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Case Report

Bacteremic pneumonia caused by Nocardia veterana in an HIV-infected patient

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SUMMARY

Disseminated *Nocardia veterana* infection has rarely been reported. We describe the first reported case of *N. veterana* bacteremic pneumonia in an HIV-infected patient. The isolate was confirmed by 16S rRNA sequencing analysis. The patient initially responded well to trimethoprim–sulfamethoxazole treatment (minimum inhibitory concentration 0.25 μg/ml), but died of ventilator-associated pneumonia.

1. Introduction

Infections caused by *Nocardia* species have been increasing because of the growing population of immunocompromised hosts. Clinical manifestations of nocardiosis range from cutaneous infections in normal hosts to severe pulmonary and central nervous system diseases in immunocompromised hosts.[1] The most common predisposing factors for opportunistic Nocardia infections are long-term steroid use, neoplastic disease, and HIV infection.[1] Due to improvements in the identification of *Nocardia* species in the clinical laboratory, the genus *Nocardia* is rapidly expanding, with at least 80 species described to date (http://www.bacterio.cict.fr/n/nocardia.html). Identification of clinical isolates beyond the genus level is important, since strains of *Nocardia* species differ in the clinical spectrum of the disease they cause and their susceptibility to antibiotics.[1] *Nocardia cyriacigeorgica*, *Nocardia nova*, and *Nocardia brasiliensis* are the most commonly encountered species in human infections.[1–5] In contrast, *Nocardia veterana*, a newly identified species, was first isolated from a 78-year-old man with a history of tuberculous pleurisy, but the strain was not considered to be clinically significant.[2] We describe herein the first reported case of *N. veterana* bacteremic pneumonia in an HIV-infected patient.

2. Case report

A 30-year-old man presented with productive cough and progressive dyspnea for 1 week. He had had one episode of moderate hemoptysis 2 days prior to visiting the hospital. His medical history included HIV infection without highly active antiretroviral treatment (HAART) for 2 years, old tuberculosis with complete anti-tuberculosis treatment, and chronic hepatitis B with positive hepatitis B surface antigen. He had been unemployed for the 10 months prior to admission.

The patient reported no headache, chest pain, vomiting, diarrhea, night sweats, chills, or myalgia. His body weight was 45 kg and body height was 178 cm. Physical examination revealed a temperature (ear) of 36.6 °C, pulse rate of 120 beats/min, respiratory rate of 32/min, blood pressure of 105/43 mmHg, and pulse oximeter saturation of 81% under ambient air. Coarse crackles were heard over both lung fields, especially the right upper lung. No heart murmur was audible. There was no lymphadenopathy or hepatosplenomegaly. Laboratory data revealed a white blood cell count of 15.31×10^9/l with neutrophil predominance (96%), hemoglobin of 10.9 mg/dl, serum urea nitrogen of 61 mg/dl, serum creatinine of 1.4 mg/dl, alanine

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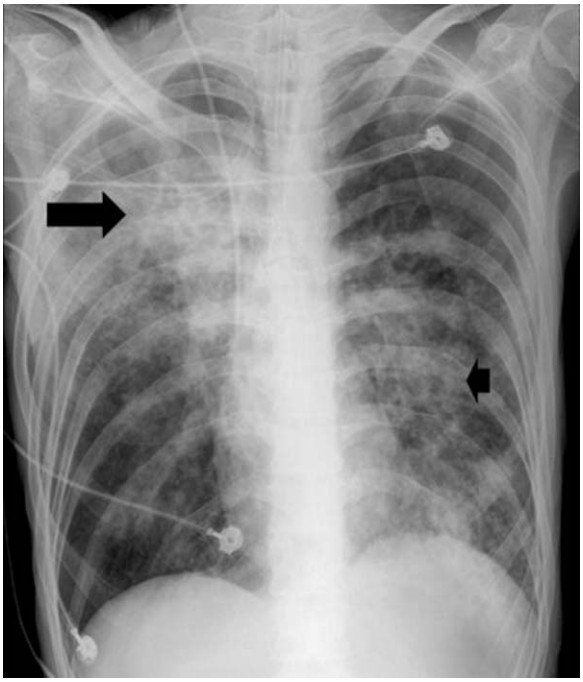

Figure 1. Chest radiograph shows patchy consolidation over the right upper lung (arrow) and diffuse infiltration over bilateral lung fields (arrow head).

aminotransferase of 71 U/l, total bilirubin of 2.86 mg/dl, albumin of 2.31 g/dl, lactate dehydrogenase of 623 U/l (reference value <460 U/l), sodium of 149 mmol/l, and C-reactive protein of 18.52 mg/dl (reference value <0.8 mg/dl). Arterial blood gas analysis under oxygen use with a non-rebreathing mask (FiO_2 of 98%) revealed pH 7.43, PCO_2 52.2 mmHg, HCO_3^- 33.9 mEq/l, and PO_2 92 mmHg. There was no pyuria or hematuria. The CD4 count was 3/μl (1%); his HIV viral load was 29 500 copies/ml.

Chest radiography on admission revealed diffuse infiltration over bilateral lung fields and patchy consolidation over the right upper lung (Figure 1). The patient was intubated due to hypoxemic respiratory failure and was admitted to the intensive care unit. Testing for *Chlamydia pneumoniae* antigen (bioMérieux, Marcy-l'Etoile, France) was negative. Serological testing for anti-*Mycoplasma pneumoniae* IgM (Savyon Diagnostics Ltd, Ashdod, Israel) was negative. The influenza rapid test (QuickVue Influenza A+B test, bioMérieux, San Diego, CA, USA) of a nasopharyngeal swab sample and Legionella urinary antigen test for serogroup 1 (Binax Inc., Portland, ME, USA) were both negative, but a Binax NOW *Streptococcus pneumoniae* urinary antigen test (Binax Inc.) was positive.

Three sets of blood cultures and one set of sputum cultures were performed. Empirical antibiotic therapy with moxifloxacin (400 mg every day) and clarithromycin (500 mg every 12 h) was started to cover the probable infection due to *S. pneumoniae* and atypical pathogens. Intravenous trimethoprim–sulfamethoxazole (800 mg/160 mg every 8 h) was administered because of the possibility of *Pneumocystis jirovecii* pneumonia (PJP). Bronchoalveolar lavage (BAL) from the right upper bronchial tree and a transbronchial lung biopsy from the lesions over the left lower lobe were performed on the third hospital day. Pathological examination of lung biopsy tissue using Gomori's methenamine silver stain revealed clusters of cysts within the alveolar space suggesting *P. jirovecii*, however there was no evidence of concomitant cytomegalovirus infection. The patient had not received trimethoprim–sulfamethoxazole prophylaxis before.

Many branching and filamentous Gram-positive and weakly acid-fast positive bacteria were found in the BAL fluid, while *P. jirovecii* was found using Giemsa stain (Muto Pure Chemicals Ltd, Tokyo, Japan). Bacterial, mycobacterial and fungal cultures of the BAL fluid were negative. Three sets of blood cultures using the Bactec 9240 automated culturing system in Aerobic/F bottles with resin (BD Diagnostic System, Sparks, MD, USA) all grew branching Gram-positive bacteria after incubation for 5 days. Using a modified acid-fast stain the isolates were also weakly acid-fast bacteria, suggesting the presence of *Nocardia* species.

The dosage of trimethoprim–sulfamethoxazole was therefore increased to 1600 mg/320 mg every 8 h for the treatment of PJP and disseminated Nocardia infection (pneumonia and bacteremia). The patient's clinical condition, including dyspnea, oxygenation and lung infiltration on chest radiography, all gradually improved. Seven days later, repeat blood cultures were performed and yielded no growth. However, one episode of ventilator-associated pneumonia caused by *Acinetobacter baumannii* occurred 10 days after admission, and moxifloxacin and clarithromycin were changed to imipenem according to the culture results. The patient's condition deteriorated and multiple-organ failure developed. The patient died 1 month after hospital admission.

2.1. Microbiology

The Nocardia isolates were branching, beaded, filamentous Gram-positive bacilli and were weakly positive with acid-fast stain. The isolate grew well on blood agar plate and had negative reactions for hydrolysis of casein, xanthine, hypoxanthine, and tyrosine. The isolate was further confirmed to the species level by 16S rRNA gene analysis. Partial sequencing analysis of the 16S rRNA gene was performed using the primers Noc1 (5′-GCTTAACACATGCAAGTCG-3′; positions 46 to 64, *Escherichia coli* numbering system) and Noc2 (5′-GAATTCCAGTCTCCCCTG-3′; positions 663 to 680, *E. coli* numbering system). The sequences were compared with published sequences in the 16S rRNA database. The sequences obtained (823 bp) were compared with published sequences in the GenBank database using the BLASTN algorithm (http://www.ncbi.nlm.nih.gov/blast). The closest match was obtained with *N. veterana* (GenBank accession No. GQ376181; maximal score 1507, E value 0.0, and maximal identity 99% (821/823)). The isolate had a positive reaction for urea hydrolysis and positive growth at 45 °C, which were compatible with the identification of *N. veterana* (not *Nocardia africana* or *N. nova*).[2–4] The minimum inhibitory concentrations (MICs) of trimethoprim–sulfamethoxazole, ciprofloxacin, clarithromycin, and imipenem were 0.25, >32, 0.03, and 0.12 μg/ml, respectively, as determined by the broth microdilution method.[1]

3. Discussion

N. veterana is an opportunistic pathogen in humans that can cause respiratory tract infection, primary cutaneous infection, and peritonitis.[2–4] Bloodstream infection due to *N. veterana* is a rare condition, which has only been reported once in the literature in a patient with chronic lymphocytic leukemia and lung cancer. The condition resolved without further sequelae after antibiotic treatment.[5]

The present case is the first report of concomitant PJP and *N. veterana* bacteremic pneumonia in an HIV-infected patient. In addition to the present case, another previous report has described a cancer patient with *N. veterana* bacteremia complicating a pulmonary infection; the patient recovered completely after 3 weeks of antibiotic treatment that included trimethoprim–sulfamethoxazole.[5] *N. veterana*, which was probably secondary to the pulmonary infection, was isolated in pure culture three times from the blood of this immunocompromised patient over the

course of 2 days. The identification of *N. veterana* was confirmed by molecular methods in addition to conventional biochemical studies. The untreated HIV infection should be considered the main predisposing factor for *N. veterana* bacteremia in the present case.

Trimethoprim–sulfamethoxazole has good in vitro activity against *N. brasiliensis* and *N. asteroides*, but its activity against other *Nocardia* species varies.[1] Based on limited in vitro studies of antimicrobial agents against *N. veterana*, most reported clinical isolates have been susceptible to trimethoprim–sulfamethoxazole.[5] Our patient initially responded well to treatment with trimethoprim–sulfamethoxazole, which showed fair in vitro activity against the isolate (MIC of 0.25 μg/ml). In addition, previous studies have shown the MIC ranges of imipenem for six clinical isolates to be as low as 0.032 to 1 μg/ml.[3–5] However, further in vitro and in vivo studies are needed to define the appropriate management for *N. veterana* infection. Although most reported cases of *N. veterana* infection have had various immunocompromising conditions, including transplantation, systemic lupus erythematosus, cancer, HIV infection and steroid use, a fatal outcome has rarely been reported.[4] Death occurred before antibiotic treatment started in only one case of *N. veterana* peritonitis in an HIV-infected patient.[4]

In conclusion, *N. veterana* can cause disseminated infection in patients of immunocompromised status, such as those with an HIV infection. Sequencing of the 16S rRNA gene is crucial for the accurate identification of this emerging pathogen.

Conflict of interest: No conflict of interest to declare.

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