Disseminated Nocardia farcinica infection in a patient with systemic lupus erythematosus

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Here, we describe a patient with disseminated systemic nocardiosis. He had a history of systemic lupus erythematosus and had received oral prednisolone for 7 months. Nocardia farcinica was isolated from the pus. There were neither clinical nor radiologic features of pulmonary nocardiosis. The patient was treated with oral trimethoprim/sulfamethoxazole, intravenous imipenem and surgical drainage with a good clinical response, and there has been no recurrence of the infection.

Introduction

Nocardia species are aerobic, Gram-positive, filamentous, partially acid-fast bacteria found worldwide as soil saprophytes. Nocardiosis in humans ranges from a self-limiting, subclinical condition to acute, life-threatening and disseminated disease (McNeil & Brown, 1994). Nocardiosis usually affects immunocompromised hosts. The most common site of infection is the lung, which may be followed by dissemination to multiple sites. Disseminated nocardiosis to the brain, kidneys, joints or eyes can occur by haematogenous spread. However, muscular involvement is uncommon. We describe an unusual case of systemic infection (manifesting as intra-muscular, subcutaneous and brain abscesses) caused by Nocardia farcinica in a patient with systemic lupus erythematosus (SLE) on long-term oral corticosteroid therapy, and review the reported cases of muscular nocardial abscesses in the English language literature.

Case report

A 52-year-old Japanese man with SLE was treated with prednisolone at 40 mg per day for 1 month. The dose of prednisolone was tapered to 20 mg per day over a period of 6 months. At this time, he noticed a subcutaneous nodule on the left flank. Within 2 months, further subcutaneous nodules developed on the trunk and left lower extremity. He had no history of injury. There was no fever, weight loss, chills or shortness of breath, and he denied any weakness, numbness, difficulties with gait or imbalance, or visual changes. He had muscular pain in the left lower thigh region. Physical examination revealed multiple subcutaneous nodules, ranging from 3 to 6 cm in diameter associated with tenderness and swelling on the left upper arm, left axilla, left thoracic region, lumbar region and the left thigh. In particular, a tender, erythematous mass measuring 15 × 17 cm was observed in the left femoral region (Fig. 1, left panel). Computed tomography (CT) of the left femoral region showed a ring-enhancing, spherical, hypodense, mass lesion in the left rectus femoris muscle (Fig. 1, right panel). Chest X-ray and CT of the chest did not reveal any masses. A magnetic resonance imaging (MRI) of the brain was performed and revealed peripherally enhancing lesions in the right parietal (Fig. 2a) and temporal (Fig. 2b) region on T1-weighted MRI, indicating the presence of brain abscesses.

Laboratory evaluations revealed the following: white blood cell count 12 700 mm⁻³ (neutrophils 88.5 %, lymphocytes 7.5 % and monocytes 3.0 %); C-reactive protein 19.1 mg dl⁻¹; CD4⁺ T-cell count 9 % (normal range, 29–59 %); CD8⁺ T-cell count 48 % (normal range, 19–48 %); and CD4/CD8 ratio was 0.19 (normal range, 6–29).

The muscular abscess was drained and yielded 18 ml of pus. Pus drawn from the intramuscular and subcutaneous abscesses was thick and yellow. Microbiological examination of the purulent material obtained from both the intramuscular and subcutaneous abscesses showed branching Gram-positive rods on the Gram stain. They were also acid-fast filamentous bacilli on Ziehl–Neelsen stain. Colonies of the micro-organism on blood agar were crumbly and orange–yellow; thus, the bacteria were suspected to be Nocardia species. Identification of Nocardia asteroides group was confirmed by hydrolysis of urea and non-degradation of...
adenine, casein, hypoxanthine, xanthine and tyrosine. The organism was then confirmed as *Nocardia farcinica* by acid production from *i*-erythritol, *d*-glucose, *l*-rhamnose and mannose. The organism was susceptible to trimethoprim/sulfamethoxazole (TMP-SMX) and imipenem, but resistant to tobramycin and kanamycin.

The diagnosis of disseminated nocardiosis caused by *N. farcinica* was made and the patient was treated with oral TMP-SMX and intravenous imipenem with a good clinical response. Intravenous therapy was continued for 4 weeks and after discharge, oral TMP-SMX therapy was administered for another 10 months. Repeat MRI of the brain performed at 2.5 months confirmed that the abscesses had healed with treatment.

**Discussion**

The patient had intramuscular, subcutaneous and brain abscesses from which *N. farcinica* was isolated. *Nocardia* species are ubiquitous soil-borne aerobic actinomycetes. Sixteen species have been implicated in human infections (Saubolle & Sussland, 2003). *N. asteroides* complex includes *N. asteroides sensu stricto*, *N. farcinica*, *N. cyriacigeorgica*, *N. nova* and *N. abscessus* (Beaman & Beaman, 1994). Recent advances in molecular methods, including PCR targeting 16S rDNA sequences (Woo et al., 2009), have shown promise as rapid and specific tools for the identification of *Nocardia* species (Corti & Villafañe-Fioti, 2003). *Nocardia* species cause localized or disseminated infection. The presence of *Nocardia* in two or more
organs of the body defines disseminated disease. The majority of nocardioses is acquired through inhalation; therefore, the lung is the most common site of infection. In the present case, no clinical or radiological features of pulmonary nocardiosis were observed.

A total of 10 reported cases (including our case) of muscular nocardial abscesses were found in the literature (Borget et al., 1992; Stamenkovic & Madden, 2001; Mousa, 2003; Smit et al., 2003; Malani et al., 2006; Agterof et al., 2007; Chatelus et al., 2007; Corti et al., 2008; Marchan et al., 2009) and the details are shown in Table 1. Deep-seated soft tissue infection can occur by local traumatic inoculation or by haematogenous dissemination. In general, haematogenous dissemination was characteristic of immunocompromised hosts (Ambrosioni et al., 2010). Disseminated disease was present in four of the ten patients. Haematogenous dissemination most commonly involves the central nervous system (CNS), bone, retina, heart, joints and kidneys (Agterof et al., 2007). Nocardiosis has been observed in conditions associated with impaired cell-mediated immunity. The organism is phagocytosed by macrophages, implying the involvement of cell-mediated immunity. T-cells have a role in immunity as suggested by experiments with T-cell-deficient mice (Gillespie & Emmerson, 1996). In our case, CD4+ T-cells were low, therefore the reduced numbers of helper T cells might have led to nocardial infection.

In reports of Nocardia muscle abscesses, seven of ten patients had predisposing factors, the most frequent being immunosuppressive therapy, transplantation, haematological neoplasm, collagen diseases and HIV infection.

Brain abscesses were present in two patients. N. farcinica was isolated in these two patients. CNS involvement is a well known complication of nocardiosis (Corti & Villafranca-Fioti, 2003). Although focal neurological deficits and seizures were the most common clinical manifestations in patients with Nocardia brain abscesses (Lee et al., 2002), no neurological symptoms were observed in the two patients. N. farcinica was much more resistant than other Nocardia species (Torres et al., 2000). Brain abscesses caused by N. farcinica are associated with a high mortality rate of up to 20% in immunocompetent patients and 55% in immunocompromised patients (Mamelak et al., 1994).

In 10 reported cases, the outcome was favourable and they survived. Early diagnosis and appropriate therapy are important for a good outcome (Chung et al., 2009). Management of nocardiosis involves antimicrobial therapy in conjunction with surgical debridement/drainage and improvement of immune function (Agterof et al., 2007).

**Table 1. Summary of clinical characteristics and antimicrobial therapy of previous reported cases of muscular nocardial abscesses**

<table>
<thead>
<tr>
<th>References</th>
<th>Age/sex</th>
<th>Underlying disease or condition</th>
<th>Site of infection</th>
<th>Other site(s) of infection</th>
<th>Species</th>
<th>Therapy</th>
<th>Predisposing factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borget et al. (1992)</td>
<td>73/M</td>
<td>Giant cell arteritis</td>
<td>Deltoid</td>
<td>None</td>
<td><em>N. asteroides</em></td>
<td>TMP-SMX, amikacin</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Stamenkovic &amp; Madden (2001)</td>
<td>58/M</td>
<td>Cardiac transplantation</td>
<td>Adductor</td>
<td>None</td>
<td><em>N. asteroides</em></td>
<td>Incision, TMP-SMX, imipenem</td>
<td>Cyscosporine, azathioprine, prednisolone</td>
</tr>
<tr>
<td>Mousa (2003)</td>
<td>52/M</td>
<td>None</td>
<td>Psoas</td>
<td>None</td>
<td><em>N. asteroides</em></td>
<td>Incision, ampicillin, claxacillin</td>
<td>None</td>
</tr>
<tr>
<td>Smit et al. (2003)</td>
<td>42/M</td>
<td>None</td>
<td>Psoas</td>
<td>None</td>
<td><em>N. farcinica</em></td>
<td>Drainage, TMP-SMX</td>
<td>Methotrexate, vinblastine, bleomycin</td>
</tr>
<tr>
<td>Malani et al. (2006)</td>
<td>65/F</td>
<td>Hodgkin’s lymphoma</td>
<td>Vastus lateralis</td>
<td>None</td>
<td><em>N. farcinica</em></td>
<td>Drainage, TMP-SMX</td>
<td>None</td>
</tr>
<tr>
<td>Chatelus et al. (2007)</td>
<td>46/M</td>
<td>Obesity, BMI 44.8</td>
<td>Ilio-psoas</td>
<td>L5-S1 spine</td>
<td><em>N. asteroides</em></td>
<td>Drainage, imipenem, amikacin</td>
<td>Alcoholism, drug abuse, Tacrolimus, prednisolone</td>
</tr>
<tr>
<td>Agterof et al. (2007)</td>
<td>76/M</td>
<td>Polymyalgia rheumatica</td>
<td>Gracilis</td>
<td>None</td>
<td><em>N. farcinica</em></td>
<td>Drainage, TMP-SMX</td>
<td>Prednisolone</td>
</tr>
<tr>
<td>Corti et al. (2008)</td>
<td>32/M</td>
<td>AIDS</td>
<td>Psoas</td>
<td>Subcutaneous abscesses</td>
<td><em>N. asteroides</em></td>
<td>Incision, imipenem, linezolid</td>
<td>None</td>
</tr>
<tr>
<td>Marchan et al. (2009)</td>
<td>69/M</td>
<td>Liver transplantation</td>
<td>Lower abdomen</td>
<td>Brain, left adrenal gland</td>
<td><em>N. farcinica</em></td>
<td>Incision, TMP-SMX</td>
<td>None</td>
</tr>
<tr>
<td>Present report</td>
<td>52/M</td>
<td>SLE</td>
<td>Rectus femoris</td>
<td>Brain, subcutaneous abscesses</td>
<td><em>N. farcinica</em></td>
<td>Drainage, TMP-SMX, imipenem</td>
<td>Prednisolone</td>
</tr>
</tbody>
</table>
Antimicrobials may improve survival when used alone or in combination with other antimicrobials. The standard treatment is TMP-SMX. *Nocardia* is also susceptible to ciprofloxacin, linezolid and imipenem (Brown-Elliott et al., 2006). Patients with immunodeficiency should receive prolonged therapy because of high relapse rates (Smego et al., 1983). The duration of therapy is variable and depends on the site of the lesions and the patient’s immune status (Ambrosioni et al., 2010). If the CNS is involved, therapy must last for at least 12 months (Lerner, 1996). Mamela et al. (1994) recommended the use of aspiration or craniotomy and excision for brain abscesses larger than 2.5 cm, and abscesses that fail to shrink after 4 weeks of antibiotic therapy. Our patient was treated with oral TMP-SMX, which crosses the blood–brain barrier, for 11 months plus intravenous imipenem with a good clinical response.

In conclusion, we report a case of disseminated infection due to *N. farcinica* in an SLE patient receiving long-term steroid therapy, which was successfully treated with antibiotic therapy and surgical drainage. Isolation of *Nocardia* species from an intramuscular lesion is uncommon; therefore, muscular nocardial infection may be misdiagnosed. Nocardiosis should be suspected in immunosuppressed patients who present with abscesses in multiple organs.

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**References**


