

A 60-Year-Old Woman with Pulmonary Nodules

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WHAT IS YOUR DIAGNOSIS?

A 60-year-old woman was admitted due to persistent right-sided vague chest pain since two months ago. She also complained of 5 kg weight loss and productive cough.

On admission, she was stable and afebrile with mild crackles in both lungs without tachypnea or remarkable respiratory distress.

She lived in a rural region in southwest of Iran and was being treated with combined fluticasone-salmeterol and ipratropium bromide due to chronic bronchitis since five years ago. Exposure to biomass fuels used for cooking and heating was a possible etiology for her chronic respiratory symptoms. She denied using systemic corticosteroids in recent months.

Laboratory analysis revealed normal complete blood count, arterial blood gases, liver and renal function tests, serum lactate dehydrogenase and angiotensin converting enzyme levels. Human immunodeficiency virus antibody was negative and plasma immunoglobulin revealed no abnormality.

Chest roentgenographic studies (Figure 1) revealed multiple nodules in both lung fields.

Based on chest computed tomography (CT) findings and negative repeated sputum smears, the patient underwent CT-guided biopsy of lung nodules. Histopathological examination was unremarkable and the procedure was complicated by pneumothorax.

Finally, bronchoscopy and bronchoalveolar lavage were performed. No abnormality was detected in the airways.

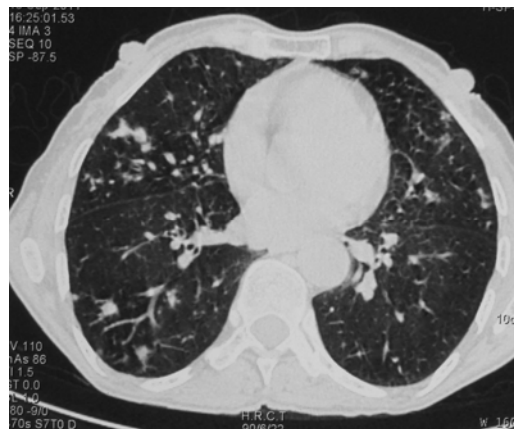


Figure 1. Chest computed tomography revealed multiple scattered nodules in both lungs

Answer

Diagnosis: Pulmonary Nocardiosis

Bronchoalveolar lavage (BAL) smear revealed many filamentous, beaded and branching gram positive bacilli (Figure 2) and finally the culture confirmed Nocardia in BAL specimen.

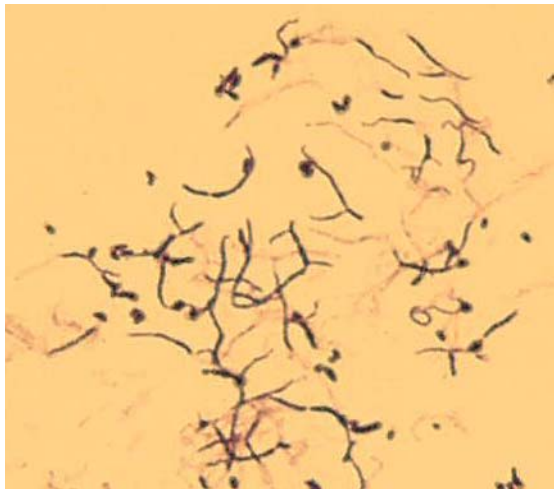


Figure 2. Direct gram smear of bronchoalveolar lavage revealed many filamentous, beaded and branching gram positive bacilli.

According to The Infectious Diseases Society of America, nocardial infections are not rare. Estimated annual incidence of Nocardiosis in the United States is about 500-1000 cases per year (1). There is limited data available about its true incidence in other countries. Difficulties in isolation of the organism, incubation experience and lack of systematic report for Nocardia infection in health system are the probable reasons (2).

It is very important to inform the microbiologist when Nocardiosis is suspected (3). Sometimes incubation of the samples for a prolonged period of time up to 3 weeks may help in making the diagnosis.

The microorganism has the ability to interfere with host phagocytic mechanisms (phagosome-lysosome fusion inhibition in phagocytes, phagosomal acidification neutralization, phagocyte function modification) and to grow within phagocytic cells. Penetration and growth

within host cells describe the virulence of Nocardia (4). Thus, phagocytic and cell mediated immunity play an important role in protection against Nocardia infection particularly the disseminated form of disease (5). Human immunodeficiency virus infection, alcohol abuse, pulmonary alveolar proteinosis, organ transplantation, and lymphoreticular neoplasms are the most frequent conditions that can lead to disseminated Nocardiosis (5,6). In an observational report, 31 adult patients were identified with disseminated pulmonary Nocardiosis; the predisposing conditions were chronic obstructive pulmonary diseases (COPD) (23%), transplantation (29%), HIV infection (19%), alcoholism (6.5%) and treatment with steroids (64.5%) (7).

Lung transplant patients have the highest frequency of Nocardiosis among recipients of solid organs. Receipt of high-dose steroids, cytomegalovirus disease in the preceding 6 months and a high median calcineurin inhibitor level in the preceding 30 days were found to be independent risk factors for Nocardia infection in this population (8).

The radiological manifestations of pulmonary Nocardiosis are very diverse, and include non-segmental consolidation and pulmonary nodules. Cavitory nodules most commonly appear in AIDS patients, and are uncommon in non-AIDS patients (9).

Based on clinical and imaging findings, fungal infections particularly aspergillosis, zygomycosis, cryptococcosis, tuberculosis and atypical mycobacteria, and malignancies including primary lung cancer as well as lung metastases should all be considered in differential diagnosis of pulmonary Nocardiosis (10). Thus, a high index of suspicion for Nocardiosis should be maintained in susceptible hosts with pulmonary infiltrates, particularly when there is evidence for metastatic infection, and in patients with skin infections and a history of outdoor injury.

Considering the propensity of *Nocardia* to the brain, presence of any symptoms indicative of CNS disease warrants brain imaging to exclude the presence of a brain abscess particularly in immunocompromised patients with cutaneous or pulmonary Nocardiosis even without neurologic manifestations.

Occasionally, isolation of *Nocardia* is due to colonization (11), but clinical decision making to receive treatment is based on apparent *Nocardia* related manifestations and existence of immunodeficiency and comorbidity. However, pulmonary colonization in healthy people without disease is not rare (12).

Although sulfonamides in combination with other antibiotics are the drug of choice, other regimens including combination of imipenem and amikacin are preferred in some centers. Linezolid is a useful alternative therapeutic agent due to its oral availability and activity against most of the isolates (13). Occurrence of *Nocardia* in patients on SMX-TMP prophylaxis occurs rarely, which means that this drug does not provide full protection against Nocardiosis (14,15).

The patient was treated with combination of imipenem and amikacin for two weeks and then changed to oral SMX-TMP. Pulmonary nodules were diminished; and pneumothorax was managed properly with chest tube insertion and significantly healed after one week (Figure 3). She was discharged in healthy condition on SMX-TMP for at least 6 months.



Figure 3. Chest high resolution computed tomography two weeks after treatment. Note the diminished nodularity of lung and mild pneumothorax in the right side.

Pulmonary Nocardiosis should be taken into account in patients with predisposing factors, particularly when clinical resolving is not satisfactory under usual antimicrobial agents. Clinicians must be alert about the possibility of Nocardiosis in otherwise healthy people without previously recognized immune deficiency.

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