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CASE REPORT
OLGU SUNUMU

Pulmonary nocardiosis caused by *Nocardia abscessus* mimicking pulmonary thromboembolism in a patient with atypical anti-glomerular basement membrane glomerulonephritis

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ABSTRACT

Pulmonary nocardiosis caused by *Nocardia abscessus* mimicking pulmonary thromboembolism in a patient with atypical anti-glomerular basement membrane glomerulonephritis

Nocardia species are opportunistic bacteria that are frequently contagious by inhalation. Recently, Nocardia abscessus has been described as a different species. We report a 54-year-old male who presented with acute pleuritic chest pain, mimicking pulmonary thromboembolism on the 5th day of discharge from the hospital. The patient was receiving immunosuppressive therapy for newly diagnosed atypical anti-glomerular basement membrane disease. Thorax computed tomography revealed a 17x19 mm soft tissue lesion in the lateral segment of the middle lobe of the right lung. After further examinations, a biopsy decision was made and Nocardia abscessus was isolated in the aerobic culture of the aspiration material.

Key words: *Nocardia abscessus; pulmonary nocardiosis; opportunistic infection; anti-GBM*

ÖZ

Atipik anti-glomerüler bazal membran glomerülonefriti tanılı hastada pulmoner tromboemboliyi taklit eden *Nocardia abscessus* nedenli pulmoner nokardiyozis

Nocardia türleri sıklıkla inhalasyonla bulaşan fırsatçı bakterilerdir. Bunlardan Nocardia abscessus yakın zamanda farklı bir tür olarak tanımlanmıştır. Biz bu çalışmada, taburculuğunun 5. gününde pulmoner tromboembolizmi taklit eden akut plöritik göğüs ağrısı ile başvuran 54 yaşında erkek hastayı sunduk. Hasta yeni tanı atipik anti-glomerüler bazal membran hastalığı nedeniyle immunsupresif tedavi almaktaydı. Göğüs ağrısı etyolojisini araştırmak için çekilen toraks bilgisayarlı tomografisinde sağ akciğer orta lob lateral segmentinde 17x19 mm yumuşak doku lezyonu saptandı. İleri incelemeler sonrası biyopsi kararı alındı ve aspirasyon materyalinin aerobik kültüründe Nocardia abscessus izole edildi.

Anahtar kelimeler: *Nocardia abscessus; pulmoner nokardiyozis; fırsatçı enfeksiyon; anti-GBM*

INTRODUCTION

Nocardia genus consists of gram-positive, aerobic, variable acid-fast bacteria, and is included in the family of Actinomycetales (1). Currently, the genus is composed of 111 validly identified species (2). One of these, *Nocardia abscessus*, was first described as a different species in 2000 by Yassin et al. (3). *Nocardia* spp. are filamentous bacteria found in soil, water, rotted vegetation, and other organic matter. The bacteria are transmitted to humans by inhalation or, less commonly, through the skin. Although pulmonary nocardiosis is encountered in more than 70% of the cases, the infection can also spread to the central nervous system (CNS) and can be fatal. *Nocardia* spp. are uncommon opportunistic pathogens, and approximately two-thirds of the cases are immunosuppressed patients with malignancy, solid organ or hematopoietic stem cell transplantation, human immunodeficiency virus infection/acquired immunodeficiency syndrome, or on long-term steroid use (4).

CASE PRESENTATION

A 54-year-old male patient who was on corticosteroid therapy for atypical anti-glomerular basement membrane (anti-GBM) glomerulonephritis presented with a complaint of acute-onset, sharp, stabbing right chest pain that worsens during breathing. The patient also had fatigue, gross hematuria, and a body temperature of 38.5°C, but he did not have cough, sputum, hemoptysis, or dyspnea. Physical examination revealed reduction of right hemithorax expansion and pleural rubbing sound in the right middle zone.

Two months prior, the patient had been diagnosed with atypical anti-GBM disease by renal biopsy performed to investigate mild hematuria, proteinuria [urine protein-to-creatinine ratio (UPCR) was 432.3 mg/g] and creatinine increase (3.28 mg/dL). Following the diagnosis, he had received plasmapheresis five times every other day, 500 mg intravenous pulse methylprednisolone (MP) for 3 consecutive days, and two courses of 500 mg cyclophosphamide. Six weeks prior, oral immunosuppressive therapy had been commenced with 48 mg of MP per day and the patient had been discharged five days before the current hospital visit without any complaint.

During the current hospitalization, hemoglobin concentration was 8.1 g/dL (11.7-15.5), white blood cell (WBC) count $5.3x10^3$/µL ($4.3-10.3x10^3$/µL), neutrophil count $4.87x10^3$/µL ($2.1-6.1x10^3$/µL), erythrocyte sedimentation rate (ESR) 13 mm/hour, C-reactive protein (CRP) 7.78 mg/dL (0-0.8 mg/dL), procalcitonin 0.54 ng/mL (0-0.1 ng/mL), blood urea nitrogen (BUN) 128 mg/dL (6-20 mg/dL), creatinine 5.09 mg/dL (0.67-1.17 mg/dL), UPCR 2556.5 mg/g and there was no electrolyte abnormality. Urine and blood cultures did not reveal any pathogenic growth. Serology for hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) were negative. C3 and C4 were within normal limits and anti-GBM antibody, anti-nuclear antibody (ANA), anti-dsDNA, antineutrophil cytoplasmic antibodies (ANCA) were negative, too.

Chest radiography demonstrated peripheral opacity in the right middle zone, and therefore low-dose thorax computed tomography (CT) was performed. Computed tomography revealed a newly developed 17x19 mm soft tissue lesion in the lateral segment of the middle lobe of the right lung, which was not present in the chest radiography two weeks ago (Figure 1a). In differential diagnosis, pulmonary infarction due to segmentary pulmonary embolism or septic embolism was considered. As the patient had elevated creatinine levels, CT angiography could not be performed. However, lower extremity Doppler ultra-

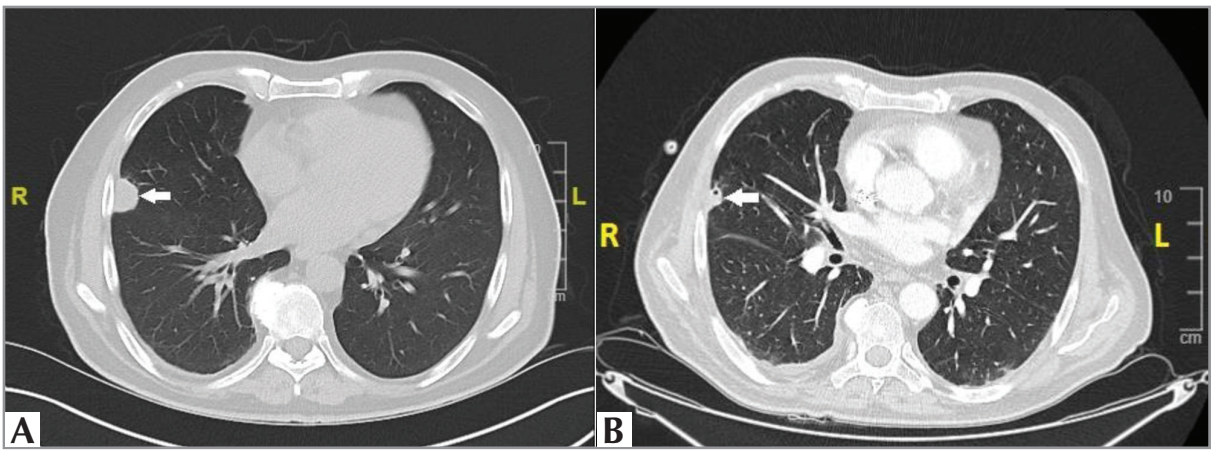

Figure 1. Thorax computed tomography demonstrating: **A.** A 17x19 mm soft tissue lesion in the lateral segment of the middle lobe of the right lung. **B.** A 10x13 mm lesion containing cavitation in the lateral segment of the middle lobe of the right lung, which has shrunk in the first month of antibiotic treatment, compared to previous imaging.

sonography and ventilation perfusion scan revealed neither deep vein thrombosis nor any finding compatible with pulmonary thromboembolism. Transthoracic echocardiography performed to investigate for a possible septic embolism did not reveal any mass or vegetation in the heart valves. As the lesion progressed and the patient expressed severe pain, a CT-guided fine-needle aspiration (FNA) biopsy was performed for definitive diagnosis, and dark pink-brown purulent fluid was aspirated from the lesion. Cytology and cell block section of the sample were characterized by necrotic debris and mixed-type inflammatory cells.

Direct gram staining of the samples showed filamentous, branching gram-positive bacilli and moderate polymorphonuclear leukocytes (11-25 cells/lpf, 10X). The aerobic culture of the aspiration material was inoculated into Columbia 5% sheep blood agar (BD,USA), MacConkey (BD,USA), chocolateagar plates (BD,USA), and Brain Heart Infusion liquid medium (BD,USA). All plates were incubated at 37°C under atmospheric and 5% CO_2 conditions. Small, rough, dry and non-haemolytic chalky white colonies having distinctive odor of moist basement were seen after 48 hours of incubation on sheep blood agar and chocolate agar (Figure 2a). Gram staining from the purified colony revealed gram-positive filamentous, branching gram-positive bacilli (Figure 2b). Thin branching bacilli were evident inmodified Ziehl-Nielsen stain using 1% sulfuric acid as decolorizer. The isolate was identified as *Nocardia abscessus* by matrix-assisted laser desorption ionization time-of-flight mass spectrometry [MALDI-TOF MS (Bruker,Germany)] with score value of 2.1 that yielded to species level identification. antimicrobial susceptibility testing (AST) was performed and minimum inhibitory concentrations (MICs) were assessed by a gradient test (bioMerieux,France), as described previously for *Nocardia* spp. for amikacin, trimethoprim-sulfamethoxazole (TMP-SMX), ciprofloxacin, imipenem, ceftriaxone, amoxicillin-clavulanate, linezolid, and tobramycin (5). The isolate had intermediate susceptibility to tobramycin (MIC=12 µg/mL) and ceftriaxone (MIC=12 µg/mL), and was susceptible to amikacin (MIC=4 µg/mL), TMP-SMX (MIC=0.0160 µg/ml), ciprofloxacin (MIC=1 µg/mL), imipenem (MIC=1 µg/mL), amoxicillin-clavulanate (MIC=0.19 µg/ml), linezolid (MIC=0.50 µg/mL) (6).

The patient was put on intravenous TMP-SMX 7.5 mg/kg/day (TMP component) in 4 divided doses and imipenem-cilastatin 250 mg QID. The MP dose was tapered and eventually discontinued. No pathological findings were detected in the brain CT performed to rule out CNS involvement. Kidney functions deteriorated with the reduction of immunosuppressive therapy and hemodialysis was initiated. In the first month of antibiotic treatment, a control thorax CT showed that the lesion has shrunk to 10x13 mm, and a cavity was formed in it (Figure 1b). At this time, ESR was 14 mm/hour, CRP was 1.29 mg/dL, and procalcitonin was 0.47 ng/mL. The patient's pleuritic chest pain improved, and he had no fever. Thereafter, antibiotic therapy was switched to oral TMP-SMX 7.5 mg/kg/day (TMP component) and was planned to

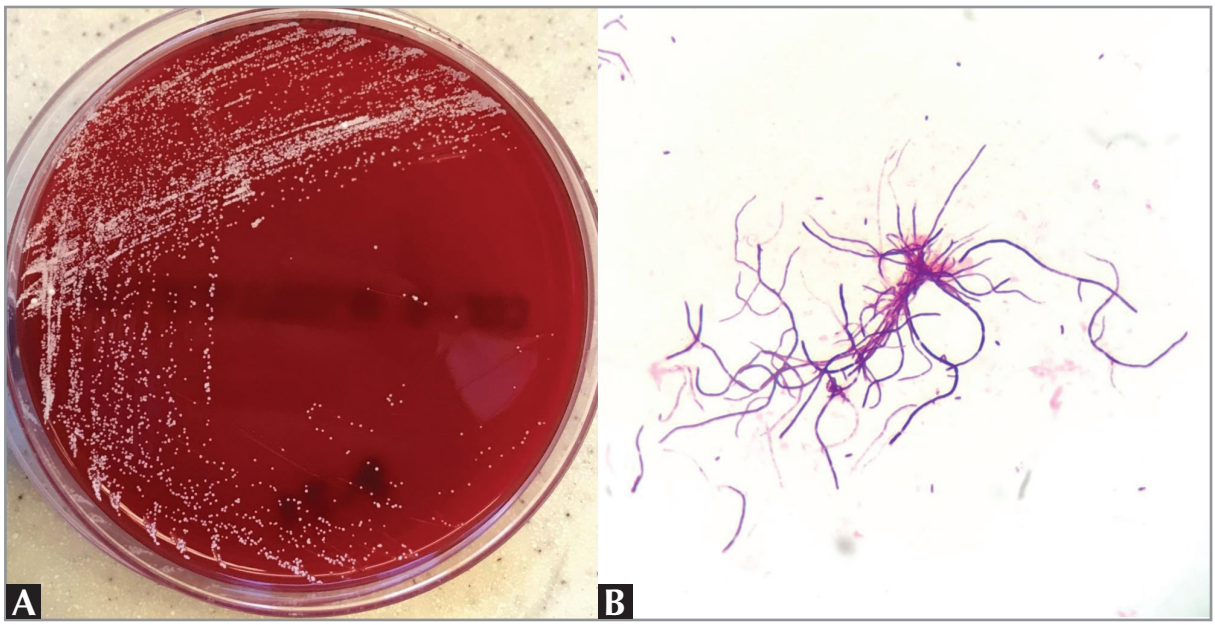

Figure 2. Microbiological examination. **A.** Colony morphology of *N. abscessus* on Columbia %5 sheep blood agar. **B.** Gram stain preparation of the isolated colony (Gram stain × 1,000).

continue for at least 6 months, with outpatient follow-up.

DISCUSSION

Above, we presented a case of pulmonary nocardiosis with acute-onset, sharp, pleuritic chest pain mimicking pulmonary thromboembolism in a high-risk patient for venous thromboembolic events. Pulmonary nocardiosis might be difficult to diagnose as it presents with nonspecific symptoms such as cough, sputum, fever, dyspnea, or hemoptysis (7). In addition, variability of radiographic findings may cause delays in diagnosis and treatment, unless nocardiosis remains on the list of possible diagnoses. The mean time between the emergence of symptoms to diagnosis varies from 30 to 42 days (8,9). In our patient, a definitive diagnosis was made 10 days after the development of symptoms. The most common CT findings of pulmonary nocardiosis were reported to be a nodule/mass (94.4%), ground-glass opacity (77.8%), interlobular septal thickening (77.8%), and cavitation (66.7%) (9). Although these findings are not specific to *Nocardia*, nodule/mass, interlobular septal thickening, and cavitation are significantly more common in pulmonary nocardiosis than other types of bacterial pneumonia.

In 80% of cases, *Nocardia* can be isolated from sputum, but bronchoscopic sampling or CT-guided FNA may be required in the remaining patients (7). In patients who do not produce sputum as in our case, the early use of invasive diagnostic methods may be beneficial, especially in the presence of immunosuppression and suspected infection.

There are no definite guidelines for the initial treatment of nocardiosis. Each *Nocardia* species has specific antimicrobial susceptibilities. Therefore, treatment recommendations are based on species identification and AST. The most frequently active antibiotics against *Nocardia* are linezolid, amikacin, TMP-SMX, minocycline and imipenem, respectively (10). In practice, TMP-SMX is often used and its combination with other agents is recommended for effective treatment. It may be necessary to extend treatment up to 12 months for complete response (4).

In conclusion, nocardiosis is an uncommon opportunistic infection and its diagnosis is challenging, leading to mortality and morbidity if not treated timely and appropriately. Pulmonary nocardiosis may mimic pulmonary thromboembolism and septic emboli due to other bacterial and fungal infections, and its diagnosis may be missed or delayed if nocardiosis is not on the possible diagnoses list. Therefore, clinicians should consider nocardiosis, especially in immunosuppressed patients in the presence of suspected infection with pulmonary involvement. In suitable

patients, withholding empirical antimicrobial therapy and early use of invasive methods such as bronchoscopic biopsy or CT-guided FNA may be useful.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: RI, MDT

Analysis/Interpretation: RI, Nİ, GTD

Data Acqusition: RI, NK, Nİ

Writing: RI

Clinical Revision: MDT, GH, MA

Final Approval: MDT, MA

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