International Journal of Research in Medical Sciences
Castillo Martinez DB et al. Int J Res Med Sci. 2022 Oct;10(10):2291-2295
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20222537

Case Report

Pulmonary artery mycotic aneurism owing to aspergillus in SARS-CoV-2 convalescent: a case report and literature review

Daniel Benito Castillo Martínez[1]*, Doris Michelle Palacios Rivera[1], José Luis Ruiz Pier[2], Álvaro Mendoza Carranza[3]

[1]Department of General Surgery, North Central PEMEX Hospital, Mexico City, Mexico
[2]Department of Cardiothoracic Surgery, North Central PEMEX Hospital, Mexico City, Mexico
[3]Department of Imaging and Radiology, North Central PEMEX Hospital, Mexico City, Mexico

Received: 06 August 2022
Accepted: 03 September 2022

***Correspondence:**
Dr. Daniel Benito Castillo Martínez,
E-mail: drdancastillo@icloud.com

ABSTRACT

Invasive aspergillosis is a severe illness described in immune-compromised and critically ill non-immuno-compromised patients. Aspergillosis and COVID-19 co-infection cases harbor multiple unfavorable prognostic factors, with a 44% mortality versus 19% without aspergillosis. We presented the case of a 61-year-old man known with hypertension, diabetes, and smoking that went through COVID-19 infection, during the convalescent period presented multiple hemoptoic events due to *A. fumigatus* mycotic pseudoaneurysm, successfully resolved by selective angioembolization. Selective angioembolization is an effective alternative for high surgical risk due to comorbidities in the treatment of pulmonary mycotic aneurism.

Keywords: Mycotic aneurism, Pulmonary aspergillosis, SARS-CoV-2

INTRODUCTION

Aspergillosis is a major health problem that, despite prevention measures in vulnerable populations, continues to register a significant number of cases per year in its severe forms.[1]

Invasive aspergillosis is a serious disease described in immunosuppressed patients and critically ill non-immunosuppressed patients where autopsy studies suggest that the incidence may be underestimated, COPD, hematological malignancies, bacterial infection, malnutrition, diabetes, renal replacement therapy, frequent use of inhalers and systemic steroids have been considered as risk factors for aspergillosis with a recorded mortality of more than 80%.[2-6]

Distinguishing between benign colonization of the respiratory tract and disease represents a diagnostic challenge because it infrequently causes inflammation or invasion, remaining subclinical in most cases.[7] On the other hand, viral pneumonia increases the susceptibility of patients to invasive bacterial and fungal infections since respiratory viruses cause direct damage to respiratory tissue, in addition to hindering ciliary and conidia clearance, which leads to local immune dysfunction manifested as a state of pulmonary immunosuppression.[3,6]

The role of the lung microbiome is not yet fully understood, however, its involvement in the immune response is recognized and imbalance in the microbiome is an important factor in the development and severity of lung infections.[5] COVID-19 infection leads to decreased T cell populations, especially in patients with severe disease, which modifies the immune response and favors the growth and proliferation of microorganisms.[7,8]

Some studies suggest a higher risk of co-infection with Aspergillus in critically ill patients, mainly due to changes in immune kinetics.[5-7,9]

Cases of co-infection with COVID-19 and aspergillosis harbor many baseline prognostic factors with negative effects on survival, with mortality of 44% versus 19% in patients without aspergillosis.[8]

CASE REPORT

A 61-year-old male with a history of systemic arterial hypertension treated with bisoprolol, type 2 diabetes mellitus treated with vidagliptin in combination with metformin, prostatic growth treated with tamsulosin, and long-standing positive smoking habit, diagnosed with COVID-19 on 28 January 2021 by PCR, managed with dexamethasone, ceftriaxone, prednisone and theophylline, required low-flow home oxygen, persisting with chronic cough.

Fourteen weeks later, he presented an event of isolated hemoptysis, which was repeated on 3 other occasions in the following 7 days without hemodynamic repercussions with an estimated volume per event of less than 100 milliliters, he underwent a panendoscopy with no abnormalities and a chest tomography finding an intracavitary pseudoaneurysm dependent on the right interlobar artery (Figure 1), a sputum culture was performed, which was positive for *Klebsiella Oxytoca* and *Aspergillus fumigatus*, he received treatment with ertapenem, tranexamic acid and voriconazole for 4 weeks initially and later with itraconazole.

Spirometry was performed with FEV1 of 44%, vital capacity 1.18 l, Gupta score 2.5 %, Ariscat score 68 points with a 42.1% risk of perioperative complications, so the case was held in session and an interventional radiology approach was decided, which was performed in the catheterization room under sedation, with right femoral cannulation, Pigtail (6 FR×100 cm) was advanced to the pulmonary trunk, an arteriography was performed with blood pressure of 65/31 mmHg, showing retention of the contrast medium at the level of the upper segmental artery of the right lower lobe corresponding to the image of the pseudoaneurysm with a neck of approximately 7-7.8 mm, adequate distal perfusion and 10% pneumothorax by Kircher index (Figure 2).

The aneurysmal neck was cannulated with a wire guide (0.36 mm×300 cm) and subsequently with a microcatheter (2.6 Fr×150 cm) through which 2 Penumbra COILS (60 cm×51 mm) were advanced with release in the pseudoaneurysmal body, subsequently, a 10×7 mm amplatzer vascular occluder plug was placed, releasing the first disc in the distal neck, the second and third disc in the proximal segment, control angiography was performed, confirming adequate placement without evidence of passage of the contrast medium into the lumen of the pseudoaneurysm with total occlusion without complications or incidents (Figure 3).

Tomographic control was performed at the end of the procedure and at 90 days. He progressed with satisfactory evolution without recurrence in outpatient follow-up for 6 months (Figure 4).

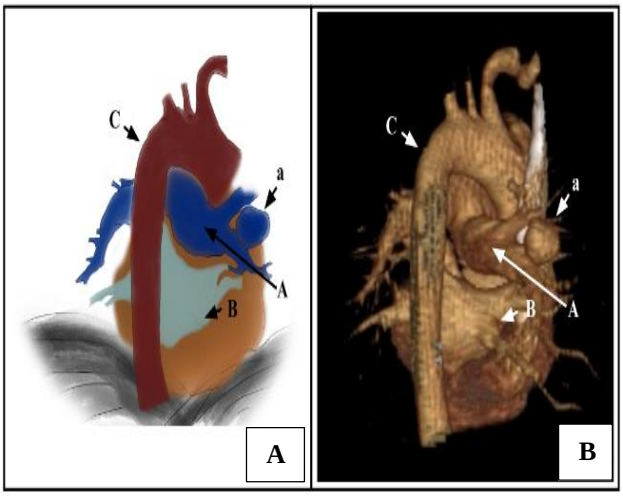

Figure 1: Pseudoaneurysm dependent on the right interlobar artery (rear view)- (A) representative illustration; and (B) three-dimensional tomographic reconstruction.

Note: A- Right pulmonary artery, a- pseudoaneurysm, B- pulmonary veins, and C- aortic arch.

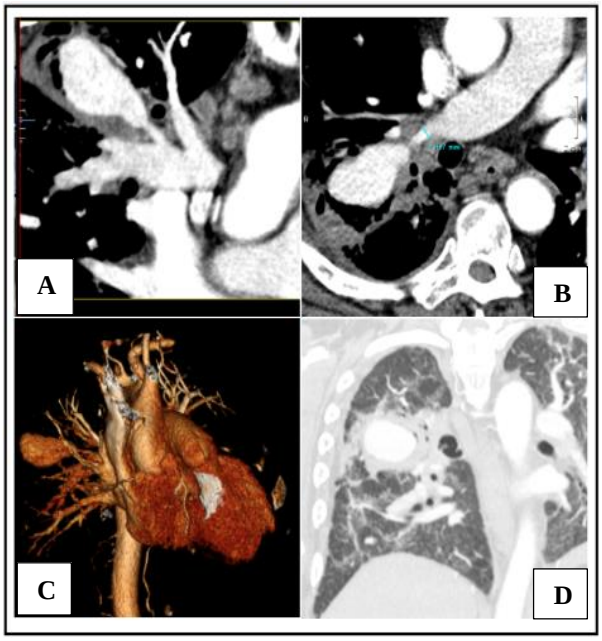

Figure 2: Tomographic control 7 days prior to the procedure- (A) chest angiotomography with curviplanar reconstruction showing pulmonary cavitation and inside the right interlobar pseudoaneurysm with dimensions of 5×2.5×3 cm; (B) chest angiotomography with measurement of the neck of the pseudoaneurysm with a diameter of 6.7 mm and a length of 2 cm; (C) 3D volume rendering reconstruction, where the pseudoaneurysm is observed at the upper right interlobar level (right lateral view); and (D) coronal section with pulmonary window where post-COVID changes are observed.

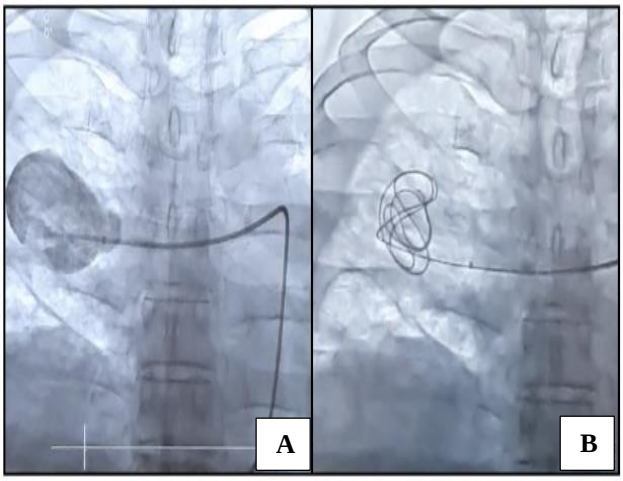

Figure 3: Angiographic controls- (A) angiography showing pseudoaneurysm; and (B) fluoroscopic control where placement of coils is observed.

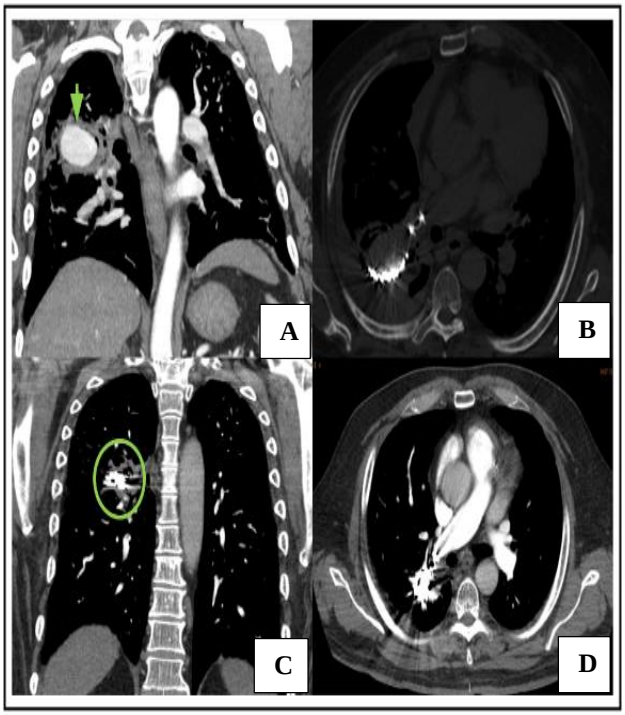

Figure 3: Tomographic controls 90 days after the procedure- (A) coronal reconstruction angiotomography of the chest prior to the procedure showing the right superior interlobar pseudoaneurysm (arrow); (B) axial section with bone window showing the coils in the lumen and occluder in the neck of the pseudoaneurysm (vascular plug); (C) coronal section showing the coils and collapsed cavitation (circle); and (D) axial section with collapsed pseudoaneurysm and no evidence of flow.

DISCUSSION

Aspergillus is a saprophytic fungus of the Thricomaceae family, of which 900 species have been described, classified into 18 groups, of which 12 are known to be capable of causing disease in humans: *Aspergillus fumigatus, A. flavus, A. niger, A. terreus, A. versicolor, A. nidulans, A. glaucus, A. clavatus, A. cervinus, A. candidus, A. flavipes, and A. ustus, A. fumigatus* being the most frequent species in human diseases.[5,10]

Structurally, *A. fumigatus* has a cell wall that is composed in its internal portion of an organized fibrillar structure composed of branched chitin with galactomannan, 1,3-β-glucans and 1,4-β-glucans linked by covalent bonds that are immersed in a matrix composed of 1,3-α-glucans and galactosaminogalactan.[11] In the external portion of the wall in the hypha, cell adhesion glycoproteins, inducers of apoptosis and platelet activation are expressed, on the other hand, in the conidia, RodA hydrophobin, melanin and 1,3-α-glucans are expressed.[12] A. *fumigatus* disperses specialized hyphae into the air in the form of conidiospores which can be isolated in air samples in hospitals, the spores have a size of 2 to 3 µm, so they have the capacity to reach the alveoli and on average the human being inhales 100 to 1000 spores per day, if they are not removed by the ciliary system and alveolar macrophages, the spores germinate within 4-6 hours at 37°C, forming germ tubes.[13,14] During colony formation, *A. fumigatus* incorporates its hyphae into the extracellular matrix, forming a biofilm known as aspergilloma.[15]

A. fumigatus has one of the fastest growth rates which, along with other factors, correlates directly with its virulence, in addition, it has the capacity for metabolic plasticity that is not yet fully understood and at the pulmonary level it requires degradation by serine proteases and metalloproteinase to obtain nutrients for its survival and development, due to the immune response, *A. fumigatus* is subjected to metabolic stress due to deprivation of nitrogen sources, which is why it is capable of adapting its metabolism to carbon sources, a response that is regulated by the transcription factor CreA.[16-18] Among the essential requirements of *A. fumigatus* is iron, which although it is abundant in humans, obtaining it is a challenge because most of it is bound to proteins, especially transferrin and the heme group, being regulated by the transcription factors SreA and Hapx.[19] The acquisition and storage of iron is carried out by the sideropore, which is composed of four subunits, two extracellular subunits for obtaining (fusarinin C and triacetylfusarinin C) and two intracellular subunits for storage (ferricrocin for storage in the hyphae and hydroxyferricrocin in the conidia).[20] On the other hand, calcium is necessary for growth and zinc for survival.[21,22]

In immunocompetent subjects, clinical manifestations depend largely on the host, such as simple aspergilloma, aspergillus nodule, and chronic cavitary pulmonary aspergillosis.[4] Clinically, they present with fever of variable intensity, cough, sputum, dyspnea, pleuritic chest pain, bronchospasm, and hemoptysis. It may present with antibiotic-resistant fever as the only sign in the early stages of the disease, making its diagnosis difficult, and although

the clinical presentation of isolated massive hemoptysis is infrequent, it represents a life-threatening complication with an estimated mortality rate of 38%.[5,23]

Angioinvasion is an important feature of invasive aspergillosis.[4,5] One of the main theories in the pathogenesis of vascular invasion is the endovascular seeding of multiple emboli causing destruction of the wall from the inside.[24,25] The presence of pulmonary artery aneurysms associated with fungal infections is more frequent in patients with endocarditis and they represent approximately 0.6-2% of all aneurysms.[24,26] Vascular invasive lesions associated with fungal infections are pseudoaneurysms, an important distinction since they have a higher risk of bleeding, with severe hemoptysis usually being fatal in these patients.[9,25,27]

The use of antibiotics has been associated with a decrease in the incidence of these, although medical treatment with antibiotics is usually insufficient and carries a risk of persistent infection.[2,25] Open surgical management is the most frequently performed because it avoids the implantation of synthetic material in the focus, however, in some cases it is not feasible due to the morbidity and mortality rate of up to 40% mainly due to comorbidities and it is in these cases that endovascular therapy emerges with favorable results in selected patients, being an effective and minimally invasive procedure, it may even be considered as the first line of treatment by some authors.[9,24,26,28,29]

Traditionally, the management of mycotic or infectious aneurysms has consisted of surgical repair with resection of the affected segment, extensive local debridement and repair in situ or with extra-anatomical bridges, these treatment modalities present mortality between 22 and 36%.[26] Due to the potential risk of high mortality of up to 50% secondary to the growth of the pseudoaneurysm and its rupture, context in which immediate treatment is mandatory.[24,30,31] Some consider bronchial artery embolization simply as a bridging therapy until definitive treatment can be provided.

Risk factors for recurrence are active aspergillosis, hemoptysis that required blood transfusion, and continuous hemoptysis in the first week after embolization.[23] Due to the low incidence of this pathology, few bibliographies mention the indication of treatment, the recommendation is based on the hemoptoic volume, oxygenation and extension of the arterial damage, a suggested cut-off point is a volume <200 ml in 24-48 hours to consider the interventional radiology approach with embolization.[24,29,30]

Successful intraluminal coiling requires an intact coagulation cascade and reduced blood pressure to promote thrombosis, making this option challenging because mycotic pseudoaneurysms commonly present with sepsis and coagulopathy.[25] The placement of stents or grafts in patients with active bacteremia or resistant microorganisms should be avoided due to the high possibilities of graft seeding.[25]

CONCLUSION

The management of mycotic pulmonary aneurysm by interventional radiology with embolization is an effective therapeutic alternative that should be considered within the main therapeutic options, especially in cases in which comorbidities represent a high perioperative risk for the patient, and can be considered as first-line treatment, however, more studies are needed to extend this recommendation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Brown GD, Denning DW, Gow NA, Levitz SM, Netea MG, White TC. Hidden killers: human fungal infections. Sci Transl Med. 2012;4(165):165rv13.
2. Cooper V, Bera R, Sherman R, Beed M. Pulmonary Artery Aneurysm Caused by Aspergillus Pneumonia Presenting as an Endobronchial Mass Lesion. J Intens Care Soc. 2013;14(3):263-5.
3. Tudesq JJ, Peyrony O, Lemiale V, Azoulay E. Invasive Pulmonary Aspergillosis in Nonimmunocompromised Hosts. Semin Respir Crit Care Med. 2019;40(4):540-7.
4. Piracha S, Mahmood A, Qayyum N, Ganaie MB. Massive haemoptysis secondary to mycotic pulmonary artery aneurysm in subacute invasive aspergillosis. BMJ Case Rep. 2018;2018:bcr2017223088.
5. Ledoux MP, Guffroy B, Nivoix Y, Simand C, Herbrecht R. Invasive Pulmonary Aspergillosis. Semin Respir Crit Care Med. 2020;41(1):80-98.
6. 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.
7. Marr KA, Platt A, Tornheim JA, Zhang SX, Datta K, Cardozo C, et al. Aspergillosis Complicating Severe Coronavirus Disease. Emerg Infect Dis. 2021;27(1):18-25.
8. Koehler P, Bassetti M, Chakrabarti A, Chen SCA, Colombo AL, Hoenigl M, et al. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. Lancet Infect Dis. 2021;21(6):149-62.
9. Asai M, Houtte O, Sullivan TR, Garrido M, Pineda DM. Endovascular Repair of Three Concurrent Mycotic Pseudoaneurysms. Vasc Endovascular Surg. 2018;52(6):473-7.
10. Raper KB, Fennell DI. The genus Aspergillus. Baltimore: Williams and Wilkins; 1965: 686.

11. Latgé JP, Beauvais A. Functional duality of the cell wall. Curr Opin Microbiol. 2014;20:111-7.
12. Aimanianda V, Latgé JP. Fungal hydrophobins form a sheath preventing immune recognition of airborne conidia. Virulence. 2010;1(3):185-7.
13. Pini G, Faggi E, Donato R, Sacco C, Fanci R. Invasive pulmonary aspergillosis in neutropenic patients and the influence of hospital renovation. Mycoses. 2008;51(2):117-22.
14. Latgé JP. Aspergillus fumigatus and aspergillosis. Clin Microbiol Rev. 1999;12(2):310-50.
15. Loussert C, Schmitt C, Prevost MC, Balloy V, Fadel E, Philippe B, et al. In vivo biofilm composition of Aspergillus fumigatus. Cell Microbiol. 2010;12(3):405-10.
16. Rhodes JC. Aspergillus fumigatus: growth and virulence. Med Mycol. 2006;44:S77-81.
17. Vries RP, Visser J. Aspergillus enzymes involved in degradation of plant cell wall polysaccharides. Microbiol Mol Biol Rev. 2001;65(4):497-522.
18. Ries LN, Beattie SR, Espeso EA, Cramer RA, Goldman GH. Diverse Regulation of the CreA Carbon Catabolite Repressor in Aspergillus nidulans. Genetics. 2016;203(1):335-52.
19. Schrettl M, Kim HS, Eisendle M, Kragl C, Nierman WC, Heinekamp T, et al. SreA-mediated iron regulation in Aspergillus fumigatus. Mol Microbiol. 2008;70(1):27-43.
20. Haas H. Iron - A Key Nexus in the Virulence of Aspergillus fumigatus. Front Microbiol. 2012;3:28.
21. Brown NA, Goldman GH. The contribution of Aspergillus fumigatus stress responses to virulence and antifungal resistance. J Microbiol. 2016;54(3):243-53.
22. Moreno MA, Ibrahim-Granet O, Vicentefranqueira R, Amich J, Ave P, Leal F, et al. The regulation of zinc homeostasis by the ZafA transcriptional activator is essential for Aspergillus fumigatus virulence. Mol Microbiol. 2007;64(5):1182-97.
23. Ding WY, Chan T, Yadavilli RK, McWilliams R. Aspergilloma and massive haemoptysis. BMJ Case Rep. 2014;2014:bcr2013200019.
24. Chen Y, Gilman MD, Humphrey KL, Salazar GM, Sharma A, Muniappan A, et al. Pulmonary Artery Pseudoaneurysms: Clinical Features and CT Findings. AJR Am J Roentgenol. 2017;208(1):84-91.
25. Koneru H, Biswas Roy S, Islam M, Abdelrazek H, Bandyopadhyay D, Madan N, et al. Pulmonary Artery Pseudoaneurysm: A Rare Cause of Fatal Massive Hemoptysis. Case Rep Pulmonol. 2018;2018:8251967.
26. Patrón M, Russo A, Sosa F, González SG, Esperón A. Experiencia en el tratamiento endovascular de pseudoaneurismas arteriales infecciosos: presentación de tres casos. Angiología. 2021;73(2):95-9.
27. Herbst N, Truong AD. A case of pulmonary artery pseudoaneurysm caused by invasive pulmonary aspergillosis. Chest. 2020;158.
28. Didier M, Guedin P, Staub F, Catherinot E, Rivaud E, Scherrer A, et al. Pulmonary arterial mycotic pseudoaneurysms in a patient with invasive pulmonary aspergillosis. Successful occlusion by coils. Am J Respir Crit Care Med. 2014;190(1):112-3.
29. Khalil A, Fedida B, Parrot A, Haddad S, Fartoukh M, Carette MF. Severe hemoptysis: From diagnosis to embolization. Diagn Interv Imaging. 2015;96(7-8):775-88.
30. Garg A, Chandrasekaran K, Jadhav S, Chandok G, Ringe A, Sankhe A. Intra-aneurysmal glue embolisation of a giant pulmonary artery pseudoaneurysm after left upper lobe lobectomy: case report. Korean J Radiol. 2013;14(3):455-9.
31. Bhatty D, Srivali N. Pulmonary artery pseudoaneurysm: a rare cause of hemoptysis. QJM. 2020;113(5):351-2.

Cite this article as: Castillo Martinez DB, Palacios Rivera DM, Ruiz Pier JL, Mendoza Carranza AM. Pulmonary artery mycotic aneurism owing to aspergillus in SARS-CoV-2 convalescent: a case report and literature review. Int J Res Med Sci 2022;10:2291-5.