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Pulmonary Nocardiosis: A Rare Diagnosis in an Intensive Care Unit

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Abstract

Nocardiosis is an acute, subacute, or chronic bacterial infection that is typically acquired through inhalation and usually presents with pulmonary, central nervous system, and cutaneous manifestations. In critically ill patients, Nocardiosis has an unusually high morbidity and mortality. The authors present the case of a 43-years old female with a history of severe alcoholism and undernutrition that was admitted to ICU with refractory hypoxemic respiratory failure. Chest CT showed bilateral and diffuse pulmonary parenchymatous densification, with extensive areas of consolidation that demonstrate cavitation, but the sputum gram stain showed gram-positive branching rods, confirmed in culture as *Nocardia farcinica*. Antibiotic therapy comprised a combination of sulfonamide and meropenem for fourteen days and the patient was successfully weaned from the ventilator at the eight day at the ICU. Pulmonary infection with *Nocardia* spp show clinical symptoms similar to those suspected with pulmonary tuberculosis, but in patients with weakened immune system possibility of human Nocardiosis should always be considered.

Keywords: Pulmonary nocardiosis; infection; *Nocardia farcinica*; intensive care unit

Introduction

Nocardia are aerobic Gram-positive bacteria of the order Actinomycetales. They are found in dust, sand, soil and stagnant water. Nocardiosis is mainly an opportunistic infection but can also affect nonimmunocompromised hosts. Innoculation occurs via inhalation and the most common species causing human infection is the Nocardia asteroides complex, which includes N. asteroides sensu stricto type VI, *N. farcinica*, *N. nova*, and recently *N. abcessus* [1]. Infections with Nocardia spp usually occur in individuals with weakened immune system and can include patients suffering from diabetes, malignancies, HIV/AIDS, lung disorders like pulmonary alveolar proteinosis, individuals with connective tissue disorders, chronic alcoholism, transplant patients, and patients on corticosteroid therapy [2]. The incidence of pulmonary Nocardiosis is low. In the USA, it is estimated that 500–1000 new cases are diagnosed each year and there are few descriptions of pulmonary Nocardiosis in the literature [1]. It´s an infrequent, but serious and potentially fatal pulmonary infection, even though, patients rarely present with symptoms severe enough to warrant admission to the Intensive Care Unit (ICU). Nocardiosis has an unusually high morbidity and mortality in critically ill patients [3].

Case Report

We present the case of a 43-years old female with a history of severe alcoholism and undernutrition that was admitted in the emergency department complaining about persistent shortness of breath, prostration and fever, for 5 days. On the admission, the temperature was 38ºC, the blood pressure 92/68 mmHg, the pulse 100 beats per minute, the respiratory rate 25 breaths per minute, and the oxygen saturation 83% with no oxygen supplementation. Besides an extreme cachexia, the remaining examination was unremarkable. Lack of response to progressive increasing oxygen requirements resulted in refractory hypoxemic respiratory failure such that the patient was intubated and admitted to the Intensive Care Unit (ICU). Chest CT showed bilateral and diffuse pulmonary parenchymatous densification, with extensive areas of consolidation that demonstrate cavitation with central disappearance of pulmonary reticulum, findings suggestive of bilateral necrotizing pneumonia with attainment of all lobes (Figure 1 and 2). Microbiological identification was performed using standard methods: Gram stain, acid resistance and modified acid resistance. Sputum gram stain showed gram-positive branching rods, suspicious for *Nocardia* species, which were later confirmed in culture as *Nocardia farcinica*. Antibiotic therapy comprised a combination of sulfonamide (trimethoprim/ sulfamethoxazole) and meropenem for fourteen days. The patient improved clinically and was weaned from the ventilator at the eight day at the ICU. Was discharged with no respiratory insufficiency already, and after a period of five days in Internal Medicine service, she was admitted to a continuous care unit to carry out a rehabilitation program.

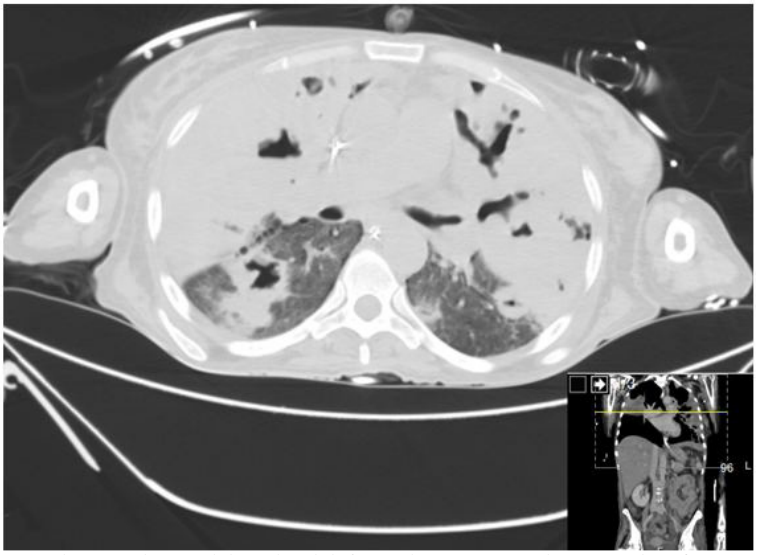

Figure 1: Chest CT showing bilateral and diffuse pulmonary parenchymatous densification, with extensive areas of consolidation that demonstrate cavitation with central disappearance of pulmonary reticulum, findings suggestive of bilateral necrotizing pneumonia with attainment of all lobes.

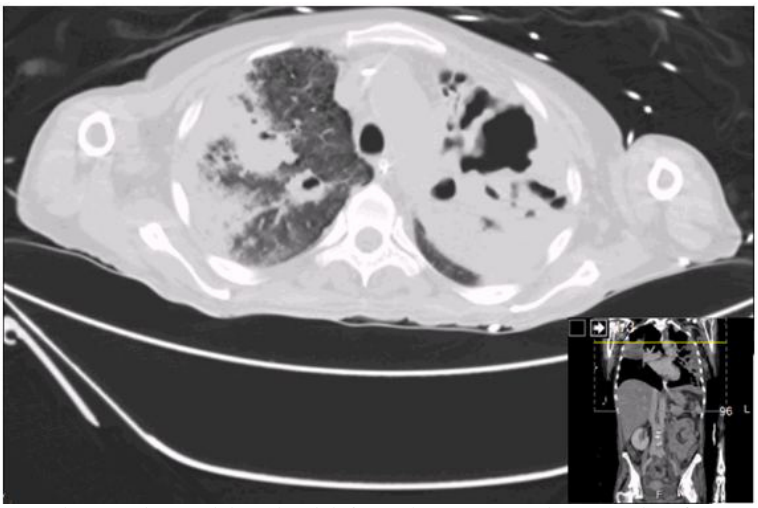

Figure 2: Chest CT showing bilateral and diffuse pulmonary parenchymatous densification, with extensive areas of consolidation that demonstrate cavitation with central disappearance of pulmonary reticulum, findings suggestive of bilateral necrotizing pneumonia with attainment of all lobes.

Discussion and Conclusion

Pulmonary infection with *Nocardia* spp show clinical symptoms similar to those suspected with pulmonary Tuberculosis (fever, cough, chest pain, weight loss and pneumonia), but in patients with weakened immune system possibility of human Nocardiosis should always be considered. Since the clinical and radiologic manifestations are nonspecific, and the microbiological diagnosis is often difficult, it seems likely that, in some patients, pulmonary Nocardiosis will be mistaken for other infections [4]. Alertness to the possibility of Nocardiosis can expedite the diagnostic work-up, especially in patients with predisposing factors. The diagnosis of *Nocardia* requires the isolation and identification of the organisms from a clinical specimen. Since nocardial colonies may take up to 2 weeks to appear, it is important to notify the laboratory when *Nocardia* infection is suspected, so that appropriate measures can be taken to optimize the recognition and recovery of the organism. *Nocardia* can disseminate to virtually any organ and, thus, clinical samples can vary. As most cases are pulmonary, the most frequent samples are sputum and bronchoalveolar lavage, or other respiratory specimens. Other samples are skin biopsies, aspiration from fluid collections, cerebrospinal fluid, and biopsy material [5]. So, if sputum examinations do not yield the diagnosis in a suspected case and the diagnosis cannot be made easily from lesions elsewhere in the body, more invasive diagnostic procedures like bronchoscopy, needle aspiration, and open lung biopsy should be performed [4]. *Nocardia* is a gram-positive bacterium that grows aerobically. Unlike other gram-positive bacteria, *Nocardia* appears as a filamentous bacterium with hyphaelike branching on direct microscopy. *Nocardia* exhibits varying degrees of acid-fastness, depending on the mycolic acid composition in the cell wall and type of stain used [1]. Laboratory diagnosis of human nocardiosis includes microscopy and culture. Identification of *Nocardia* is more rapid, precise, and accurate with polymerase chain reaction (PCR) and 16S rDNA sequencing than with conventional phenotypic methods, which include microscopic, cultural, and

biochemical properties. Modified acid-fast staining using 1% sulphuric acid as a decolorizer is employed to identify *Nocardia* microscopically in clinical samples, where pink colored filamentous branching bacilli are observed as shown in (Figure 3) [3]. *Nocardia* is rarely considered as a contaminant in the laboratory, and each isolate must be carefully evaluated. Serology is usually not useful, as no single serological technique can detect all of the clinically relevant species. Moreover, antibody response is usually impaired in immunocompromised patients. Microscopic and macroscopic examination of specimens submitted for culture is the first step in providing a diagnosis. Staining with modified acid-fast stain, and especially gram stain, is particularly important to provide a rapid presumptive diagnosis while awaiting the results of the culture [5]. General treatment recommendations for Nocardiosis are hindered by the lack of prospective controlled trials. Optimal antimicrobial treatment regimens have not been firmly established. *Nocardia* displays variable in vitro antimicrobial susceptibility patterns, and management of nocardial infections must be individualized [3]. No prospective randomized trials have determined the most effective therapy for nocardiosis. In addition, it is unlikely that such trials will ever be performed since a large number of patients with similar clinical manifestations would be required. Two hallmarks of nocardiosis are its relative rarity and the diversity of the clinical presentation in different patients. Thus, the choice of antimicrobials is based upon cumulative retrospective experience [6]. Sulphonamides have been the antimicrobials of choice since they were introduced 50 years ago. However, changes in the host and concurrent diseases, immune factors, the increase in resistance and adverse effects have led to an increased need for more powerful and safer antibiotics. Currently, TMP-SMZ is widely used for the treatment of this infection, despite the lack of data supporting the need for this combination. Amikacin, imipenem, third generation cephalosporins, minocycline, netilmicin and amoxicillin-clavulanic acid are drugs that are active in vitro against a large percentage of *Nocardia* isolates. Experimental studies have shown in vitro synergy with imipenem-cefotaxime, cefotaxime-amikacin and imipenem-amikacin with good clinical results. The appearance of resistance of *N. asteroides* to TMP-SMZ has led to proposals of combined therapy that take into account the clinical response, which are now included in several clinical guidelines. However, the susceptibility results do not always correlate with the clinical outcomes. When the CNS is involved, treatment with cefotaxime or ceftriaxone is recommended. Among the new beta-lactams, cefmetazole has shown a better in vitro susceptibility and clinical resolution. Antimicrobial susceptibilities should be performed on all *Nocardia* isolates as a guide to therapy. Susceptibility testing is particularly important in patients infected with *Nocardia* species known to have high frequencies of antimicrobial resistance, such as *N. farcinica* or other newly identified species [18]. One caveat is that immune compromised patients may fail therapy even though susceptibilities indicate that the organism is sensitive. Susceptibility testing is also repeated for patients who fail to respond to initial therapy 7. Immuno competent patients with pulmonary Nocardiosis or disseminated Nocardiosis outside the CNS should be treated for 6–12 months. In the case of immunosuppressed patients, treatment should continue for 1 year and, if possible, the dose of the immunosuppressant drug should be reduced. Likewise, the duration of treatment must be at least 1 year for patients with CNS involvement [1]. The extent of disease and underlying conditions may significantly influence the outcome of *Nocardia* therapy. Poor prognosis is often associated with a delay in diagnosis and/or premature discontinuation of appropriate therapy [8]. Clinical improvement is usually seen within two weeks after initiation of appropriate therapy like it was present in this clinical case. Patients who continue to be symptomatic or have progression of their primary lesions after two weeks of therapy should be carefully revaluated. Poor response may represent primary drug resistance, inadequate serum antibiotic concentrations, poor penetration of drug into the infected tissue compartment, or the presence of an abscess requiring surgical drainage. Patients should be monitored for the response to therapy and possible drug toxicity. Following discharge from the hospital, patients should be seen frequently (example, at least monthly) to monitor for changes in signs and symptoms as well as to detect any adverse drug effects [8].

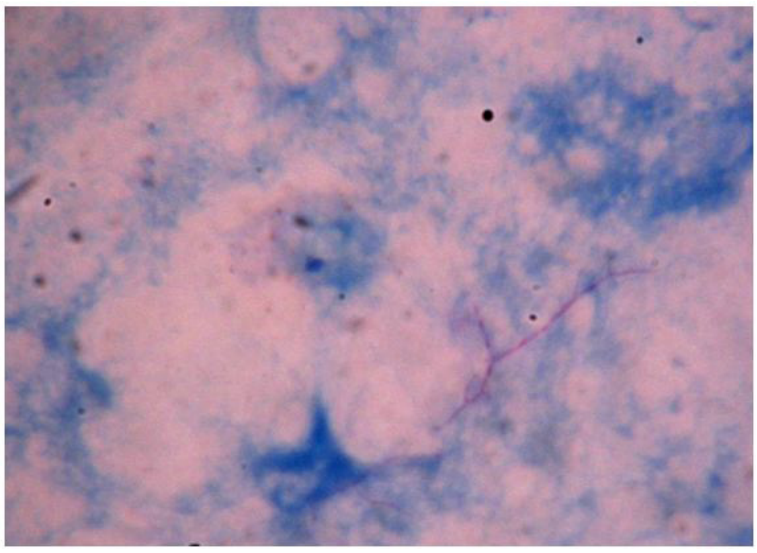

Figure 3: Pink colored filamentous and branched bacilli appearing in modified acid fast stained smear of respiratory secretions.

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