

Emergence of a Microbe in a New Geographic Area

Disseminated *Nocardia transvalensis* complex and *farcinica*: First case in an immunocompetent

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ARTICLE INFO

Handling Editor: Patricia Schlagenhauf

Keywords:

Nocardia transvalensis

Wallacei and *farcinica*

Immunocompetent

Disseminated

Community-acquired pneumonia

ABSTRACT

Background: Nocardiae is an opportunistic infection mainly of the immunocompromised patient without sparing the immunocompetent subject or without any identified risk factors. They can be localized or disseminated. The extreme rarity of this infection often results in a deleterious diagnostic delay.

Case presentation: We report a first case of community acquired pneumonia with asymptomatic disseminated brain abscess due to *Nocardia transvalensis/wallacei* and *farcinica* in an immunocompetent man. The patient fully recovered after receiving optimized antimicrobial therapy.

Conclusions: This case suggests that health care professionals should always evoke this diagnosis when confronted to atypical community-acquired pneumonia, even in immunocompetent patients.

1. Introduction

Nocardiae species are Gram-positive, aerobic actinomycetes found ubiquitously in nature all around the world, but more frequently in warm and humid regions. The primary mode of contamination is airborne transmitted via the respiratory tract [1]. Nocardiae is primarily considered an opportunistic pathogen that primarily affects immunocompromised patients. However, it may cause infections in immunocompetent patients as well [2]. Nocardiae organisms can be classified into these following complexes: *N. transvalensis* complex (*N. blacklockiae*, *N. transvalensis*, and *N. wallacei*) and *N. farcinica* complex (*N. farcinica*, *N. kropstedtii*) [3]. To our knowledge, our case report is the first case described in the literature of disseminated infection caused by *N. transvalensis/wallacei* and *farcinica* in an immunocompetent patient.

2. Case report

A 29-year-old man with no medical or surgical history, no medication taken for the 6 months before the onset of the signs and not smoking is referred to the emergency department for fever and dry cough in a context of alteration of general condition. He had lost 13 kg in 3 months.

He also complained of right chest pain and intermittent hemoptysis. Clinical examination showed the presence of crackles in the right lung field. The rest of the clinical examination showed no particularity. Initial blood samples revealed a high leucocyte count of 28 giga/l, including neutrophils at 25.62 giga/l, hemoglobin was 8.7 g/l and the C-reactive protein was high at 176 mg/L. Biological tests for immune deficiency, such as blood count, plasma protein electrophoresis, immunoglobulin (Ig) G, A and M, HIV serology, complement assay (C3 and C4, CH50) and total IgE all came back negative in our patient. Chest X-ray and CT scan showed right apical pneumonia (Image 1a and Image 2a). Empirical antibiotherapy with Amoxicillin/clavulanic was initiated. The persistence of fever motivated therapeutic escalation with ceftriaxone 1g/day. The patient's health has improved dramatically with apyrexia and biological improvement. However, there was a recurrence of fever after stopping antibiotics. Given the evocative radiological images, the patient was prescribed on anti-tuberculosis treatment for about two weeks, but without significant improvement and all the results of search for Koch bacilli (BK) came back negative. Due to the degradation of the clinical picture, a new cytobacteriological examination of the sputum (ECBC) was carried out which revealed multiple branched filaments suggestive of nocardiosis (Image 3). The diagnosis was then confirmed in a reference

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<https://doi.org/10.1016/j.nmni.2023.101148>

Received 28 January 2022; Received in revised form 17 February 2023; Accepted 8 May 2023

Article published online: 20 May 2023

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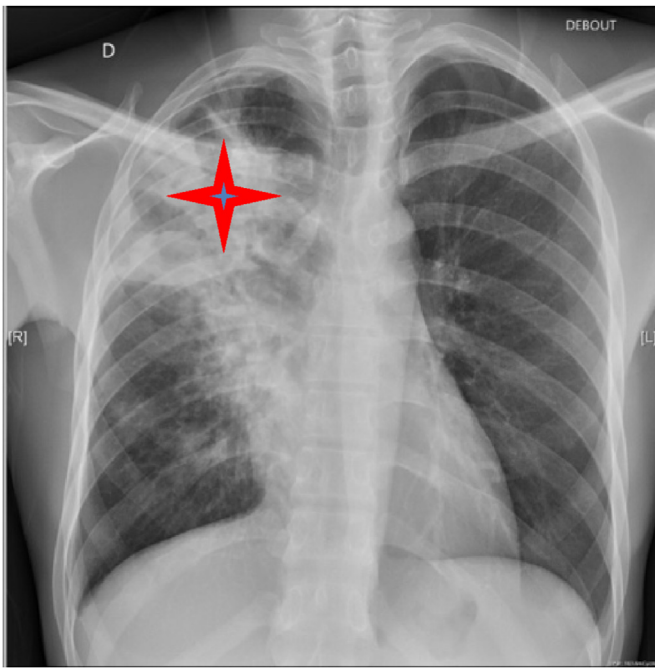


Image 1a. Face chest x-ray: Right hilar and apical alveolar condensation closing an air bronchogram, associated with a bubble of right superior lobe.

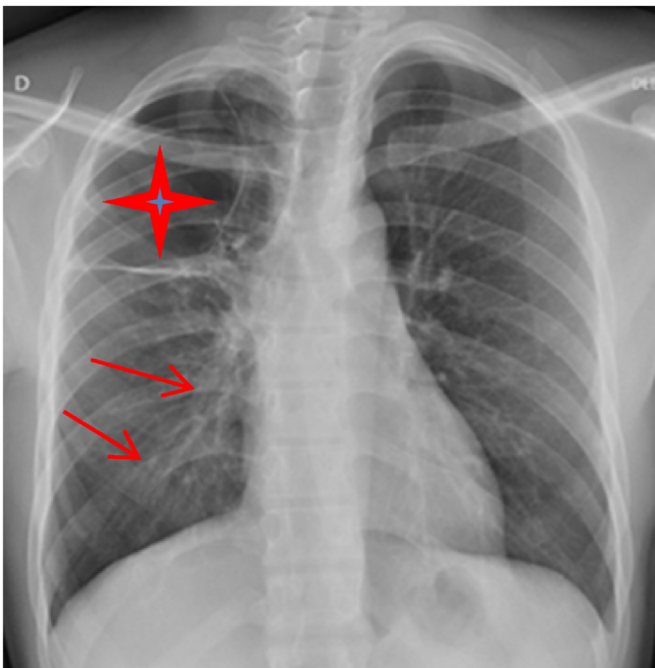


Image 1b. Face chest x-ray: Control at 12 months showing a large right apical bubble without sign of secondary infection (star), associated with a cylindrical dilation of the bronchi of the right middle and lower lobes (arrows).

laboratory of nocardiosis (Laboratory of Mycology of Lyon) with identification of the two species of *Nocardia transvalensis/wallacei* and *farcinica*. The identifications were made by PCR and sequencing a 600 nt fragment targeting 16S gene. The primers and conditions used for amplification and sequencing are found in Rodriguez-Nava et al., 2006 [4]. For antibiograms we used the disc method, the conditions used as well as the reference thresholds are found in the publication of Lebeaux et al., 2018 [5].

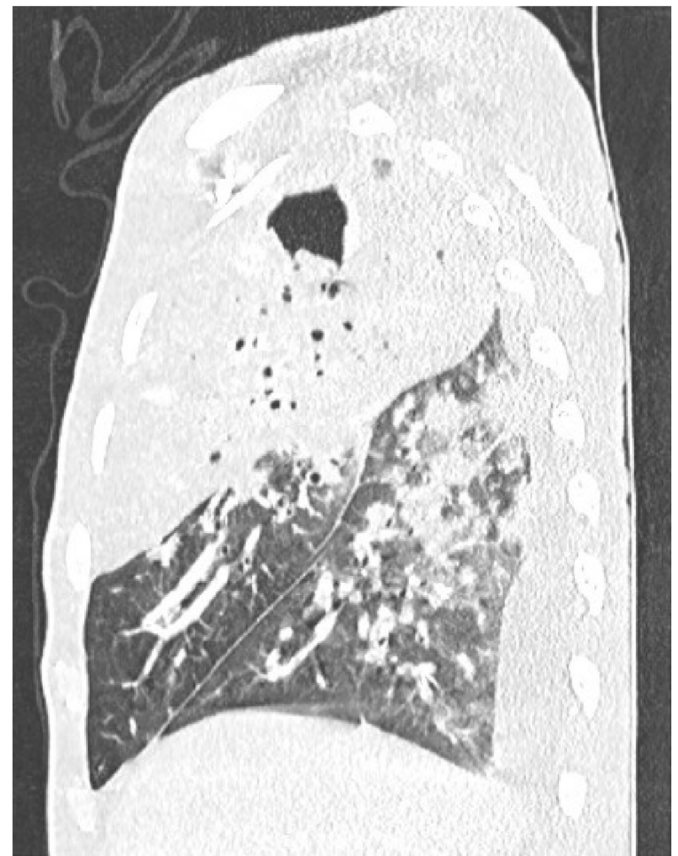


Image 2a. CT scan in sagittal parenchymal window reconstruction: Alveolar condensations taking the right upper lobe with an excavated lesion and an air bronchogram, the lower lobe. Thickening of the septal lines.

The evaluation of the extension of the disease was carried out by brain magnetic resonance imaging (MRI) in search of a brain location despite the absence of neurological manifestations. It showed a left cerebellar abscess of 20 mm and a sub-left frontal cortex measured a small abscess of 5 mm (Image 4a).

Treatment with triple therapy Meropenem 6g/d in IV, Sulfamethoxazole-trimethoprim intravenously 12 ampoules/d and Amikacin 750mg/d for 15 days was instituted and then relayed by Sulfamethoxazole-trimethoprim 800/160mg 3 tablets x 3 per day and moxifloxacin 400mg/d and folinoral 25mg/d for 6 months. Post-therapeutic follow-up at 12 months to show a large right apical bubble with no signs of secondary infection (star) associated with cylindrical dilation of the bronchi of the right and lower lobes (Image 1b) and thoracic CT scans for cystic and cylindrical dilatation of the bronchi of the right upper lobe with a voluminous sequential emphysema bubble (Image 2b). The cerebral MRI was back to normal (Image 4b). Unfortunately, the patient will remain with lung sequelae.

3. Discussion

To our knowledge, this is the first case reported case is of a disseminated infection caused by concomitant association of two *Nocardia* species, *N. transvalensis* complex and *N. farcinica* in an immunocompetent patient. At the beginning of his disease, he complained of pulmonary symptoms and no other complaints. Nevertheless, asymptomatic cerebral involvement was found in the form of multiple small cerebellar abscesses. *Nocardia* is an opportunistic pathogen that may affect predominantly the immunocompromised patient. In our case, the patient had no significant medical history and no argument for underlying immunosuppression. In a retrospective study of 253 cases of pneumonia due to *Nocardia* Beaman



Image 2b. CT scan in sagittal parenchymal window reconstruction: Cystic and cylindrical dilation of the bronchi of the right upper lobe (arrow) with voluminous bubble of sequel emphysema at control at 12 months.

et al. reported that only 15% of the affected patients were immunocompetent [6]. The lung is the most frequent organ involved [7] and the bacteria can spread hematogenously to other sites such as brain, bones, joints, kidneys, heart, spleen and sinus [8].

Despite the patient showed only signs of lung disease and no signs or neurological symptom, brain MRI showed multiple cerebral abscesses. The data suggest that neurological or potentially other organs should be routinely researched in these patients to assess the spread of the disease and to provide guidance for the type and length of treatment. Pulmonary Nocardia may initially mimic necrotic or non-necrotic community-

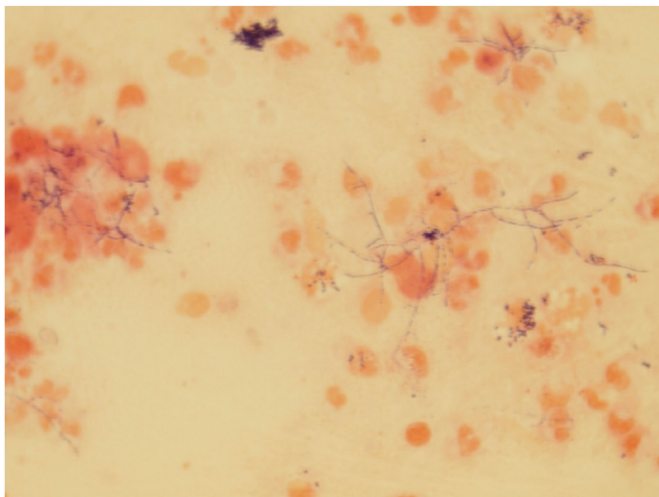


Image 3. A Gram stain ($\times 1000x$) of sputum showed branching Gram-positive filaments suggesting a Nocardia infection.



Image 4a. Brain sagittal MRI 3D T1 FFE with gadolinium injection: Left cerebellar contrast enhancement evoking a micro-abscess (arrow) [Image 4a](#) which disappears at control at 12 months. [Image 4b](#).

acquired bronchopneumopathy, pulmonary tuberculosis. Our patient was initially empirically put under antituberculous therapy for a high suspicion of pulmonary tuberculosis. However, the diagnosis of pulmonary tuberculosis was not confirmed for many reasons: Koch bacillus sputum was all negative and so were the cultures, which is atypical regarding the pulmonary images. Furthermore, the thoracic CT scans realized 1 month after the treatment was introduced revealed contralateral nodular lesions of the parenchyma. Thus, sputum was performed again with specific coloration and the diagnosis of Nocardia was made thanks to the presence of the filamentous bacteria. Many Nocardia

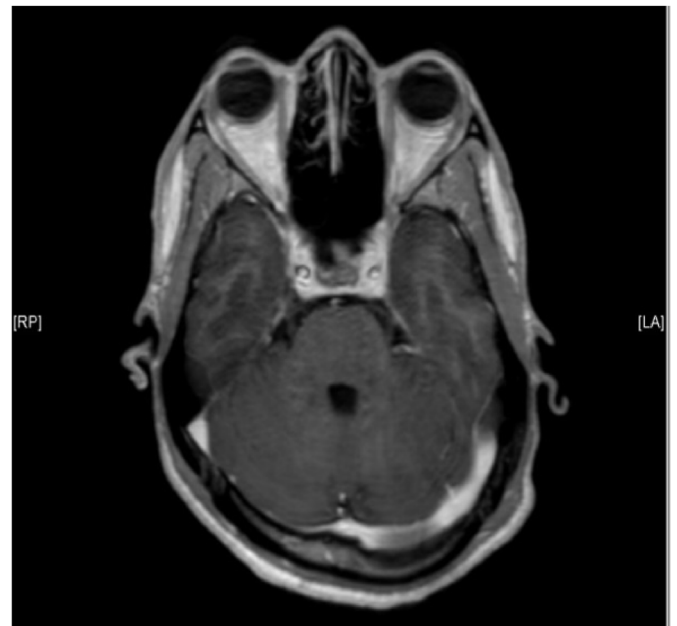


Image 4b. Brain sagittal MRI 3D T1 FFE with gadolinium injection: Left cerebellar contrast enhancement evoking a micro-abscess (arrow) [Image 4a](#) which disappears at control at 12 months. [Image 4b](#).

Table 1
Antibiogram the two germs (*N. transvalensis/wallacei* and *N. farcinica*)

| Germs | <i>N. transvalensis/wallacei</i> | <i>N. farcinica</i> |
|-------------------------------------|----------------------------------|---------------------|
| Carbapenem | | |
| Imipenem | I | I |
| Ertapenem | R | R |
| Meropenem | R | R |
| Aminoglycoside | | |
| Gentamicin | R | R |
| Tobramycin | R | R |
| Amikacin | I | S |
| Quinolone | | |
| Ciprofloxacin | S | S |
| Levofloxacin | S | S |
| Moxifloxacin | S | S |
| Penicillins - Cephalosporins | | |
| Amoxicillin clavulanic acid | S | S |
| Amoxicillin | R | R |
| Ceftriaxone | S | R |
| Other | | |
| Trimethoprim-sulfamethoxazole | S | S |
| Linezolid | S | S |

I: intermediate, R: resistant, S: sensitive, N: nocardia.

species are gathered in complexes based on their predicted antimicrobial susceptibility patterns. *N. transvalensis* complex one of the less frequent *Nocardia* species and has a natural resistance to aminoglycosides, while other *Nocardia* species are not, such as *N. wallacei* [9]. In our case, we find the germ resistant to aminoglycosides and sensitive to cotrimoxazole, third generation cephalosporin, moxifloxacin and linezolid (Table 1).

The most frequently isolated species is *N. farcinica*, with, up to a third of cases in the literature. It differs from other species by its clinical severity: As it is virulent, it tends to disseminate more especially to neural tissue. Moreover, it is naturally resistant to third generation Cephalosporins, aminoglycosides except for amikacin, sensitive to ciprofloxacin, linezolid, trimethoprim-sulfamethoxazole (TMP-SMX) as it can be seen on the antibiogram of our case (Table 1).

The treatment options and the pattern of antibiotic susceptibility among different *Nocardia* species vary considerably. The trimethoprim-sulfamethoxazole is the gold standard for the treatment of nocardiosis, thanks to its broad spectrum of action and its good tissue diffusion [10].

Our patient was treated with trimethoprim-sulfamethoxazole and moxifloxacin for 6 months, which is the recommendation in immunocompetent [11].

4. Conclusion

This case suggests that health care professionals, especially Pulmonologists, Infectious Disease Specialists and Neurologists should always evoke this diagnosis when confronted to atypical community-acquired pneumonia, even in immunocompetent patients. When the diagnosis of pulmonary nocardiosis is confirmed, neuroradiological assessment is required even in the absence of neurological signs or symptoms, as both lung and brain involvement may coexist in the same patient.

Ethical approval

The authors certify that they comply with the Principles of Ethical

Publishing.

Informed consent

The patient has consented to the submission of the case report to the journal.

Authors' contributions

AD, YD, IY were involved in the design of the study, data collection, supervision, data processing, cleaning, analysis, and interpretation of the results, as well as the writing of the manuscript. MN and PM participated in the review of the manuscript. TBC participated in the identification of the germs and the correction. SP reviewed the manuscript. All the authors made a significant contribution and approved the final version of the manuscript.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Abbreviation

BK: Koch bacilli
 CT scan: Computerized tomography
 ECBC: Cytobacteriological sputum examination
 G: Gram
 MRI: Magnetic resonance imaging
 TMP SMX: Trimethoprim-sulfamethoxazole
 TB: Pulmonary Tuberculosis