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Letter to the Editor

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Cavitary pneumonia and empyema thoracis caused by multidrug resistant *Nocardia otitidiscaviarum* in an elderly patient

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Sir,

Female of 86 years with background of arterial hypertension and chronic thromboembolism secondary to severe pulmonary hypertension. She went to the Emergency Service where she was admitted for dyspnoea, coughing without expectoration, pleuritic-type thoracic pain of one week of evolution. Blood analysis showed a slight elevation of acute phase reactants, the rest was normal. In the thoracic X-ray (Figure 1), condensation was observed in the right middle lobe (RML) with mild uncomplicated pleural effusion. The detection of pneumococcal antigens and of *Legionella pneumophila* serogroup 1 were negative, with negative sputum culture. She was treated for ten days with 500 mg/24 h of intravenous (IV) levofloxacin and 1 g/24 h of IV ceftriaxone, and after clinical improvement, she was discharged. The patient returned 48 hours later with clinical and radiological worsening. A diagnostic pleural puncture showed non-purulent hematic exudate with the following characteristics: pH 7.22, red blood cells 29,000 cells/µL, leucocytes 37,426 cells/µL (87.8% neutrophils), lactate dehydrogenase 4329 U/L, glucose 68 mg/dL. The pleural liquid was seeded in chocolate agar, trypticase soy agar with 5% of sheep blood (TSA), Columbia CNA agar, MacConkey agar, Brucella agar with Hemin and vitamin K1, as well as in thioglycolate enrichment broth. The chocolate and TSA agars were incubated in aerobiosis at 37ºC and 5% of CO_2, the CNA and MacConkey agars in aerobiosis at 37ºC, and the Brucella agar in anaerobiosis. The aerobic and anaerobic cultures were negative after 5-7 days of incubation; however, in the subculture of the enrichment medium, dry whitish colonies were isolated. The identification of the species was made through sequencing the 16S gene of the rRNA, using the 27F primers (5'-AGAGTTTGATCCTGGCTCAG-3') and 533-R (5'-CTTGAGGCTCTGGTATCTTATTGC-3'), obtaining a sequence of 439 pairs of bases. The sequence was entered in BLAST® and the identification of *N. otitidiscaviarum* was obtained with 99.54% homology with the referenced strains, and the sequence was registered in GenBank of the NCBI® with accession number "OQ439630". The antibiotic susceptibility was performed through Thermo Scientific Sensititre® (Thermo Fisher Scientific, Massachusetts, United States) using the Sensititre® NOCARDIA panel. The strain was sensitive to co-trimoxazole (MIC= 0.25 mg/L), amikacin (MIC= 1 mg/L) and linezolid (MIC= 1 mg/L) and resistant to imipenem (MIC= 16 mg/L), amoxicillin-Clavulanic acid (MIC > 32/16 mg/L), and ceftriaxone (MIC= 64 mg/L).

Treatment was initiated with 240 mg/1200 mg/12 h of IV trimethoprim-sulfamethoxazole for one week. In the thoracic CT scan performed for control a right hydropneumothorax was observed with cavitated condensations in RML (Figure 2), while a head CT scan ruled out acute intracranial pathology or disseminated infection. An assessment with thoracic surgery was requested installing a drainage tube. For 25 days 600 mg/24 h of linezolid IV was initiated and subsequently 200 mg/24 h of oral tedizolid for 5 months. After the antibiotic and surgical treatment, the patient presented clinical improvement and was released with oral antibiotic treatment with subsequent controls for one year. During this monitoring, there was no resistance to the antibiotic treatment, or secondary effects, achieving a good clinical (clinical improvement, with no recurrence of infection on subsequent chest X-ray and blood tests) and microbiological response.

Nocardia spp. have worldwide distribution and are found in soil, water and plants. By being found suspended in dust particles, its inhalation is frequent, being one of the most frequent transmission channels. It can also be ingested through contaminated food or it can cause infection after cutaneous inoculation [1]. The majority of the infections caused by bacteria of the *Nocardia* genus occur in immunosupressed patients, which include immunosupressive treatment, solid organ transplant, HIV infection or tumours, among others [2]. In our environment, the most frequently isolated species of *Nocardia*

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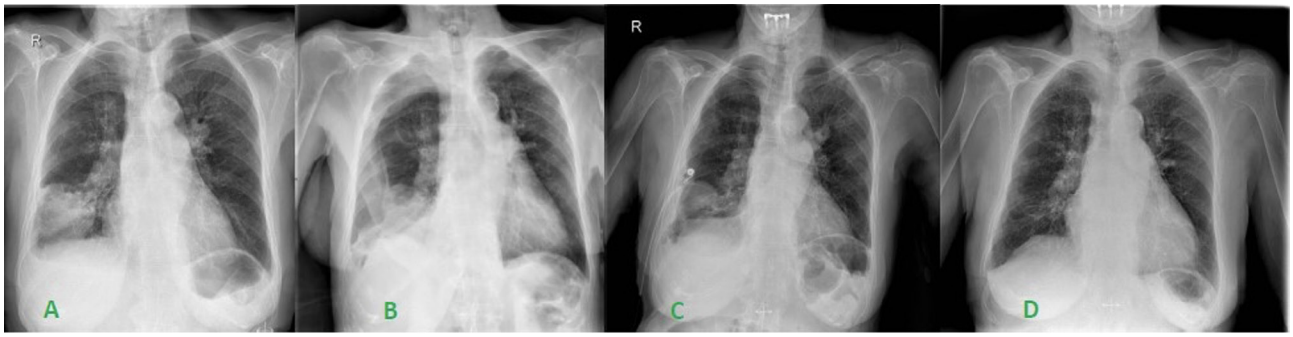

Figure 1 **A: Partially cavitated consolidation-mass in middle lobe (ML) and slight bilateral pleural effusion with right predominance. Cardiac silhouette increased in size in probable relation with cardiomegaly and bilateral hilar prominence, probably vascular. B: Decreased size of the partially cavitated consolidation mass in ML. Appearance of moderate right hydropneumothorax with contralateral deviation of the mediastinum. Rest without changes. C: Placement of pleural drainage tube in right hemithorax. The mass-consolidation in ML persists stable. Rest without changes. D: After resolution of the episode, three years later, without pulmonary consolidations or pleural effusion.**

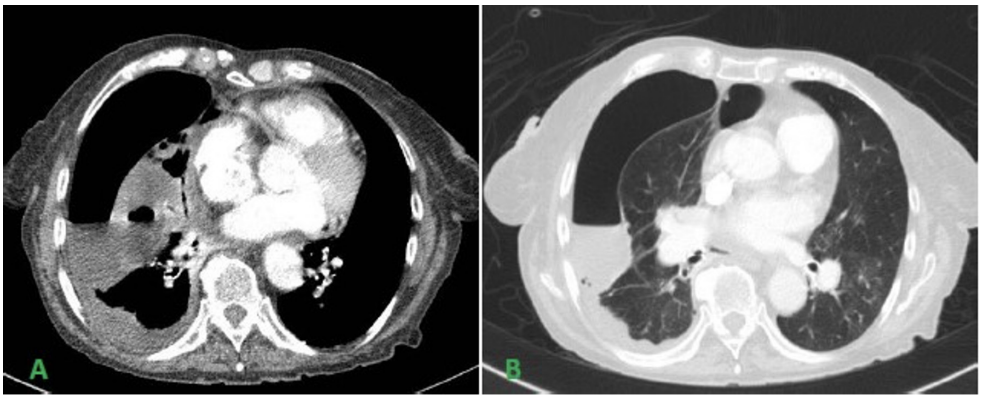

Figure 2 **Thoracic CT with intravenous iodinated contrast in axial cuts. A) soft-tissue window: Cavitated pulmonary mass consolidation in ML. B) lung window: moderate right hydropneumothorax (liquid component in posterior segment of the thorax and air component in anterior segment of the thorax, forming a hydro-aerial level) with mediastinal deviation to the left.**

are *Nocardia cyriacigeorgica, Nocardia abscessus* and *Nocardia farcinica* [3] while the isolation of strains of *N. otitidiscaviarum* is infrequent. The multi-centre study by Ercibengoa M et al., microbiological data were collected from 55 cases of pneumonia [4] caused by different species of *Nocardia*, and *N. otitidiscaviarum* was isolated on only four occasions.

N. otitidiscaviarum has been reported previously as cause of severe pneumonia [5,6] empyema thoracis [7], brain abscess [8], skin infection [9] or disseminated infection [10] even in immunocompetent patients [11]. In some cases, the differential diagnosis of pulmonary nocardiosis is considered with pulmonary metastatic diseases or even tuberculosis, particularly if the affected pulmonary lobes are the upper ones and slightly acid-resistant filaments are observed in our respiratory samples. The presumptive diagnosis is made by means of direct vision of gram-positive branched-chain filamentous bacilli. The diagnostic yield of the cultures is increased by maintaining them approximately four weeks, since it deals with slow-growing bacteria. When invasive diagnostic methods are used, the cultures are positive in even up to 85-90% of the cases. Currently, the identification of the species has been simplified thanks to the introduction of the MALDI-TOF mass spectrometer [6], although in some cases molecular methods such as the sequencing of the 16S gene of the rRNA hsp65, gyrA or rpoB, among others, may be necessary.

The initial regimens suggested for pleuropulmonary nocardiosis generally include the combination of trimethoprim-sulfamethoxazole (15 mg/kg/day) plus imipenem (500 mg IV every

6 hours), with the option of adding amikacin (7.5 mg/kg IV every 12 hours) in serious infections. Linezolid or tedizolid have been also used in the treatment of infections caused by *Nocardia* spp., even in a long-term antibiotic regimens [12,13]. After 3 to 4 weeks of intravenous therapy and documented clinical improvement, the patients can change to oral monotherapy [14]. The duration of the treatment with antibiotics is generally long (6-12 months). However, it is necessary to identify the species of *Nocardia* due to the intrinsic resistance of each species. In addition, the susceptibility of each strain must be analysed, due to the fact that some of the antibiotics considered as the first option such as Trimethoprim-sulfamethoxazole have been found resistant in some reports of infections produced by *N. otitidiscaviarum* [5,9].

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

REFERENCES

1. Traxler RM, Bell ME, Lasker B, Headd B, Shieh WJ, McQuiston JR. Updated Review on Nocardia Species: 2006-2021. Clin Microbiol Rev. 2022 Dec 21;35(4):e0002721. doi: 10.1128/cmr.00027-21.
2. Peleg AY, Husain S, Qureshi ZA, Silveira FP, Sarumi M, Shutt KA, Kwak EJ, Paterson DL. Risk factors, clinical characteristics, and outcome of Nocardia infection in organ transplant recipients: a matched case-control study. Clin Infect Dis. 2007 May 15;44(10):1307-14. doi: 10.1086/514340.
3. Valdezate S, Garrido N, Carrasco G, Medina-Pascual MJ, Villalón P, Navarro AM, Saéz-Nieto JA. Epidemiology and susceptibility to antimicrobial agents of the main Nocardia species in Spain. J Antimicrob Chemother. 2017 Mar 1;72(3):754-761. doi: 10.1093/jac/dkw489.
4. Ercibengoa M, Càmara J, Tubau F, García-Somoza D, Galar A, Martín-Rabadán P, Marin M, Mateu L, García-Olivé I, Prat C, Cilloniz C, Torres A, Pedro-Botet ML, Ardanuy C, Muñoz P, Marimón JM. A multicentre analysis of Nocardia pneumonia in Spain: 2010-2016. Int J Infect Dis. 2020 Jan;90:161-166. doi: 10.1016/j.ijid.2019.10.032.
5. Saksena R, Rynga D, Rajan S, Gaind R, Dawar R, Sardana R, Sen MK, Suri JC. Fatal pulmonary infection by trimethoprim-sulfamethoxazole resistant *Nocardia otitidiscaviarum*: report of two cases and review. J Infect Dev Ctries. 2020 Feb 29;14(2):214-222. doi: 10.3855/jidc.10169.
6. Liu C, Feng M, Zhu J, Tao Y, Kang M, Chen L. Severe pneumonia due to *Nocardia otitidiscaviarum* identified by mass spectroscopy in a cotton farmer: A case report and literature review. Medicine (Baltimore). 2017 Mar;96(13):e6526. doi: 10.1097/MD.0000000000006526.
7. Huang CH, Hsueh PR, Chen YH. Empyema thoracis due to *Nocardia otitidiscaviarum*. J Microbiol Immunol Infect. 2015 Oct;48(5):580-1. doi: 10.1016/j.jmii.2014.05.004.
8. Einstein EH, Bonda D, Khan S, Zlochower AB, D'Amico RS. Multiple Brain Abscesses Due to *Nocardia otitidiscaviarum*: Case Report and Treatment Implications. Cureus. 2021 Apr 8;13(4):e14362. doi: 10.7759/cureus.14362.
9. Clark NM, Braun DK, Pasternak A, Chenoweth CE. Primary cutaneous *Nocardia otitidiscaviarum* infection: case report and review. Clin Infect Dis. 1995 May;20(5):1266-70. doi: 10.1093/clinids/20.5.1266.
10. Barry M, AlShehri S, Alguhani A, Barry M, Alhijji A, Binkhamis K, Al-Majid F, Al-Shahrani FS, Muayqil T. A fatal case of disseminated nocardiosis due to *Nocardia otitidiscaviarum* resistant to trimethoprim-sulfamethoxazole: case report and literature review. Ann Clin Microbiol Antimicrob. 2022 May 16;21(1):17. doi: 10.1186/s12941-022-00511-9.
11. Jiang Y, Huang A, Fang Q. Disseminated nocardiosis caused by *Nocardia otitidiscaviarum* in an immunocompetent host: A case report and literature review. Exp Ther Med. 2016 Nov;12(5):3339-3346. doi: 10.3892/etm.2016.3755.
12. Shen T, Wu L, Geng L, Wei Z, Zheng S. Successful treatment of pulmonary *Nocardia farcinica* infection with linezolid: case report and literature review. Braz J Infect Dis. 2011 Sep-Oct;15(5):486-9. doi: 10.1016/s1413-8670(11)70234-3.
13. Chomei Y, Nishimura S, Iwata K. Long-term use of tedizolid for pulmonary nocardiosis. J Infect Chemother. 2022 Aug;28(8):1172-1176. doi: 10.1016/j.jiac.2022.03.020.
14. Margalit I, Lebeaux D, Tishler O, Goldberg E, Bishara J, Yahav D, Coussement J. How do I manage nocardiosis? Clin Microbiol Infect. 2021 Apr;27(4):550-558. doi: 10.1016/j.cmi.2020.12.019.