Official journal of the Spanish Society of Chemotherapy

Revista Española de Quimioterapia
doi:10.37201/req/075.2024 - Advance Access published October 10, 2024

Letter to the Editor

Marina Fayos[1,2]
Andrea Severo[3]
María Dolores García-Cosío[3]
Carlos Prados[4]
Marina Alonso[4]
Francisco López-Medrano[1,2]

Nocardia and mucoral co-infection in heart transplant recipient

[1]Unit of Infectious Diseases, Hospital Universitario "12 de Octubre", Instituto de Investigación Sanitaria Hospital "12 de Octubre" (imas12), Madrid, Spain.
[2]Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.
[3]Department of Cardiology, Hospital Universitario "12 de Octubre". Madrid, Spain.
[4]Department of Pathological anatomy. 12 de Octubre University Hospital. Madrid, Spain.

Article history
Received: 19 July 2024; Revision Requested: 12 September 2024; Revision Received: 13 September 2024; Accepted: 20 September 2024; Published: 10 October 2024

Sir,

Bacterial and fungal coinfection presents a significant diagnostic and therapeutic challenge in solid organ transplant recipients. This case involves a heart transplant recipient who developed pulmonary consolidation and multiple brain lesions. *Nocardia farcinica* was isolated from a subcarinal adenopathy, but despite targeted treatment, new lesions appeared in the lungs, brain, and stomach. Additionally, *Cunninghamella* spp. was detected in a bronchoalveolar lavage, leading to a complicated clinical course.

A 64-year-old male underwent heart transplantation in March 2022 for ischemic cardiomyopathy. The patient received induction therapy with basiliximab (2 doses) and was on immunosuppressive therapy with tacrolimus 1,5 mg every 12 hours (last levels 9.7 ng/ml), everolimus 0,5 mg every 12 hours (last levels < 0.30 ng/ml), and prednisone 15 mg per day. In October 2023, he was admitted for Ogilvie syndrome following a hernioplasty, where he received meropenem due to respiratory symptoms and radiological findings (Figure 1A). A follow-up computed tomography (CT) revealed a decrease in consolidation after treatment, along with a subcarinal adenopathy (Figure 1B). Despite initial improvement, the patient's condition deteriorated, leading to readmission and further diagnostic challenges.

A transbronchial biopsy of the subcarinal adenopathy performed on day +7 of admission revealed the presence of *N. farcinica* in the culture, leading to targeted therapy with cotrimoxazole 1600/320 mg every 8 hours and meropenem 1 g every 8 hours. However, the patient's clinical condition continued to deteriorate, with the development of multiple abscesses detected on brain magnetic resonance imaging (MRI) performed on day +21 of admission (Figure 1C). Suspecting disseminated nocardiosis, the dosage of meropenem was increased to 1,5 g every 8 hours, but the patient's condition worsened further. On day +24, the patient exhibited a reactivation of cytomegalovirus (CMV) infection with 8800 copies/ml. A follow-up chest CT scan on day +35 showed worsening consolidation in the left upper lobe with cavitation and involvement of the right upper lobe. The serum levels of Wako beta-D-glucan were 37.84 pg/ml, and galactomannan was negative. Suspecting an invasive fungal superinfection, liposomal amphotericin B was started at a dose of 5 mg/kg/24h. Additionally, moxifloxacin was added to the meropenem and cotrimoxazole regimen due to concerns about Nocardia progression.

Further complications arose, and the patient required admission to the Intensive Care Unit (ICU) on day +39. Complications included gastrointestinal bleeding, respiratory distress, and neurological deficits. A cranial CT scan revealed a subacute ischemic lesion newly appearing in the left parietal area, with improvement of the previous lesions observed on the MRI. Additionally, an endoscopy showed multiple necrotic gastric ulcers. Due to the progression of the condition, the patient continued to receive an antibiotic regimen for *Nocardia* consisting of cotrimoxazole, imipenem, and amikacin. The antifungal treatment was changed to isavuconazole after *Aspergillus fumigatus* was isolated from a sputum culture taken on day +35. A subsequent bronchoalveolar lavage on day +41 revealed non-septate mycelia consistent with mucorales and the isolation of *Cunninghamella* spp. in the culture. Surgical intervention for suspected disseminated mucormycosis was ruled out by the thoracic surgery department at that time. Despite intensive medical support and treatment in the ICU, the patient deteriorated rapidly and passed away on day +45 of hospitalization.

A clinical autopsy confirmed the presence of mucormycosis in the lungs, gastric ulcers, spleen, and central nervous system, as well as *Nocardia* infection in lymph nodes and the central nervous system (Figure 2). The cause of death

Correspondence:
Marina Fayos
Hospital Universitario 12 de Octubre. Madrid.
Av. Cordoba, s/n, Usera, 28041. Madrid, Spain.
E-mail: marina.fayos.perez@gmail.com.

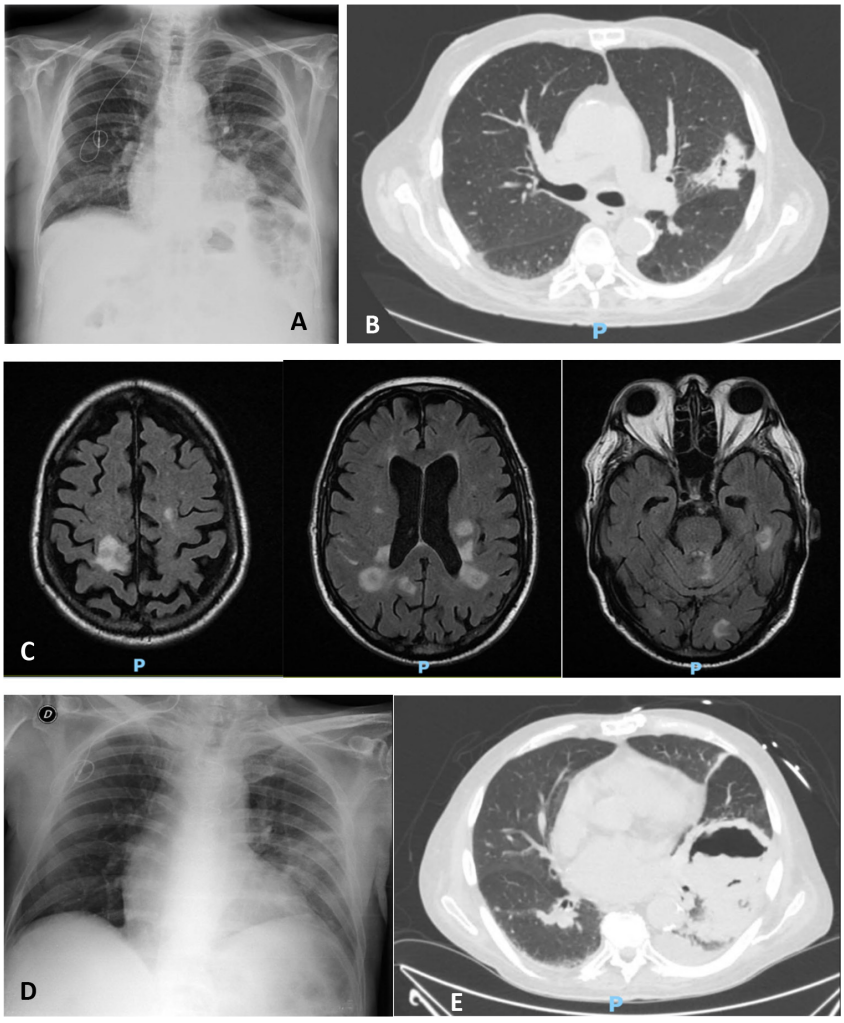

Figure 1 Image A presents a chest X-ray performed on day +4 of the previous admission, due to dry cough and fever. It shows a subsegmental parenchymal consolidation with air bronchogram in the left upper lobe (LUL). Image B presents a CT scan performed on day +10 of the last admission, due to dry cough and fever. The CT scan reveals a decrease in consolidation after 5 days of antibiotic treatment, along with a subcarinal adenopathy cluster. Image C: Brain MRI performed on day 21 of admission, showing 2 infratentorial and 20 supratentorial lesions. These lesions are ring-shaped, subcentimetric, and associated with vasogenic edema. The FLAIR sequence depicts signal hyperintensity in some right convexity sulci, suggestive of meningitis. Image D shows the patient's chest X-ray 7 days after discharge, revealing progression of pulmonary consolidation in the left upper lobe. Image E shows a control chest CT on day +35 of the new admission, depicting worsening lung lesions. Extensive consolidation in LSI with a large area of cavitation, cavitating satellite nodules, and contralateral involvement of the RUL, all consistent with necrotizing pneumonia.

was attributed to invasive fungal infection by mucormycosis, highlighting the challenges of managing co-infections in transplant recipients. This case underscores the complexities involved in diagnosing and treating concurrent mucormycosis and *Nocardia* infections. Differential diagnosis considerations include opportunistic infections, neoplasms, and interstitial lung disease [1]. Nocardia, a member of actinomycetes, presents diagnostic challenges, emphasizing the need for comprehensive diagnostic approaches such as fibrobronchoscopy [2,3]. Mucormycosis, known for its aggressive nature, requires prompt diagnosis through biopsy for direct microscopy, culture, and histopathological examination [4]. This patient exhib-

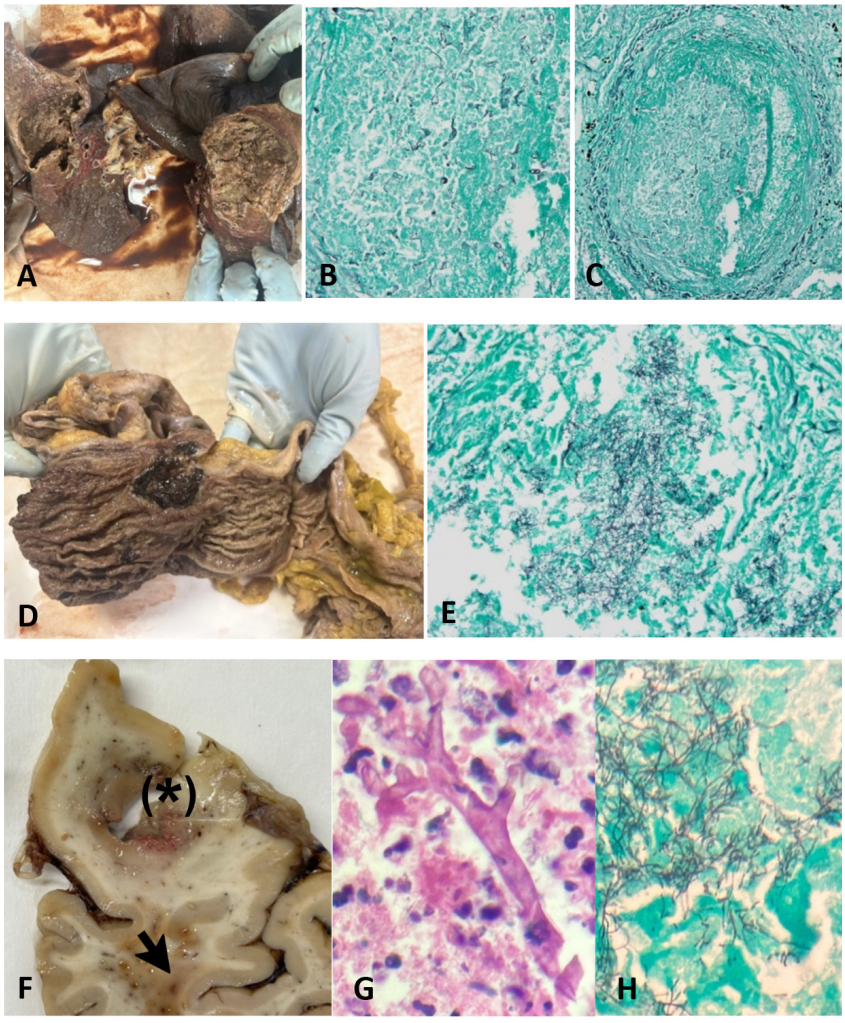

Figure 2 Macroscopic and histopathological study of clinical autopsy. Image A shows areas of necrosis and abscess formation in the left lung, consistent with mucormycosis. Image B and C shows areas of necrosis and abscess formation in the left lung, with thick, sparsely septate hyphae within vessels as observed in Grocott stain, with mucoral (scale bar 100 µm and 200 µm). Image D shows a gastric ulcer with transmural necrosis, consistent with mucoral Image E presents a cavitated lesion with areas of necrosis in a lymph node, Grocott stain positive for positive filamentous bacilli, consistent with Nocardia (scale bar 100 µm). Image F shows the macroscopic piece of central nervous system study, in which an acute necrotic lesion consistent with mucoral is observed (asterisk) upon a previous lesion in remission consistent with Nocardia (arrow). Image G shows the microscopic findings from the nervous system study, revealing sparsely septate hyphae at 90° in hematoxylin-eosin stain, consistent with mucoral (scale bar 50 µm). Image H reveals positive Grocott stain lesions with positive filamentous bacilli, consistent with *Nocardia* (scale bar 100 µm).

ited multiple risk factors for invasive fungal infection, including CMV infection, prolonged hospitalization, and subsequent admission to the ICU. Treatment involves a multidisciplinary approach combining antifungals and surgical interventions due to the rapid progression of mucormycosis [4].

Solid organ transplant recipients are particularly susceptible to opportunistic infections like nocardiosis and mucorales. These infections can occur in both post-transplant patients and those with normal immune function, often mimicking other diseases clinically and radiologically. Unfortunately, ac-

curate diagnosis may only occur when these diseases have already spread extensively. Therefore, it is crucial to remain vigilant for signs and symptoms to identify and treat these conditions early on. Highly immunosuppressed patients may develop multiple simultaneous opportunistic infections, posing a challenge for diagnosis and treatment when superinfections arise during ongoing treatment for a previous infection.

FUNDING

None to declare

CONFLICTS OF INTEREST

The authors declare the absence of conflicts of interest.

REFERENCES

1. Kanne JP, Yandow DR, Mohammed TL, Meyer CA. CT findings of pulmonary nocardiosis. AJR Am J Roentgenol. 2011;197(2):W266-272. doi: 10.2214/AJR.10.6208
2. Wilson JW. Nocardiosis: updates and clinical overview. Mayo Clin Proc. 2012;87(4):403-407. doi: 10.1016/j.mayocp.2011.11.016
3. Hardak E, Yigla M, Berger G, Sprecher H, Oren I. Clinical spectrum and outcome of Nocardia infection: experience of 15-year period from a single tertiary medical center. Am J Med Sci. 2012;343(4):286-290. doi: 10.1097/MAJ.0b013e31822cb5dc
4. Cornely OA, Arikan-Akdagli S, Dannaoui E, Groll AH, Lagrou K, Chakrabarti A, et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. Clin Microbiol Infect. 2014;20 Suppl 3:5-26. doi: 10.1111/1469-0691.12371.