Case Report: Nocardia asteroides Mycetoma

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Abstract. Primary cutaneous infections with Nocardia asteroides are rare and have been reported in immunocompromised patients. Herein, we report a case of primary cutaneous Nocardia asteroides mycetoma of the skin in an immunocompetent individual. The infection was treated successfully with trimethoprim-sulfamethoxazole. Because a prolonged incubation time is required for the cultures and since additional biochemical tests are necessary for identification of this species, the clinician should alert the microbiology laboratory when such an infection is suspected clinically. (received 3 January 2003; accepted 15 May 2003)

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Case Report

A 28-yr-old woman presented with an 8-10 month history of a non-healing, slightly painful, plaque with multiple, occasionally discharging, lesions on the right lateral aspect of her back. The condition started as a single, painless nodule, followed by development of multiple tan-brown papular nodules over a period of 6 to 8 mo. A few nodules showed draining sinuses. The patient was otherwise healthy. She denied any history of trauma to the region. A few weeks prior to her initial visit to the dermatology clinic, she had been treated with acyclovir for a presumed herpes zoster infection. The patient noted no improvement and the intermittent discharge and mild discomfort persisted.

The physical examination revealed an 8 x 5 cm, indurated, cutaneous plaque on the right lateral aspect of her back (Fig. 1). The plaque was mildly tender and comprised multiple, brown, hyperpigmented papules and a few discharging sinuses. As a presumptive diagnosis, a deep mycosis, (eg, Actinomyces or atypical mycobacteria) was considered. A punch biopsy of a nodule was performed and submitted for histopathologic examination. In addition, the serosanguinous discharge from the cutaneous sinuses was collected for bacterial, fungal, and mycobacterial cultures, including a special request for a culture for Actinomyces.

Histopathological and Culture Findings

The H&E-stained sections showed a suppurative and granulomatous dermatitis involving the dermis and subcutaneous fat (Fig. 2a). There was dermal fibrosis indicating that the process was chronic in nature. The Gomori methenamine silver (GMS), periodic acid Schiff (PAS), and Fite stains were negative for organisms. However, a tissue Gram stain revealed clusters of short, beaded, variably Gram-positive rods within suppurative areas, suggesting infection either with Nocardia or Actinomyces (Fig. 2b). The discharge from the sinuses was cultured on blood, MacConkey, phenol ethyl-alcohol agar (PEA), and thioglycolate broth. These bacterial cultures were negative for growth. However, the fungal culture plates (inhibitory mold agar and brain-heart infusion agar with blood) grew white colonies. When stained with a Gram stain and a modified acid-fast stain (Kinyoun stain), these colonies showed variably Gram-positive (Fig. 3a) and faintly acid-fast positive, slender, non-branching,
filamentous bacilli (Fig. 3b), features characteristics of *Nocardia* species. These colonies were subcultured on bromcresol purple (BCP) milk agar for various biochemical reactions to identify the organism further. The organism showed non-reactivity for xanthine, tyrosine, and casein hydrolysis, but demonstrated the production of urease and nitrate reductase without gelatinase. Resistance to lysozyme was also noted. Based on these metabolic results, culture characteristics, histopathological findings, and clinical features, the definitive diagnosis was *Nocardia asteroides* mycetoma.

**Clinical Course, Treatment, and Follow-up**

The patient was seen 3 weeks after the biopsy. Based on the clinical presentation and presumptive biopsy findings of *Nocardia* or *Actinomycetes* infection, treatment with trimethoprim-sulfamethoxazole double strength (Septra-DS) was begun and administered every day. Examination of the patient 6 weeks later showed no significant clinical improvement. However, the patient was continued on the same treatment and was seen at the end of 4 mo. The patient showed marked clinical improvement with less discomfort, complete absence of discharge from sinuses, and gradually healing of the papules, nodules, and sinuses. Physical examination revealed decreased induration of the skin and subcutaneous tissue. The patient was continued with the same therapy for another 6 mo. Examination of the patient a yr after the diagnosis revealed a healing scar with no evidence of recurrence.

Fig. 1. A plaque of primary cutaneous *Nocardia asteroides* mycetoma showing multiple hyperpigmented papules and discharging sinuses on the right lateral aspect of the patient's back.
**Discussion**

*Actinomycetales* is an order of bacteria consisting of Gram-positive and variably acid-fast positive diphtheroid-like to branched, filamentous, aerobic bacteria [1]. Many of these microorganisms are present in soil, plants, compost, house dust, beach sand, and swimming pools [2]. However, some exist as normal commensal organisms on the human skin, oropharynx, and gastrointestinal tract [3]. The *Actinomycetales* that are considered human pathogens include *Nocardia, Actinomadura, Streptomyces, Rhodococcus, Corynebacterium,* and *Mycobacterium* [3,4]. The first human infection with *Nocardia* was reported in 1924. The infection was then considered either a type III or type IV hypersensitivity reaction to repeated and chronic exposure to *Actinomyces* antigen from decaying vegetation [3,4].

Human *Nocardia* infections are rare. The incidence of nocardiosis in the United States is approximately 1,000 cases/yr [4]. The respiratory tract is the most commonly involved system, but CNS and cutaneous diseases have also been described. The majority of *Nocardia* infections in the United States are caused by *N. asteroides* complex, which includes *N. asteroides sensu stricto, N. farcinica,* and *N. nova. N. brasiliensis* accounts for most of the infections in tropical and subtropical regions.

The skin and subcutaneous tissues are the second most common sites involved by *Nocardia.*
The majority of these infections are caused by \textit{N. brasiliensis}. Infection with \textit{N. asteroides} has been reported rarely, but generally in immunocompromised patients, eg, those with malignancies receiving chemotherapy, post-transplant patients, and AIDS patients [5,6]. There have been a few case reports of primary cutaneous nocardiosis caused by \textit{N. asteroides} in immunocompetent patients [2,5-8]. Herein, we report another case of the rare primary skin infection caused by \textit{N. asteroides} in an otherwise healthy woman.

Cutaneous nocardiosis occurs in 4 clinical forms. These are (a) superficial skin infections that present as ulcers, pustules, abscesses, granulomas, or cellulitis, (b) lymphocutaneous infections that resemble sporotrichosis, with an initial ulcerated papule after trauma, followed by advancing lymphangitis and subcutaneous erythematous nodules, extending proximally along the lymphatic drainage, (c) actinomycetomas that are indurated masses with draining sinuses [7,9], and (d) disseminated infections where skin involvement is usually secondary to an advanced pulmonary infection. Of the patients with disseminated disease, 10% show cutaneous involvement. The mortality rate for the disseminated infections is approximately 40% [10]. \textit{Nocardia asteroides} is the prevalent pathogen, but infection with \textit{N. brasiliensis} has also been described [11,12].

Histopathologically, a skin biopsy may show suppurative and/or chronic inflammation with dermal fibrosis. Within the foci of suppuration the
bacteria form loosely arranged clumps and pseudogranules. The granules are small, measuring 25-150 µm, and contain filamentous bacteria undergoing fragmentation. These bacteria, when stained with tissue Gram stain (Brown & Brenn) or modified acid-fast stains, demonstrate variably Gram-positive and acid-fast-positive, short, beaded clumps within foci of microabscesses. PAS and GMS stains fail to demonstrate these coccobacilli. These morphological features help to make a provisional diagnosis of Nocardia infection [8].

Culture morphology and biochemical characteristics remain the gold standard tests for definitive diagnosis of Nocardia and species identification. This organism’s slow growth is likely to generate negative results on aerobic and anaerobic cultures. It is essential to hold these cultures for several weeks to allow for growth of the organism [5,8,9]. Hence, it is critical for the clinician to inform the microbiology laboratory if such an infection is suspected.

Macroscopically, cultures of Nocardia present as glabrous, either orange or white chalky, “gypsoides” colonies. Microscopically, when stained with Gram stain and Kinyoun stain, these colonies show delicate, branching, filamentous coccobacilli that are variably Gram-positive and weakly acid-fast positive. In biochemical tests, Nocardia species characteristically produce urease and are resistant to lysozyme. Nocardia asteroides is further identified by its inability to peptonize (hydrolyze) casein, xanthine, or tyrosine in bromcresol purple (BCP) milk agar and its abilities to produce nitrate reductase and metabolize citrate [3-5].

Most cases of localized nocardial infection have been treated successfully with trimethoprim-sulfamethoxazole (TMP-SMX) double strength. Other antimicrobials that have proven effective in treating nocardiosis are minocycline, amikacin, dapsone, imipenem, tetracycline, and aminoglycoside antibiotics [9,13,14]. The optimum duration of therapy for nocardial infections can range from 6 wk for minor infections to 1 yr for severe systemic diseases [2,9,10]. Surgical drainage of cutaneous abscesses is also important [9].

In conclusion, we report a rare case of actinomycetoma caused by N. asteroides that responded well to prolonged treatment with TMP-SMX. Nocardia infection should be considered in the differential diagnosis of a suppurative and granulomatous dermatitis that presents clinically as multiple discharging sinuses with papules and nodules. We emphasize that the microbiology laboratory should be informed if such an infection is suspected clinically.

References