Case Report

Miliary nocardiosis:
Fatal sepsis in an immunocompromised patient

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ABSTRACT

We present a rare case of pulmonary nocardiosis presenting as rapidly progressive sepsis with a miliary radiologic pattern in an immunocompromised patient, with a history of idiopathic membranous nephritis under treatment with cyclosporine and methylprednisolone. Pulmonary nocardiosis presents high mortality and nonspecific clinical and radiological features. The most usual radiological patterns are alveolar opacities, consolidation, nodules, masses, reticulonodular opacities, and pleural effusion. On the other hand, a miliary pattern can occur in tuberculosis, fungal infection, viral pneumonia, malignancy, sarcoidosis, tropical pulmonary eosinophilia, hypersensivity pneumonitis, silicosis and other rare conditions. Clinical suspicion is important as microbiological isolation requires 2-7 days. Awareness around nocardiosis needs to be raised as its frequency increases in parallel with the increase of cytotoxic and steroid treatment.
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INTRODUCTION

Immunosuppression is a well-known risk factor for infection. Choice of treatment can be extremely challenging, especially in patients presenting sepsis, as the isolation of the pathogen is either impossible or time-consuming, requiring prompt initiation of broad-spectrum antibiotic treatment before microbiological diagnosis. We present a case of pulmonary nocardiosis in an immunocompromised patient that presented in the emergency department with rapidly progressive sepsis.

CASE REPORT

A 46-year-old Caucasian man presented in the Emergency Department with hypotension (79/42 mmHg), mild respiratory insufficiency (pO_2 59 mmHg on room air) and acute on chronic renal failure with anuria. He had a history of idiopathic membranous nephritis and was receiving treatment with cyclosporine 150 mg twice daily and methylprednisolone 32 mg daily

during the last 6 months. He had a smoking history of 20 pack/years, he lived in his house, with no pets, was currently unemployed, and never travelled during the past year. On presentation, he was febrile (38.6 °C) and presented crackles in lung auscultation. Initial laboratory findings revealed diminished white blood cell count (2.500 cells/dL, neutrophils 1.400 cells/dL), anaemia (Hct 35%), elevated c-reactive protein (16 mg/L) and elevated serum creatinine (6.6 mg/dL). Chest x-ray revealed bilateral infiltrations forming a micronodular pattern (Figure 1). Rapid deterioration of gas exchange (pO_2 62 mmHg on FiO_2 of 60%) led to urgent chest computed tomography and pulmonary angiography that was negative for pulmonary embolism, thus revealed diffuse, bilateral micronodular lesions and dense infiltrates of the basal parts of the lower lobes (Figure 2). The patient was placed empirically on imipenem/cilastatin, azithromycin, voriconazole and trimethoprim/sulfamethoxazole, and underwent urgent hemodialysis. A few hours after presentation, he developed severe hemodynamic instability and acute respiratory distress syndrome and was intubated. Hemodiafiltration was also started in the ICU as the patient was anuric presenting severe metabolic acidosis. Unfortunately, the patient did not respond to antibiotic treatment and supportive care and died 24 hours after admission at the ICU. Blood cultures confirmed post mortem the presence of *Nocardia* spp.

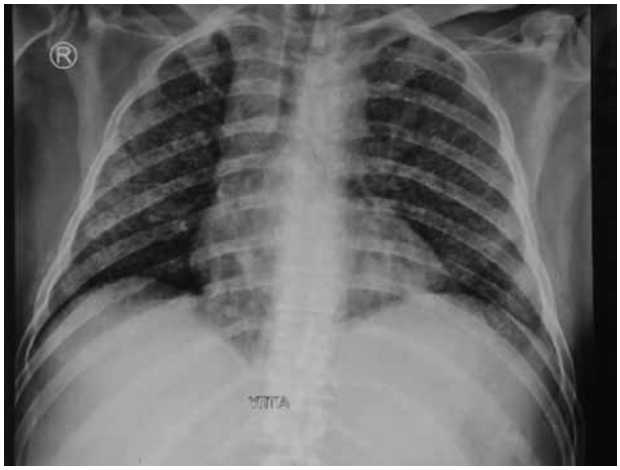

FIGURE 1. Chest x-ray showing diffuse micronodular infiltrations.

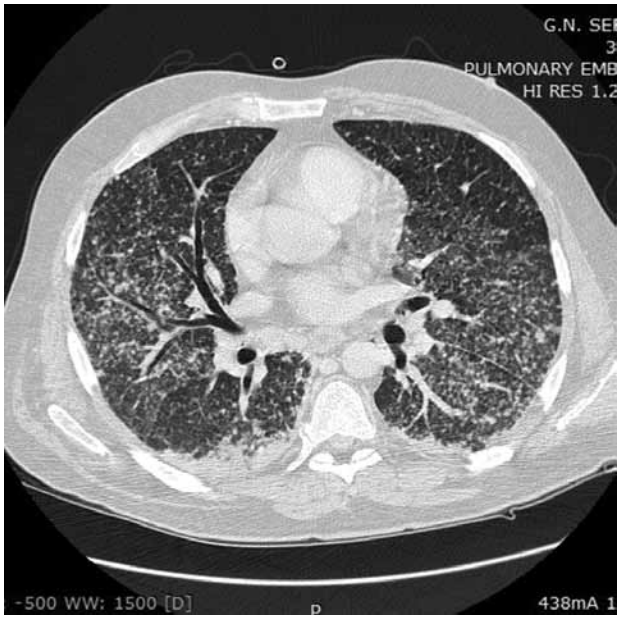

FIGURE 2. Diffuse, bilateral micronodular lesions and dense infiltrates of the basal parts of the lower lobes.

DISCUSSION

Sepsis is a major cause of morbidity and mortality in the immunocompromised patients[1]. Immunosuppression attenuates the signs of infection posing obstacles in early diagnosis of sepsis. The differential diagnosis should include conventional and opportunistic pathogens, with consideration of probable site of infection, immune status, chronic comorbidities, social history[1-2].

Prompt initiation of antibiotic treatment within the first hour of documented hypotension is associated with increased survival[2]. In the above case, a combination of broad-spectrum antibiotics such as imipenem/cilastatin plus azithromycin was immediately started, following the current recommendations[1-3]. Voriconazole was added due to the miliary nodularity that can often occur in a fungal infection. Trimethoprim/sulfomethoxazole (TMP/SMX) was also initiated targeting *Pneumocystis jiroveci* pneumonia, which is also probable in an immunosuppressed host and can present with various radiological patterns, including miliary nodularity. TMP/SMX is also considered the therapy of choice for nocardiosis[4]. Carbapenems, third-generation cephalosporins, and amikacin are alternative choices. Combination therapy has been recommended for serious infections. In our case, sepsis was not contained despite prompt initiation of two antibiotics that *Nocardia* spp. are known to be susceptible to.

Nocardia spp. is a Gram-positive aerobic bacillus of

the genus *Nocardia*. Pulmonary nocardiosis is rather infrequent demanding high clinical suspicion in patients with depressed cellular immunity such as patients under corticoid or cytotoxic treatment. It presents as an acute, subacute or chronic infection with diversity in clinical and radiological patterns[4]. However, the patient of this case had an extremely rare presentation with miliary appearance and rapidly progressive septic shock. Miliary appearance is reported only twice in the literature and fatal sepsis is also infrequently reported[5-8].

The most usual radiological patterns of pulmonary nocardiosis are alveolar opacities, consolidation, nodules, masses, reticulonodular opacities, and pleural effusion. Empyema and necrotizing pneumonia with subsequent cavitation can also occur[4,9,10].

Furthermore, the miliary radiological appearance can occur in other infectious conditions such as tuberculosis, fungal infection (histoplasmosis, mycoplasmosis, and blastomycosis) and viral pneumonia[9,10]. Other causes of such an appearance can be: a) malignant (bronchoalveolar carcinoma, hematogenous metastases from thyroid or kidney cancer, lymphagitic carcinomatosis), b) other (sarcoidosis, tropical pulmonary eosinophilia, hypersensivity pneumonitis silicosis and pulmonary siderosis), c) rare (allergic bronchopulmonary aspergillosis, leiomyoma, pulmonary alveolar microlithiasis, complication of BCG immunotherapy)[9-11].

Pulmonary nocardiosis presents high mortality and nonspecific clinical and radiological features. Clinical suspicion is important as microbiological isolation requires 2-7 days[12]. Awareness around nocardiosis needs to be raised as its frequency increases in parallel with the increase of cytotoxic and steroid treatment.

CONFLICTS OF INTEREST
None.

ΠΕΡΙΛΗΨΗ

Κεχροειδής νοκαρδίωση: Θανατηφόρος σήψη σε ανοσοκατεσταλμένο ασθενή

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Το περιστατικό που παρουσιάζεται αφορά πνευμονική νοκαρδίωση σε ανοσοκατεσταλμένο ασθενή, η οποία εκδηλώθηκε κλινικά ως ταχέως εξελισσόμενη σήψη και απεικονιστικά με κεχροειδές πρότυπο. Ο ασθενής έπασχε από ιδιοπαθή μεμβρανώδη νεφρίτιδα υπό θεραπεία με κυκλοσπορίνη και μεθυλπρεδνιζολόνη. Η πνευμονική νοκαρδίωση εμφανίζει υψηλή θνητότητα και μη ειδικά κλινικά και απεικονιστικά χαρακτηριστικά. Τα πιο συνήθη απεικονιστικά ευρήματα είναι: κυψελιδικές και δικτυοζώδεις διηθήσεις, πύκνωση, όζοι, μάζες και πλευριτική συλλογή. Αντίθετα, το κεχροειδές πρότυπο απαντάται σε φυματίωση, πνευμονία από μύκητες και ιούς, κακοήθεια, σαρκοείδωση, τροπική πνευμονική ηωσινοφιλία, πνευμονίτιδα εξ υπερευαισθησίας, πνευμονοκονίωση και άλλες σπάνιες παθήσεις. Η κλινική υπόνοια είναι σημαντική, καθώς η μικροβιολογική απομόνωση απαιτεί 2-7 ημέρες. Η εξοικείωση με το φάσμα των εκδηλώσεων της νοκαρδίωσης οφείλει να αυξηθεί, καθώς αυξάνεται η συχνότητά της, παράλληλα με την αυξανόμενη χρήση ανοσοκατασταλτικών θεραπειών.

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Λέξεις - Κλειδιά: *Κεχροειδή οζίδια, Νοκαρδίωση, Ανοσοκαταστολή, Σηπτικό σοκ*

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