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Case report

First case of fatal bacteremia due to *Nocardia neocaledoniensis*

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ABSTRACT

Nocardia neocaledoniensis is an uncommon cause of human-infections. Few cases are reported in the literature. We describe the first case of bacteremia caused by *N. neocaledoniensis*. This article underlines the importance of mass spectrometry for easy and rapid identification of such bacterium.

Introduction

Nocardia species are Gram-positive aerobic bacilli belonging to the order of *Actinomycetales*. These ubiquitous environnemental bacteria can be responsible for opportunistic infections, particularly in immunocompromised patients. Thanks to the developement of 16S rDNA sequencing and mass spectrometry, the number of *Nocardia* species has increased and more than 100 species are currently described [1,2]. Among them, *Nocardia neocaledoniensis* was first isolated from soil in New Caledonia and identified using 16S rDNA sequencing in 2004 [3]. Herein, we report the first case of bacteremia due to *N. neocaledoniensis* in an immunocompromised patient.

CASE PRESENTATION

An 88-year-old man suffering from chronic lymphocytic leukemia was admitted to the geriatric unit for persistant febrile respiratory syndrome. He was treated with amoxicillin-clavulanic acid and ciprofloxacin for fifteen days without resolution.

On admission, physical examination revealed deterioration of his general condition with fever at 38 °C. The patient was conscious and oriented. A productive cough with clear sputum without respiratory distress was observed. Heart sounds were regular without heart murmur. Blood pressure was at 115/54 mmHg, pulse rate at 72/min and oxygen saturation at 95 %. Biological results indicated an elevated white blood cells (16.6×10^9/l with 9.6×10^9/l polymorphonuclear neutrophils) and an inflammatory syndrome with high level of C-reactive protein (27 mg/mL). Chest X-ray revealed after-effects of left basal pneumonia.

The influenza RT-PCR was negative. Urine soluble antigen testing for *Streptococcus pneumoniae* and *Legionella pneumophila* was not performed. Culture of sputum only showed an oro-pharyngeal flora. Two sets of blood cultures (BD BACTEC™ FX; Becton Dickinson, Franklin Lakes, New Jersey, United States) were positive after more than 72 h of culture. The direct examination of the blood culture showed a branched Gram-positive rod (Fig. 1). After 24 h of culture on blood agar plate, the culture showed cerebriform white colonies with sugary appearance, pitting into the agar. Identification was performed by MALDI-TOF spectrometry mass on the VITEK MS® (BioMérieux, Marcy l'Etoile, France) with an excellent confidence value (>99 %) for *N. neocaledoniensis* and was confirmed using 16S rDNA sequencing by the National Reference Center for nocardiosis.

Susceptibility testing was performed using the CLSI-recommended method of broth microdilution [4]. The organism was susceptible to amikacin (MIC < 0.5 mg/L), imipenem (MIC = 0.5 mg/L), clarithromycin (MIC = 2 mg/L), linezolid (MIC = 2 mg/L), trimethoprim-sulfamethoxazole (MIC = 1 mg/L), and resistant to amoxicillin-clavulanic acid (MIC > 32 mg/L), cefotaxime (MIC = 32 mg/L), ciprofloxacin (MIC > 4 mg/L).

Unfortunately, the respiratory and hemodynamic functions of our patient declined rapidly. He finally died five days after his admission from an acute respiratory distress syndrome.

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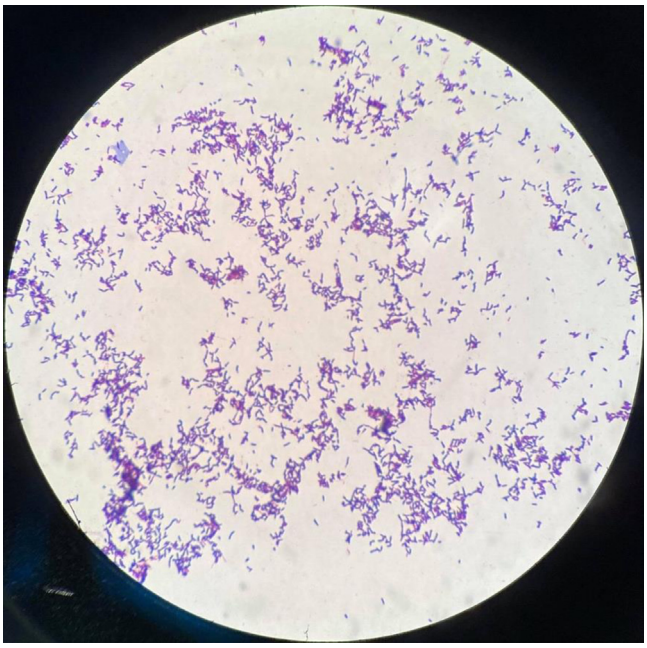

Fig. 1. Gram strain microscopic examination of Nocardia neocaledoniensis at magnification 1000 × . Presence of Gram-positive branched filamentous bacilli.

Discussion

The review of the literature including key-words "*Nocardia neocaledoniensis*" and "human infection" related few cases caused by this bacterium. After its first description in 2004 from a hypermagnesian ultramafic soil, this species was isolated from milk samples of dairy cows with mastitis; its isolate identification was confirmed by 16S rDNA sequencing [5]. Since then, few human infections have been described. In 2007, Yin et al. identified three cases of conjunctivitis caused by *N. neocaledoniensis* out of 11 ocular infections, using *hsp*65 gene sequencing for species identification of *Nocardia* spp. [6]. In 2012, McGhie et al. described the first case of skin and soft tissue infection caused by *N. neocaledoniensis* in a 68-year-old man on immunosuppressive therapy for rheumatoid arthritis [7]. In 2020, Azadi et al. isolated *N. neocaledoniensis* from an abscess following a surgery in an immunocompetent patient [8].

In our case, we describe a fatal bacteremia due to *N. neocaledoniensis* identified using MALDI-TOF spectrometry mass. This technique allows a rapid and accurate identification of *Nocardia* species. Its performance was evaluated by Body et al. on a panel of 312 isolates representing 21 different *Nocardia* species. Of the 312 isolates, 3 % were incorrectly classified by this method, including 3 strains of *N. asteroides* which were misidentified as *N. neocaledoniensis* [9]. Concerning *Nocardia* bacteremia, the last study of Williams et al. reported more than 100 cases of invasive infections [10]. The most frequent species isolated were *N. farcinica* (33 %) followed by *N. nova* complex (10 %). In this study, 80 % of patients were immunocompromised, and the blood was the only site where *Nocardia* yielded in 38 % of cases, as described in our case. However, *Nocardia* species are slow-growing organisms: while incubation time of blood cultures is sufficient to detect them, media used for respiratory samples are conventionnally not looked for as long as. As in our study, it could have been underestimated in respiratory samples for this reason, while respiratory tract is the main entrance wound for these bacteria. The outcome of these patients was lethal in 40 % of the cases. Finally, the majority of strains were susceptible to linezolide (100 %), amikacin (98 %), imipenem (85 %) and trimethoprim-sulfamethoxazole (89 %) whereas 50 % of them were resistant to amoxicillin-clavulanic acid and ciprofloxacin. These data were confirmed in our case with the failure of the initial pneumonia treatment (amoxicillin-clavulanic acid and ciprofloxacin) and the secondary bacteremia. This case demonstrates the importance of quick detection and identification of *Nocardia* in clinical samples in order to prescribe an antibiotic deemed to be more effective (linezolide, imipenem, amikacin). Moreover, in case of persistant atypical pneumonia, physicians should consider requesting specifical *Nocardia* research to permit a long incubation of culture media. Although *Nocardia* may be isolated within 3–5 days of culture, prolonging the culture media incubation time to 2 weeks may be needed in cases with high clinical suspicion.

Authorship statement

All authors meet the ICMJE authorship criteria

AR, CL and FW wrote the first draft of the article.

AR, CD, AV, CL, FW and PC were responsible for biological analyses.

AR, AV and AEP were responsible for collection of patients' data.

All authors contributed to the writing and approved the final manuscript.

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Ethical approval

The authors have read and complied with the journal's ethical consent policy. No specific ethical approval was required for this study.

Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish the case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, the Editor in Chief must be made aware of all such conditions. Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

Declaration of Competing Interest

There are no conflicts of interest to declare.

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