

Primary Soft-Tissue Nocardial
Abscess with a Complication of Severe
Pneumonia: A Case Report and
Literature ReviewShufang Zhang^{1#}, Feifei Zhou^{2#}, Xiuhui Lin³, Lihong Wang⁴, Wei Cui³ and
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CC-BY 4.0**Keywords** Primary soft-tissue
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Abstract

Although very rare, nocardiosis is considered as an important opportunistic infection, especially in immunocompromised patients with long-term corticosteroid use or organ transplantation. Lung and skin involvements are frequent, but primary soft-tissue nocardiosis is very rare. Herein, we described a 48 year-old Chinese man with a primary soft-tissue nocardial abscess caused by multidrug-resistant nocardia asteroides, which was sensitive only to imipenem and resistant to trimethoprim-sulfamethoxazole and other antibiotics like amikacin and vancomycin. An initial treatment with a combination of surgical drainage and imipenem was conducted, but a secondary severe pneumonia was complicated two weeks later. Then, the antimicrobial regimen was shifted to sulbactam sodium/cefoperazone and itraconazole injection for the severe pneumonia. For nocardiosis, drainage was continued and minocycline was administered instead of imipenem for maintenance therapy for 9 months. Eventually, the patient recovered well from the primary soft-tissue nocardial abscess and the secondary severe pneumonia. To our knowledge, this is the first case with a combination of primary soft-tissue nocardial abscess, multidrug-resistant nocardia asteroides and complication of severe pneumonia.

Introduction

Nocardiosis is an opportunistic infection that has been noted in patients with malignancies, autoimmune diseases, long-term steroid users and transplant recipients [1-5]. Lungs and skin involvements are frequent, whereas bone and cerebral tissue involvements are rare [2-5]. Soft tissue nocardiosis is often a sign of a disseminated nocardia infection or secondary to primary cutaneous nocardiosis [6], but primary soft-tissue nocardiosis is very rare. Although Trimethoprim-Sulfamethoxazole (TMP/SMZ) is considered as the most efficacious regimen for nocardiosis, resistance has been reported [7]. Herein, we described a very rare case of primary soft-tissue nocardial abscess caused by multidrug-resistant nocardia asteroides, which was sensitive only to Imipenem and resistant to TMP/SMZ and other antibiotics like amikacin and vancomycin. The patient was complicated with secondary severe pneumonia, but he was successfully recovered with a combination of alternative antibiotic therapy and continuous surgical drainage.

Case Report

A 48-year-old Chinese man was admitted to our hospital with fever, sore swellings on his left inferior thigh and numbness on the left dorsal foot for a month. He had been treated with Prednisone at 10 mg/day for one year for his rheumatoid arthritis. On examination, he was conscious and his body temperature was 38.3°C, pulse rate was 108/min, blood pressure was 118/68 mm Hg, and respiratory rate was 20/min. Left thigh movements were painful and excessively restricted. A palpable soft tissue mass (10 cm×8 cm) with rigidity was found on the left inferior thigh, but no ulcer or injury on the skin. Numbness was found on the left dorsal foot. Other physical findings were unremarkable. Laboratory findings included a leukocyte count of 23.3×10⁹/l with 92% neutrophils, a hemoglobin level of 13.2 g/dl, elevated C-reactive protein level of 128 mg/l, and a low albumin level of 2.66 g/dl. HIV test was negative. Electrolytes and other biochemical parameters were normal. Chest radiograph was normal (Figure 1A). Magnetic Resonance Imaging (MRI) showed a multifocal cystic mass in the left inferior thigh (Figure 1B-1D).

The primary diagnosis was considered as soft-tissue abscess, and he was treated empirically

with intravenous Piperacillin/Tazobactam and Levofloxacin. Percutaneous aspiration guided by Computed Tomography (CT) was performed, which revealed purulent fluid with large leucocytes with 68% neutrophils. The pus sample was sent for microbiologic culture. A Gram stain of purulent material demonstrated delicate branching gram-positive rods. The nocardia infection was suspected and antibiotic therapy regimen was shifted to a combination of TMP/SMX and amikacin. A week later, the microbiological culture of pus revealed nocardia asteroides, and the antibiotic sensitivity testing determined susceptibility only to imipenem and resistances to Penicillin, Amoxicillin, Trimethoprim-Sulfamethoxazole, Amikacin, Rifampicin, Clindamycin, and Vancomycin. Thus, the antibiotic therapy regimen was shifted to intravenous imipenem (0.5g, q6h). At the same time, incision and drainage of the abscess were performed, and the sample of abscess wall was sent for pathological examination. On the next day after the drainage, the patient was strikingly improved with decreased fever and reduced numbness on the left dorsal foot. The pathology of the abscess wall revealed an acute suppurative inflammation (Figure 1E). To investigate whether the soft-tissue nocardial abscess was primary or secondary, blood cultures were performed several times, and they were negative. CT scans of brain, lung, abdomen, and pelvis were performed and no abnormality was found. So the diagnosis of primary soft-tissue nocardial abscess was finally established based on the above findings.

The patient recovered well after the initial therapy for nocardia asteroides and subsequent cultures of the drainage fluids from the lesion were negative. However, the situation of the patient was deteriorated two weeks later after imipenem administration, he complained with high fever with a high body temperature of 39.3°C, productive cough and dyspnea, and extensive moist rales were heard in both lungs on auscultation. A complete blood count showed an elevated white count of $16.6 \times 10^9/l$ with a high percentage (94%) of neutrophils. An analysis of arterial blood gas in room air showed pH 7.423, PCO_2 23.9 mm Hg, PO_2 56.8 mm Hg, SaO_2 90.2%. Chest radiograph showed diffuse blurred shadows in both lung fields (Figure 2A), which was further confirmed by chest CT scan (Figure 2B and 2C). The sputum smears showed large Gram-negative bacteria and yeast with spore and fungal hyphae. Severe pneumonia was diagnosed. In view of the possibility of super infection/secondary infection, Imipenem was withdrawn. Intravenous sulbactam sodium/cefoperazone (3.0 g, q8h) and itraconazole injection (0.2 g, qd) for Gram-negative bacteria and yeast were administered respectively as an initial antibiotic regimen for the severe pneumonia. Though minocycline was not included in the sensitivity testing, it has an excellent in vitro activity [8]. So oral minocycline (0.1 g, bid) was administered instead of Imipenem for maintenance therapy of nocardiosis, and surgical drainage of the abscess was continued. Two days later, sputum culture showed large candida tropicalis and stenotrophomonas maltophilia with sensitivity to itraconazole injection and sulbactam sodium/cefoperazone respectively, so the initial antibiotic regimen was appropriate and continued. On the third day after adjustment of antibiotic regimen, the patient was improved. One week later, repeated chest radiograph revealed that both lung fields were almost clear (Figure 2D). The repeated cultures of sputum and drainage fluids were negative. Ten days later, the antibiotics of sulbactam sodium/cefoperazone and itraconazole injection were replaced by levofloxacin and itraconazole

oral solution respectively, which were stopped two weeks later. Follow-up chest CT scan one month after antibiotics were completed revealed that both lung fields were almost clear with only sporadic small patchy blurred shadows in right lung field (Figure 2E and 2F). Changing dressing was performed as needed, and the wound was healed up 6 months later. To prevent the recurrent of nocardiosis, Minocycline was administered for 9 months. The patient was then followed up for 6 additional months, and showed an uneventful recovery with no relapse of nocardiosis.

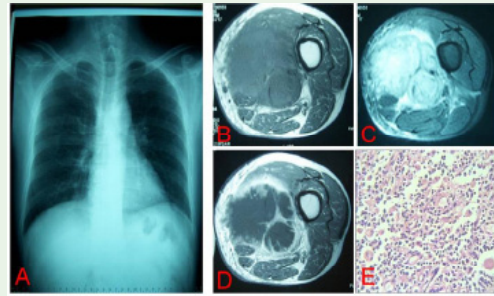


Figure 1: (A) Chest radiography of the patient on admission showed unremarkable. (B-D) Magnetic resonance imaging showed a multifocal cystic mass with long T1 and long T2 signal between muscle group in left leg (B and C). After venous injection of Gd-DTPA, the cystic wall and septa were enhanced remarkably with clear margins to adjacent soft tissues (D), which suggested an abscess. (E) The pathology of the abscess wall showed a dense inflammatory infiltrate with large of neutrophil and lymphocyte (hematoxylin and eosin, original magnification $\times 400$).

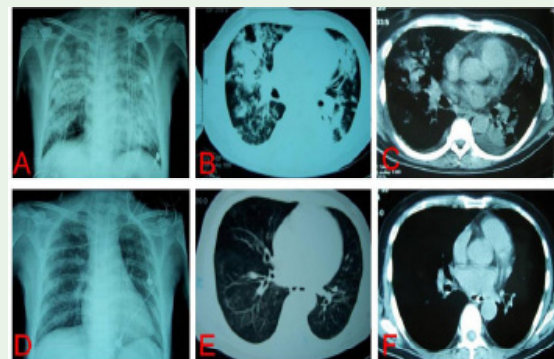


Figure 2: (A) Chest radiograph two weeks later after imipenem therapy showed widespread exudation and consolidation in both lung fields. (B and C) Further computed tomography scan also showed widespread exudation and consolidation in both lung fields. (D) Chest radiograph one week after antibiotic therapy with itraconazole injection and sulbactam sodium/cefoperazone displayed that previous exudation and consolidation lesions (shown in A) were almost absorbed. (E and F) Follow-up chest CT scan one month after antibiotics withdrawal appeared only sporadic small patching blurred shadows in the right lung field.

Discussion

Nocardia is an opportunistic microorganism that mainly affects patients under an immunosuppressive conditions such as connective tissue disorder, HIV infection, malignancies, corticosteroids and/or immunosuppressive drugs use and organ transplantation [3-5,9,10]. The entrance of nocardia species into the human body is considered either by skin lesions or by the respiratory tract as the main nocardiosis are pulmonary nocardiosis and primary cutaneous and soft tissue nocardiosis, which are also well known [3-5]. A soft

tissue nocardiosis is often a sign of disseminated nocardia infection or secondary to primary cutaneous nocardiosis [4,6], but an isolated primary soft tissue nocardiosis is very rare. Lyos, et al [11] has reported a case of primary left infrapatellar nocardiosis caused by nocardia asteroides and successfully treated with TMP/SMZ. The mechanism of primary soft-tissue nocardiosis in the present case was not well known because there was no skin injury, pulmonary/other tissue lesions or nocardia bacteremia.

The present case highlights the problem of multidrug-resistant nocardia asteroides. Though TMP/SMZ is considered as the most efficacious regimen for nocardiosis, several cases of de novo resistance have been reported with clinical failure [7,12] even with a high resistance ratio of 15% in a recent study [5]. Thus, the antibiotic sensitivity testing for nocardiosis is very important for appropriate treatment. Surgical intervention has been reported to be life-saving, in addition to the antibiotics [6,13]. In the current case, initial treatment with a combination of open surgical drainage and intravenous imipenem achieved a dramatic clinical improvement. However, the patient developed severe pneumonia two weeks later. Considering the complication of secondary severe pneumonia, imipenem was withdrawn thereafter and oral minocycline was administered for the sequent maintenance treatment. Although we didn't know whether Minocycline was sensitive to nocardia asteroides as it was not included in the antibiotic sensitivity testing, the patient obtained an uneventful recovery with no relapse. Alternative antimicrobial agents like Linezolid have shown a good clinical and microbiological efficacy for nocardiosis currently [4,14], but we could not obtain this agent at that time. In addition, continuous open surgical drainage and changing dressing might play a critical role in the recovery of the current patient. The previous study has shown that patients with soft-tissue infections obtained the same cure rate after surgical drainage regardless of appropriate or inappropriate antibiotics [15].

Another problem in the current case is the complication of secondary severe pneumonia. To our knowledge, there was no case report about complication of severe pneumonia during the therapy period of nocardia infection. Imipenem was often performed as initial treatment combined with TMP/SMZ or other agents such as amikacin in refractory cases, and then stopped for a short period [9,16]. However, the duration of imipenem for nocardiosis is not well known. Two weeks after Imipenem administration, the patient complicated severe pneumonia which resulted in acute respiratory failure. Inappropriate antibiotic therapy influences negatively the outcome of patients with severe bacterial infections [17]. Sulbactam sodium/cefoperazone and itraconazole injection were used as initially empirical antibiotics for secondary severe pneumonia according to the local microbial prevalence data and antibiotic resistance data in our ward, which was partly contributed to the successful treatment of secondary severe pneumonia in the current case. Thus, the timely and appropriate administration of initial empiric anti-infective therapy is very important, which is based upon each patient's presenting illness and local patterns of infection [18].

This case report was unique for several reasons: (i) it was a primary soft-tissue nocardial abscess without pulmonary, skin or blood stream involvements; (ii) the nocardia asteroides was multi drug-resistant including trimethoprim-sulfamethoxazole, which was only sensitive to imipenem; and (iii) a secondary severe pneumonia

resulting in acute respiratory failure was complicated, which was successfully treated by the timely and appropriate administration of initial empiric anti-infective therapy. A limitation should be pointed out from our current case that the molecular identification of the pathogen in the current nocardiosis was not performed by 16S rRNA gene analysis [19].

Conclusion

The possibility of nocardia infection should be kept in mind in patients exhibiting primary soft-tissue abscess without pulmonary involvement, direct skin injury or nocardia bacteremia, and a combination of continuous open surgical drainage and appropriate anti-infective therapy is very important. Furthermore, the superinfection should be considered when the condition is deteriorated especially after administrating broad-spectrum antibiotics such as imipenem.

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