶ , Yeganeh Karimi⁷ , Farnoosh Seirafianpour^{6*} ,
Pegah Babaheidarian⁸ and Azadeh Goodarzi^{9,10*}

Abstract

Background *Aspergillus spp.* are among the fungal pathogens that can cause life-threatening infections in patients with a history of COVID-19.

Case presentation We present the case of a 58-year-old Iranian woman with post-COVID-19 *Aspergillus fumigatus* endocarditis complicated by numerous thromboembolisms. She underwent mitral valve replacement surgery and multiple lower extremity embolectomies and was treated with voriconazole, which led to her final recovery.

Conclusions *Aspergillus* endocarditis should be considered in any patient with suspected endocarditis who has a history of COVID-19 infection and does not respond to routine antibiotic and antifungal therapy, as COVID-19 interferes with proper immune function, and lack of underlying cardiac conditions and immunodeficiencies does not preclude the diagnosis. Culture and histopathological evaluation of vegetations and emboli, as well as PCR, can confirm the diagnosis. Early initiation of antifungal therapy and surgical removal of infected valves and emboli can improve prognosis in patients with *Aspergillus* endocarditis.

Keywords *Aspergillus*, Endocarditis, COVID-19, Fungal infection, Opportunistic infection, Review

Introduction

Since the start of the coronavirus disease-2019 (COVID-19) pandemic in December 2019, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has rapidly spread worldwide, infecting over 410 million people and

causing over 5 million deaths globally up to February 2022 [1]. There have been many reports of co-infections with different fungal and bacterial organisms in COVID-19 patients, which were associated with increased mortality [2, 3]. COVID-19 patients, particularly those in need of intensive care unit (ICU) admission, have several risk factors that can predispose them to invasive fungal infections, including intubation and mechanical ventilation, corticosteroid therapy, chronic respiratory diseases, and ongoing inflammation and cytokine storm [4]. Invasive candidiasis, mucormycosis, cryptococcosis, and aspergillosis have all been reported in COVID-19

†Azadeh Goodarzi and Farnoosh Seirafianpour have contributed equally to the article, and both of them are corresponding authors

*Correspondence:

Farnoosh Seirafianpour
farnoosh.se@gmail.com

Azadeh Goodarzi

goodarzi.a@iums.ac.ir; azadeh_goodarzi1984@yahoo.com

Full list of author information is available at the end of the article



patients, involving different organs such as the lungs, brain and heart [5].

Reports indicate that a significant number of individuals experience lingering symptoms following a COVID-19 infection, with percentages varying depending on the severity of the case. Hospitalized patients can exhibit ongoing symptoms in a range of 32.6% to 87%, while non-hospitalized patients report symptoms such as fatigue (37%) and cognitive impairment (30%) [6, 7]. In Wuhan, China, 76% of those previously infected still faced at least one symptom six months after discharge, and a study in Melbourne discovered persistent symptoms in 34% of individuals even after 45 weeks [8].

The prevailing theory points to an autoimmune process characterized by an overactive innate immune response and cytokine activation [9, 10]. Severe COVID-19 cases often display significantly elevated levels of pro-inflammatory cytokines, including interleukin 6, interleukin-1 beta, interleukin-2, interleukin-8, interleukin-17, granulocyte colony-stimulating factor, granulocyte-macrophage colony-stimulating factor, chemokine ligand 2, and chemokine ligand 10, as well as tumor necrosis factor alpha. This excessive cytokine activity is recognized as a “cytokine storm” [9].

The exact cause of this post-viral syndrome, which shares similarities with chronic fatigue syndrome (now termed post-viral fatigue syndrome or PVFS), remains unknown. Notably, it occurs in both hospitalized and non-hospitalized patients, seemingly independent of the initial infection's severity [11]. Some suggest that the underlying mechanism leading to neurological damage might be indirect, involving immune-related microvascular inflammation and thrombosis, which could explain the absence of viral markers. Importantly, the extent of proinflammatory markers appears to be linked to cognitive and behavioral changes [11].

Aspergillus spp. is among the fungal organisms that can complicate COVID-19 and lead to life-threatening infections in these patients. Some of the risk factors for aspergillosis in these patients include corticosteroid use, chronic obstructive pulmonary disease, prolonged neutropenia, immunodeficiencies, impaired mucociliary clearance, and other structural lung diseases [5, 12].

Most of the reported co-infections with *Aspergillus spp.* in COVID-19 patients are pulmonary infections. In a study from Germany, invasive COVID-19-associated pulmonary aspergillosis was found in 5 out of 19 patients who had moderate to severe acute respiratory distress syndrome (ARDS) [13]. In another study from Spain, 3.3% of ICU-admitted COVID-19 patients were diagnosed with COVID-19-associated pulmonary aspergillosis. These patients were mostly immunocompetent, had

ARDS, and received corticosteroid therapy. Their mortality rate was 100% [14].

In this article, we present the first case of post-COVID-19 *Aspergillus fumigatus* endocarditis to our knowledge, complicated by numerous thromboembolisms.

Case presentation

A 58-year-old Iranian woman was admitted to a secondary healthcare center complaining of paresthesia and weakness in her left lower limb which had begun abruptly on the night before admission. Her past medical history was notable for rheumatoid arthritis (with a drug history of 5 mg of prednisolone every other day and 200 mg of hydroxychloroquine taken daily) and a hospital admission due to COVID-19 nine months ago. The patient did not report any history of heart diseases, coagulation disorders and had not received any COVID-19 vaccinations. The patient did not report any history of heart diseases, or coagulation disorders and had not received any COVID-19 vaccinations. The patient underwent color Doppler ultrasonography of the lower limbs at the mentioned center and was diagnosed with arterial thrombosis of the left lower limb. She was referred to our hospital for further treatment.

On admission, the patient's vital signs showed no fever, a blood pressure of 130/80 mmHg and a heart rate of 95 beats per minute. Physical examination revealed that the left lower limb was noticeably colder than the right lower limb, had much weaker distal pulses, and had an O₂ saturation of 85% as opposed to 95% in the right lower limb.

Initial laboratory results showed a slightly elevated leukocyte count of $10.5 \times 10^3/\text{mm}^3$ (normal $4\text{--}10 \times 10^3/\text{mm}^3$), a hemoglobin level of 9.3 g/dl (normal 12–16 g/dl), thrombocytopenia with a count of $95 \times 10^3/\text{mm}^3$ (normal $140\text{--}440 \times 10^3/\text{mm}^3$), normal liver function tests, increased lactate dehydrogenase (LDH: 891 U/L, normal 225–500 U/L), increased C-reactive protein (CRP: >24 mg/L, normal <6 mg/L), increased erythrocyte sedimentation rate (ESR: 73 mm/hour, normal <15 mm/hour), and an abnormal coagulation panel (INR: 1.16, normal 1–1.1; PT: 15.5, normal 12–13; PTT: 62.2, normal 25–45) (Table 1).

The patient underwent a CT angiography of the lower limbs and was immediately sent to the operating room (OR) for aortic and iliofemoral thrombectomy. The patient was initially started on ceftriaxone and vancomycin (in the first 48 hour), which was changed to meropenem and vancomycin (and continued for 3 weeks). After the preliminary pathology results of the lower limb emboli revealed possible fungal hyphae, amphotericin B was also added to the treatment regimen (it was used

Table 1 Laboratory findings

Laboratory indicators	In this patient	Normal range
Leukocyte count	10.5 × 10 ³ /mm ³	4–10 × 10 ³ /mm ³
Hemoglobin level	9.3 g/dl	12–16 g/dl
Platelet count	95 × 10 ³ /mm ³	140–440 × 10 ³ /mm ³
Lactate dehydrogenase	891 U/L	225–500 U/L
C-reactive protein	> 24 mg/L	< 6 mg/L
Erythrocyte sedimentation rate	73 mm/hour	< 15 mm/hour
INR	1.16	1–1.1
PT	15.5	12–13
PTT	62.2	25–45

PTT Partial Thromboplastin Time, PT Prothrombin Time, INR International Normalised Ratio, mm/hr millimeters per hour, mg/L milligrams per Liter, mm millimeter, g/dl grams per deciliter, U/L Units per Litre

for 5 days). The specimen was sent for further cultural evaluations.

The day after the surgery, the physical examination showed a significant improvement in circulation in the left lower limb, but the distal pulses of the right lower limb could not be palpated. Considering that acute signs of ischemia were not present in the right lower limb, possible thrombectomy of the right lower limb was postponed until the source of the emboli was found.

To find the source of the lower limb emboli, an echocardiogram was performed, which showed a large mobile mass on the tip of the A2 scallop [16 mm] and another mass (6 × 7 mm) attached to mitral valve chorda in the left ventricle (Fig. 1). The patient was scheduled for mitral valve replacement (MVR), which was performed one week after the left lower limb thrombectomy. The

preliminary pathology report of the cardiac vegetation was also suggestive of a fungal infection, possibly aspergillosis or mucormycosis. Accordingly, amphotericin B therapy was continued. A coronary angiography was performed before the surgery, which yielded normal results.

A day after the MVR surgery, the patient’s right lower limb showed mottling and signs of ischemia. Therefore, a superficial right femoral artery thrombo-endarterectomy and right common femoral embolectomy were performed. After the surgery, the right lower limb was still colder, and its distal pulses were weaker than those of the opposite limb. Two days after the right lower limb thrombectomy, the patient began experiencing pain in the right leg and showed signs of mottling. Color Doppler ultrasonography of the right lower extremity arteries showed a cut-off external iliac artery. Angiography of the right lower limb confirmed the findings of the Doppler ultrasonography, and percutaneous old balloon angioplasty (POBA) was performed on the right external iliac artery. Due to the high thrombosis burden of the patient, no stent was implanted, and surgical thrombectomy was suggested in case of medical failure. The patient developed a hematoma at the site of angiography and was sent to the operating room (OR) for thrombo-endarterectomy of the right common femoral artery. The day after the surgery, both lower limbs were warm, and distal pulses were strong.

The patient did not develop any further complications during admission and underwent medical therapy with Amphotericin B while waiting for the final pathology reports. Eventually, culture results of the mitral valve came back, showing the growth of *Aspergillus* spp. PCR sequencing was performed to determine the subtype

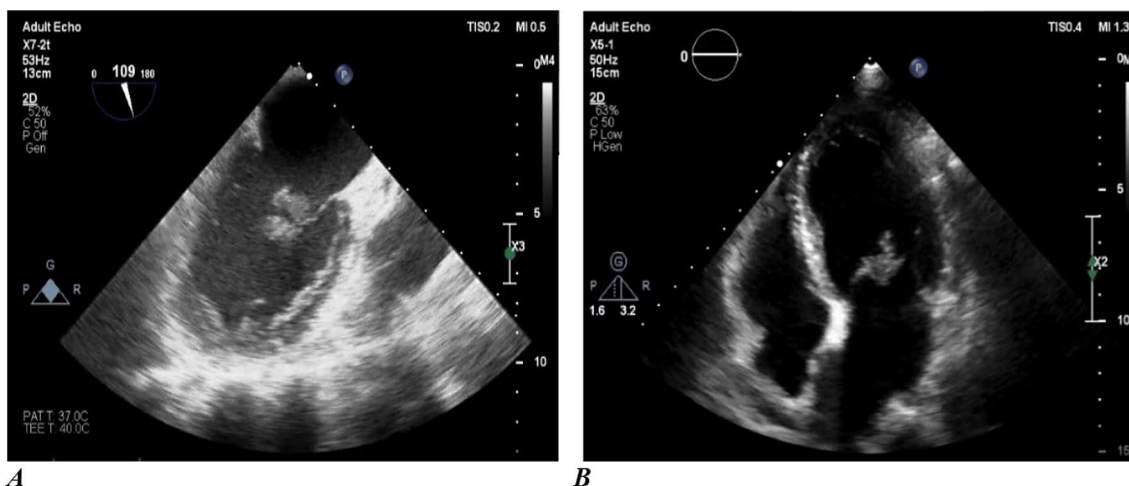


Fig. 1 Echocardiogram of the patient showing a large mobile mass on tip of A2 scallop (with a length of roughly 16 mm) and another mass (6 mm × 7 mm) attached to mitral valve chorda in the left ventricle. Left picture **a** is a transesophageal echo in a 109-degree view, and the right picture **b** is a transthoracic echo in a four-chamber view

of the organisms, and the results revealed *Aspergillus fumigatus* (*A. fumigatus*) as the culprit pathogen. The organism showed resistance to Amphotericin B in the fungogram study conducted on the cultures. Consequently, the patient’s treatment regimen was changed to Voriconazole. On day 25 of treatment, Amphotericin B was switched to Voriconazole, and the total duration of antifungal therapy was 6 months. The patient was followed for 7 months after discharge, and no further complications developed.

Discussion

Fungal endocarditis is an infrequent but lethal cause of endocarditis. After *Candida spp.*, *Aspergillus spp.* is the second most common cause of fungal endocarditis [15, 16]. Immunosuppression, bone marrow transplantation, intravenous drug use, indwelling central venous catheters, parenteral nutrition, cardiac structural abnormalities, prosthetic heart valves, cardiovascular surgery, use of steroids and cytotoxic medications, and prolonged broad-spectrum antibiotic use are some of the predisposing risk factors for fungal endocarditis [16].

According to this study, a patient can develop fungal endocarditis even with very weak immunosuppression conditions. Despite expectations regarding fungal behavior, their sensitivity and resistance must be assessed with a fungogram to guide treatment.

As mentioned, if the fungogram had not been performed for this patient, she would not have been treated with amphotericin B, potentially causing more harm to the patient.

It seems that the chronic use of prednisolone significantly contributed to these conditions for this patient, but it is undoubtedly not without the influence of contracting COVID-19 and experiencing weakened immune system and coagulation disorders.

In one study, viral load in COVID-19 patients was positively correlated with lymphocyte suppression [17]. Another study found that in COVID-19 patients, especially critically ill ones, leukocyte subpopulations were markedly reduced, and adaptive and innate immune responses, as well as T and NK cell functions, were impaired [18].

Immune dysregulation induced by COVID-19 has been implicated in the pathogenesis of other invasive fungal co-infections such as mucormycosis [19]. One study reported a case of endocarditis with *Candida tropicalis* in a COVID-19 patient with a history of cardiac valve replacement [20]. Thus, COVID-19-associated ongoing immunosuppression could have led to *Aspergillus* endocarditis in our patient. Table 2 shows a summary of reported endocarditis cases with unusual pathogens in COVID-19 patients. Additionally, SARS-CoV-2 and *A. fumigatus* were found to have common host–pathogen interaction targets. SARS-CoV-2 can recruit *Aspergillus* targets in addition to targets recruited by *A. fumigatus* itself. This can result in the development of invasive aspergillosis [21].

Most of the reported COVID-19-associated *Aspergillus spp.* infections are pulmonary [22, 23]. During severe COVID-19, infected cells release danger-associated molecular patterns (DAMPs) which are endogenous danger signals that promote the immune response and inflammation leading to lung injury. Damage to the lung epithelium and inflammation both predispose to pulmonary aspergillosis [24]. There is also a report of a brain abscess caused by *A. fumigatus* in a COVID-19 patient who had received dexamethasone and multiple antibiotics [25]. Our patient is the first case of post-COVID-19 *Aspergillus* endocarditis to our knowledge. We performed a literature review of the reported COVID-19-associated extra-pulmonary *Aspergillus* infections, which is presented in Table 3. Although most *Aspergillus*

Table 2 Summary of reported endocarditis cases with unusual pathogens in COVID-19 patients

Authors	Patient age	Patient gender	Comorbidities	Interval between COVID-19 and endocarditis	Pathogen	Outcome
Arbune et al. [27]	23	Female	Rheumatic fever	Simultaneous	<i>Streptococcus gordonii</i>	Recovery
Davoodi et al. [20]	66	Male	Mitral and aortic valve replacement	Simultaneous	<i>Candida tropicalis</i>	Death
Mouzakitis et al. [41]	83	Female	Coronary artery disease, hypertension, diabetes mellitus	Simultaneous	<i>Staphylococcus lugdunensis</i>	Death
Finch et al. [42]	Not reported (young)	Male	Seborrheic dermatitis	Simultaneous	<i>Haemophilus parainfluenzae</i>	Recovery
Benmalek et al. [26]	76	Female	Diabetes mellitus	10 days	Coagulase-negative <i>Staphylococcus</i>	Recovery

Table 3 Summary of reported cases of COVID-19-associated extra-pulmonary *Aspergillus* infections

Authors	Patient age	Patient gender	Comorbidities	Interval between COVID-19 and <i>Aspergillus</i> infection	Infection type	Medical treatment	Outcome
De Villiers De La Noue et al. [25]	60	Male	None	35 days	Brain abscess	Voriconazole	Recovery
Makhdoomi et al. [43]	85	Male	None	7 months	Spinal abscess	Liposomal Amphotericin B	Recovery
Hosseini-kargar et al. [44]	38	Male	Acute myeloid leukemia	Simultaneous	Rhinosinusitis	Fluconazole, Amphotericin B	Death
Hakamifard et al. [45]	35	Male	None	Simultaneous	Brain abscess	Voriconazole, Liposomal Amphotericin B	Death
Sahu et al. [46]	N/A	N/A	N/A	1–31 days	Endophthalmitis	Vitrectomy	Vision loss

N/A: not available

infections occurred simultaneously or within a short time frame from the initial COVID-19 infection [2, 4, 5, 21, 22, 26, 27], there have also been reports of unusual infections occurring months after COVID-19 diagnosis, presumably due to COVID-19-induced chronic immune dysregulation as discussed earlier [6–11, 17]. Accordingly, *Aspergillus* infections can involve many organs including the lungs, brain, and heart in post-COVID-19 patients and should be considered during evaluations or infections in these patients, even long after the initial COVID-19 diagnosis.

Previous studies have reported cases of *Aspergillus* endocarditis mostly in immunocompromised patients and patients with mechanical valves and other cardiac conditions [28–30]. However, there have also been a few immunocompetent patients without underlying cardiac diseases who presented with this infection [31, 32]. One study reported a case of *Aspergillus* endocarditis and fulminant mediastinitis which led to death in an immunocompetent and otherwise healthy patient [33]. Our patient also had no history of underlying cardiac diseases or surgeries. Thus, it is important to consider possible fungal infections in mildly immunosuppressed patients with suspected endocarditis and without underlying cardiac conditions, especially in those with a history of COVID-19.

Based on existing literature, among patients diagnosed with infectious endocarditis, the dominant fungal species were *Aspergillus fumigatus*, accounting for 47.5% of cases, and *Aspergillus flavus*, which constituted 24.6% of the cases. Notably, a substantial 54% of the patients exhibited embolic events as part of their clinical presentation. Treatment strategies encompassed antifungal therapy in 90.2% of cases, cardiac surgery in 85.2% of cases, or a combination of both these approaches in 78.7% of cases. The mortality rate

reached 52.5%. The immunosuppressed patients faced a significantly higher mortality rate in compared to their non-immunosuppressed counterparts, with rates of 59.4% versus 24.1%, respectively. Conversely, patients who underwent a combined treatment approach involving both cardiac surgery and azole therapy experienced a notably reduced mortality rate, standing at 28.1% compared to 65.5% for those who did not receive this dual therapy [34, 35]. In patients with *Aspergillus* endocarditis, vegetations are large and highly mobile, and peripheral emboli are common in the early stages [12]. Embolic phenomena are more common in *Aspergillus* endocarditis compared to bacterial endocarditis. The emboli can involve many organs, including brain, kidneys, spleen and lungs [36]. One study reported myocardial infarction caused by coronary artery embolism in a patient with *Aspergillus* endocarditis [36]. Lower extremity emboli similar to our patient's presentation have also been reported in previous studies [37, 38].

The diagnosis of *Aspergillus* endocarditis is obtained via 1,3- β -D-glucan testing, echocardiography, histopathologic evaluation and culture of the vegetations and emboli, as well as *Aspergillus* PCR. Transthoracic echocardiography (TTE) detects 90% of valvular vegetations [37]. The sensitivity of blood culture for the detection of *Aspergillus* infection is low. However, negative results do not exclude the diagnosis [39]. The most recent Infectious Diseases Society of America (IDSA) guidelines recommend using a combination of all the mentioned diagnostic tests for the detection of invasive aspergillosis [40]. In our patient, fungal vegetations were directly visualized on echocardiogram, and histopathological evaluation of both vegetations and emboli was suggestive of a fungal source of infection. The preliminary pathology results led to early initiation of antifungal therapy before the final confirmation of

A. fumigatus infection with PCR. This timely treatment could be the cause of our patient's good prognosis.

IDSA guidelines recommend early surgery in combination with antifungal treatment for *Aspergillus* endocarditis. A lipid formulation of amphotericin B or voriconazole is recommended as the initial treatment choice [40]. Our patient responded well to voriconazole in addition to MVR surgery and multiple embolectomies. However, her *A. fumigatus* strain showed resistance to amphotericin B, resulting in an initial lack of clinical response to treatment. Antifungal resistance has been reported among COVID-19-associated aspergillosis cases [41, 42]. This emphasizes the importance of early pathogen resistance profiling to optimize patients' treatment regimen and prognosis.

Conclusion

Aspergillus endocarditis should be considered in any patient, even with mild immunosuppression, who has a history of COVID-19 infection and does not respond to routine antibiotic and antifungal therapy, as COVID-19 interferes with proper immune function, and the lack of underlying cardiac conditions does not preclude the diagnosis. The mortality rate reported ranges from 50 to 68% in the literature. Culture and histopathological evaluation of vegetations and emboli and PCR can confirm the diagnosis. It is important to perform the fungogram test to check the sensitivity and resistance of fungi and choose the right treatment. Early initiation of antifungal therapy and surgical removal of infected valves and emboli can improve the prognosis in patients with *Aspergillus* endocarditis.

Abbreviations

ICU	Intensive care unit
COVID-19	Coronavirus disease-2019
ARDS	Acute respiratory distress syndrome
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
MVR	Mitral valve replacement
PCR	Polymerase chain reaction
TTE	Transthoracic echocardiography
IDSA	Infectious diseases society of America

Acknowledgements

The authors would like to express their gratitude to the staff of Rasool Akram Medical Complex clinical research development center (RCRDC) for their technical and editorial assistance.

Author contributions

ZY, SH and AG designed the study. MTS, MF, FS and KA wrote the paper. KA, AF, and YK reported the histopathology and immunohistochemistry of the case and F.S gathered the data and searched the literature. All authors contributed in editing the manuscript. All authors have read and approved the content of the final manuscript.

Funding

This study received no financial support.

Data availability

Data resulted from this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Informed consent was obtained and the rights of the subject were protected. To keeping ethical principles, name of the patient was not pointed in the paper. Institutional review board approval is not required for case report study at our institution. The patient received treatment consistent with the current standard of care.

Consent for publication

Written informed consent was obtained from the patients for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

None to declare.

Author details

¹Antimicrobial Resistance Research Center, Institute of Immunology and Infectious Diseases, Iran University of Medical Sciences, Niayesh Street, Sattarkhan Avenue, Rasool Akram Medical Complex, Tehran 1445613131, Iran. ²Research Center for Prevention of Cardiovascular Disease, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Niayesh Street, Sattarkhan Avenue, Rasool Akram Medical Complex, Tehran 1445613131, Iran. ³Department of Cardiology, Rasool Akram Medical Complex, Iran University of Medical Sciences, Niayesh Street, Sattarkhan Avenue, Rasool Akram Medical Complex, Tehran, Iran. ⁴Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Taleghani Ave, Nadery Ave, Tehran, Iran. ⁵Physiology Research Center, Iran University of Medical Sciences, Tehran, Iran. ⁶Razi Drug Research Center, School of Medicine, Iran University of Medical Sciences (IUMS), Iran University of Medical Sciences, Shahid Hemmat Highway, Tehran 1449614535, Iran. ⁷Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran. ⁸Pathology Department, Rasool Akram Medical Complex, Iran University of Medical Sciences, Tehran, Iran. ⁹Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center (RCRDC), School of Medicine, Iran University of Medical Sciences, Niayesh Street, Sattarkhan Avenue, Tehran 1445613131, Iran. ¹⁰Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran university of medical science, Tehran 1445613131, Iran.

Received: 29 May 2022 Accepted: 8 November 2023

Published online: 19 December 2023

References

- Allan M, Lièvre M, Laurenson-Schafer H, de Barros S, Jinnai Y, Andrews S, et al. The World Health Organization COVID-19 surveillance database. *Int J Equity Health*. 2022;21(Suppl 3):167.
- Liu HH, Yaron D, Piraino AS, Kapelusznik L. Bacterial and fungal growth in sputum cultures from 165 COVID-19 pneumonia patients requiring intubation: evidence for antimicrobial resistance development and analysis of risk factors. *Ann Clin Microbiol Antimicrob*. 2021;20(1):1–13.
- Silva D, Lima C, Magalhães V, Baltazar L, Peres N, Caligiorno R, et al. Fungal and bacterial coinfections increase mortality of severely ill COVID-19 patients. *J Hosp Infect*. 2021;113:145–54.
- Gangneux J-P, Bougnoux M-E, Dannaoui E, Cornet M, Zahar J. Invasive fungal diseases during COVID-19: we should be prepared. *Elsevier*; 2020. p. 100971.
- Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: a clinical and diagnostic perspective from China. *Mycopathologia*. 2020;185(4):599–606.
- Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. *Nat Med*. 2021;27(4):601–15.

7. Chopra V, Flanders SA, O'Malley M, Malani AN, Prescott HC. Sixty-day outcomes among patients hospitalized with COVID-19. *Ann Intern Med*. 2021;174(4):576–8.
8. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *The Lancet*. 2021;397(10270):220–32.
9. Chen C, Hauptert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global prevalence of post-coronavirus disease 2019 (COVID-19) condition or long COVID: a meta-analysis and systematic review. *J Infect Dis*. 2022;226(9):1593–607.
10. Lechner-Scott J, Levy M, Hawkes C, Yeh A, Giovannoni G. Long COVID or post COVID-19 syndrome. *Multiple Sclerosis Related Disord*. 2021;55: 103268.
11. Mueller MR, Ganesh R, Hurt RT, Beckman TJ, editors. Post-COVID conditions. *Mayo Clinic Proceedings*; 2023: Elsevier.
12. Cadena J, Thompson GR, Patterson TF. Aspergillosis: epidemiology, diagnosis, and treatment. *Infect Dis Clin*. 2021;35(2):415–34.
13. Koehler P, Cornely OA, Böttiger BW, Dusse F, Eichenauer DA, Fuchs F, et al. COVID-19 associated pulmonary aspergillosis. *Mycoses*. 2020;63(6):528–34.
14. Machado M, Valerio M, Álvarez-Uría A, Olmedo M, Veintimilla C, Padilla B, et al. Invasive pulmonary aspergillosis in the COVID-19 era: an expected new entity. *Mycoses*. 2021;64(2):132–43.
15. Badiiee P, Amirghofran AA, Nour MG, Shafa M, Nemati MH. Incidence and outcome of documented fungal endocarditis. *Int Cardiovasc Res J*. 2014;8(4):152.
16. Yuan-Min S. Fungal Endocarditis. *Braz J Cardiovasc Surg-BJCVS= Revista Brasileira de Cirurgia Cardiovascular-RBCCV*. 2016;31(3).
17. Wu H, He P, Ren Y, Xiao S, Wang W, Liu Z, et al. Postmortem high-dimensional immune profiling of severe COVID-19 patients reveals distinct patterns of immunosuppression and immunoactivation. *Nat Commun*. 2022;13(1):269.
18. Kalićniška E, Szymczak D, Zińczuk A, Adamik B, Smiechowicz J, Skalec T, et al. Immunosuppression as a hallmark of critical COVID-19: prospective study. *Cells*. 2021;10(6):1293.
19. Tabassum T, Araf Y, Moin AT, Rahaman TI, Hosen MJ. COVID-19-associated-mucormycosis: possible role of free iron uptake and immunosuppression. *Mol Biol Rep*. 2022;49(1):747–54.
20. Davoodi L, Faeli L, Mirzakhani R, Jalalian R, Shokohi T, Kermani F. Catastrophic *Candida* prosthetic valve endocarditis and COVID-19 comorbidity: a rare case. *Curr Med Mycol*. 2021;7(2):43.
21. Khan AA, Farooq F, Jain SK, Golinska P, Rai M. Comparative host-pathogen interaction analyses of SARS-CoV2 and *Aspergillus fumigatus*, and pathogenesis of COVID-19-associated aspergillosis. *Microbial Ecol*. 2021;84:1236.
22. Wu S, Yang S, Chen R, Chen H, Xu Y, Lin B. Dynamic immune response profiles and recovery of a COVID-19 patient with coinfection of *Aspergillus fumigatus* and other baseline diseases: a case report. *OMICS J Integrative Biol*. 2020;24(10):615–8.
23. Salehi M, Khajavirad N, Seifi A, Salahshour F, Jahanbin B, Kazemizadeh H, et al. Proven *Aspergillus flavus* pulmonary aspergillosis in a COVID-19 patient: a case report and review of the literature. *Mycoses*. 2021;64(8):809–16.
24. Arastehfar A, Carvalho A, van de Veerdonk FL, Jenks JD, Koehler P, Krause R, et al. COVID-19 associated pulmonary aspergillosis (CAPA)—from immunology to treatment. *J Fungi*. 2020;6(2):91.
25. De Villiers De La Noue V, Dobanton B, Rosman J, Mateu P. Intracerebral *Aspergillus fumigatus* abscess and SARS-CoV-2. *Intensive Care Med*. 2021;47(9):1032–3.
26. Benmalek R, Mechal H, Choukrallah H, Maaroufi A, Benouna EG, Habbal R, et al. Bacterial co-infections and superinfections in COVID-19: a case report of right heart infective endocarditis and literature review. *Pan Afr Med J*. 2020;35(Suppl 2):40.
27. Arbune M, Iancu AV, Lupasteanu G, Vasile MC, Stefanescu V. A Challenge of COVID-19: associated infective endocarditis with *Streptococcus gordonii* in a young immunocompetent patient. *Medicina (Kaunas)*. 2021;57(12):1298.
28. Lázaro M, Ramos A, Ussetti P, Asensio A, Laporta R, Muñoz E, et al. Aspergillus endocarditis in lung transplant recipients: case report and literature review. *Transpl Infect Dis*. 2011;13(2):186–91.
29. Nose K, Nishioka T, Hayashi T. Infective endocarditis due to *Aspergillus* following kidney transplantation. *Int J Urol*. 2011;18(11):801–2.
30. Abuzaid AA, Zaki M, Tarif H. Atypical early *Aspergillus* endocarditis post prosthetic mitral valve repair: a case report. *Heart Views*. 2015;16(1):30.
31. Ikediobi U, Sutton RE. *Aspergillus fumigatus* native valve infective endocarditis in an otherwise healthy adult. *JMM Case Rep*. 2016;3(1).
32. Singh A, Goyal A, Singh B, Sood N. Pacemaker lead infective endocarditis in immunocompetent host due to *Aspergillus*: an uncommon occurrence. *Indian J Pathol Microbiol*. 2017;60(3):441.
33. Shakoor MT, Ayub S, Ayub Z, Mahmood F. Fulminant invasive aspergillosis of the mediastinum in an immunocompetent host: a case report. *J Med Case Rep*. 2012;6(1):1–5.
34. McCormack J, Pollard J. *Aspergillus* endocarditis 2003–2009. *Med Mycol*. 2011;49(Suppl 1):S30–4.
35. Valerio M, Camici M, Machado M, Galar A, Olmedo M, Sousa D, et al. *Aspergillus* endocarditis in the recent years, report of cases of a multicentric national cohort and literature review. *Mycoses*. 2022;65(3):362–73.
36. Seo GW, Seol SH, No TH, Jeong HJ, Kim TJ, Kim JK, et al. Acute myocardial infarction caused by coronary embolism from *Aspergillus* endocarditis. *Internal Med (Tokyo, Japan)*. 2014;53(7):713–6.
37. Al-Mashdali AF, Alamin MA, Kanaan AM, Alkhulaifi A, Al Kindi DI. Fatal native aortic valve fungal endocarditis caused by *Aspergillus flavus*: a case report. *IDCases*. 2021;26: e01310.
38. Reis LJ, Barton TD, Pochettino A, Velazquez O, McGarvey M, Milas B, et al. Successful treatment of *Aspergillus* prosthetic valve endocarditis with oral voriconazole. *Clin Infect Dis*. 2005;41(5):752–3.
39. Carvalho JA, Boavida L, Amorim Ferreira I, Grima B, Delgado AJ. Native valve aspergillus endocarditis in a non-neutropenic immunocompromised patient on Anti-TNF a blockers therapy. *Cureus*. 2021;13(12): e20629.
40. Patterson TF, Thompson GR 3rd, Denning DW, Fishman JA, Hadley S, Herbrecht R, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):e1–60.
41. Mouzakitzi I, Kleinaki Z, Petropoulou T, Alexiou E, Stefanidis A. *Staphylococcus lugdunensis* native valve endocarditis in a patient with confirmed COVID-19: a cautionary tale of an old disease not to be forgotten in the pandemic era. *Cureus*. 2021;13(9): e17724.
42. Finch LC, Gerdzhikov S, Buttery R. *Haemophilus parainfluenzae* endocarditis presenting with symptoms of COVID-19. *BMJ Case Rep*. 2021;14(8):e245210.
43. Makhdoomi R, Malik N, Charan J, Malik A, Singh S. Spinal aspergillosis: a rare complication of COVID-19 infection. *Egypt J Neurosurg*. 2022;37(1):6.
44. Hosseinikargar N, Basiri R, Asadzadeh M, Najafzadeh MJ, Zarrinfar H. First report of invasive *Aspergillus rhinosinusitis* in a critically ill COVID-19 patient affected by acute myeloid leukemia, northeastern Iran. *Clin Case Rep*. 2021;9(10): e04889.
45. Hakamifard A, Hashemi M, Fakhim H, Aboutalebain S, Hajiahmadi S, Mohammadi R. Fatal disseminated aspergillosis in an immunocompetent patient with COVID-19 due to *Aspergillus ochraceus*. *J de Mycologie Medicale*. 2021;31(2): 101124.
46. Sahu ES, Lahoti K, Bhargava A, Subhedar V, Sahu A. Subretinal aspergillus abscess in post COVID-19 recovered patients—an emerging problem. *Ocul Immunol Inflamm*. 2023;31(1):127–33.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.