

# A Case of Primary Cutaneous Sporotrichoid Nocardiosis Caused by *Nocardia asteroides*

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We report a case of a 42-year-old woman who suffered from recurrent nodular skin lesions on her left foot. Sporotrichoid fungal infection was suspected and two linear nodular skin lesions that had occurred after trauma in a public pool were treated with itraconazole for 4 months. These nodular skin lesions were completely flattened. However, four months after complete flattening, a new lesion developed in the scar of a previous nodule. *N. asteroides*, which is extremely rare for sporotrichoid cutaneous nocardiosis, was cultured from the relapsed lesion. We treated this case with trimethoprim-sulfamethoxazole for 6 months under an empirical basis and this resulted in complete healing, and sensitivity of *N. asteroides* to trimethoprim-sulfamethoxazole was confirmed later. There has been no recurrence for 3 years. To our knowledge, our case is the first report in the English literature of primary sporotrichoid cutaneous nocardiosis caused by *N. asteroides* in terms of anatomic location below the knee and host immunocompetency. (*Ann Dermatol* 11(2) 90-93, 1999).

**Key Words :** Primary sporotrichoid cutaneous nocardiosis, *Nocardia asteroides*

Nocardiosis is an uncommon, potentially life-threatening, worldwide, infectious disease caused by several species of the genus *Nocardia*, it is usually opportunistic in nature especially in immunocompromised patients. Recently, reports of nocardiosis have been increasing. *Nocardia* species are gram positive, partly acid-fast, filamentous, branched bacteria. Usually, they are classified into systemic and cutaneous types. Systemic nocardiosis cases have usually developed opportunistic lung infections, mainly caused by *Nocardia asteroides*, which can then be disseminated to various organs such as the CNS system, skin, heart, liver, and kidney, etc. Primary cutaneous nocardiosis is usual-

ly caused by *Nocardia brasiliensis*, and develops as one of the following: 1) mycetoma, 2) lymphocutaneous (sporotrichoid) infection, 3) a localized superficial skin infection, such as, cellulitis, abscess, or granuloma. Sporotrichoid nocardiosis usually affects the upper extremities. It has been treated with trimethoprim-sulfamethoxazole as the drug of choice<sup>1,2</sup>.

We report a case of a patient with primary sporotrichoid cutaneous nocardiosis which differs from the usual clinical setting of cutaneous nocardiosis. We also discuss several aspects of treatment.

## CASE REPORT

A 42-year-old woman presented with two adjacent nodular lesions on the dorsum of her foot where, two months earlier, she had lacerated it at an indoor public pool. The initial nodule developed at the injured site, followed by a second nodule at the proximal site one month later. A Physical examination showed two linearly-distributed, viola-

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**Fig. 1.** Two violaceous hard nodules with central ulceration and crusts on the dorsum of the left foot.

**Fig. 3.** Several hyphae-like, branched, filamentous mycelia as narrow in width as bacteria ( $\times 100$ ).

aceous, hard nodules with central ulcerations and crusts on the dorsum of her left foot (Fig. 1). There was no regional lymphadenopathy. She had no history of previous infections, familial skin disease, or notable medical problems. She was free from systemic symptoms and signs other than intermittent epigastric soreness.

Skin biopsies were performed twice and showed acute and chronic inflammatory dermatosis with abscess, fibrosis, and granulomatous reactions, but did not demonstrate any fungal elements despite special

**Fig. 2.** Anterior view of Sabouraud dextrose agar plate cultured for 47 days. Whitish, wrinkled, heaped up, glabrous colonies.

**Fig. 4.** Complete flattening after treatment of the relapsed nodule with trimethoprim-sulfamethoxazole for 6 months.

staining (PAS, Ziehl-Nielson, Gram, and Gomori methenamine silver). The following laboratory investigations were negative or within normal limits: a complete blood count, ESR, urinalysis, chest and limb radiography, multitest CMI<sup>®</sup>, and three attempts of tissue cultures (bacterial, mycobacterial, and fungal).

Sporotrichosis was suspected and initial treatment with potassium iodide for 4 weeks resulted in

no significant improvement. Therefore, oral itraconazole 100mg daily for 4 months was used and caused complete flattening of the lesions. However, four months after this complete flattening, she noticed a newly developed nodule on the scar of the previous nodule. A histopathological examination showed almost the same findings. There were no characteristic findings representing pathogens in a skin biopsy specimen or any positive special stains, despite three independent examinations of the specimen. Finally, at 10 day, whitish, glabrous colonies appeared on a Sabouraud dextrose agar plate, and subsequently on AFB culture media (Ogawa media) at 37°C, but not at 46°C. A few weeks later, the colonies showed a heaped-up, rough, and wrinkled appearance (Fig. 2). Special staining of a smeared colony revealed gram positive, partially acid-fast bacilli. Tap-water culture showed branched, filamentous bacilli consistent with *Nocardia* species (Fig. 3). Several biochemical studies revealed the organism as *N. asteroides*; Casein (-), Tyrosine (-), Xanthine (-), Gelatin hydrolysis (-). With the diagnosis of nocardiosis, treatment with trimethoprim-sulfamethoxazole (TMP/SMX; 80/400mg) under an empirical basis, 160/800mg every 12 hours, for 6 months resulted in complete flattening of the lesion (Fig. 4). Later a sensitivity test with several antibiotics was done with cultured *N. asteroides*. The minimal inhibitory concentration (MIC) of itraconazole for *N. asteroides* was between 100 and 125 µg/ml. The strain was very sensitive to ofloxacin, vancomycin, and amikacin and less sensitive to imipenem, gentamycin, TMP-SMX, and cefotaxime. There has been no recurrence for 3 years.

## DISCUSSION

The genus *Nocardia* includes numerous species. Since their discovery by Nocard in 1889, they have been found to cause diseases in plants and animals, including humans. In USA, between 500 and 1000 cases have been reported. In humans, the commonly encountered species are *N. asteroides*, *N. brasiliensis*, and *N. otitidiscaviarum* (*N. caviae*).

Clinical manifestations of nocardiosis are classified into the systemic and cutaneous types. Cutaneous involvement is usually secondary to hematogenous dissemination from pulmonary foci, with skin in-

volvement as the primary site in 5% of the total reported cases<sup>1</sup>. However, primary cutaneous nocardiosis is increasing in both frequency and recognition. *N. brasiliensis* is the most common pathogenic agent of the genus '*Nocardia*' causing cutaneous nocardiosis. In particular, sporotrichoid nocardiosis is caused exclusively by *N. brasiliensis*<sup>1</sup>.

Reviewing the reported cases of lymphocutaneous nocardiosis, most of the patients have been healthy adults without any systemic disease and have occupations to be subjected to skin trauma or histories of puncture wounds. Affected lesions mainly involved the upper extremities, and the onset and clinical course were more acute and inflammatory than those resulting from sporotrichosis<sup>2</sup>. Causative agents were most commonly *N. brasiliensis* and extremely rarely *N. asteroides*, *N. transversalis*, or *N. farcinica*<sup>2,3</sup>, but in our case the causative agent was *N. asteroides*.

In reviewing the case reports of primary lymphocutaneous nocardiosis caused by *N. asteroides*, they had histories of lung abscesses, non-Hodgkin's lymphoma, and intestinal lymphoma. All the skin lesions occurred on the upper extremity, forearm or hand<sup>2,6,7</sup>. In contrast with these previous case reports, our case is the first in terms of anatomic location (the case involved an area below the knee which has not been reported previously) and host immunocompetency, both of which merit consideration.

Treatment of nocardiosis is usually a combined medical and surgical approach. Various antimicrobials have been used with success. Traditionally, sulfonamides are the drug of choice (especially, TMP-SMX combination) in nocardiosis, although recently several in vitro and in vivo studies have shown that *Nocardia* species were often resistant, or unresponsive, to TMP-SMX<sup>1,3,4,8</sup>. In this context, we started treatment with TMP-SMX. Later in our sensitivity tests, TMP-SMX was less effective than other drugs (ciprofloxacin, vancomycin, amikacin, imipenem, etc.), but we did not change the drug because the clinical response and compliance of the patient were good. The initial treatment in people who are allergic to sulfonamide should include amikacin, second-generation cephalosporin, and imipenem. This treatment should be continued until definitive susceptibility test results are obtained. The extreme variation in susceptibility of *Nocardia* isolates, even to chemically

similar agents, mandates in vitro susceptibility studies of each isolate. The optimal duration of therapy for nocardial infection is uncertain. Suggested duration of therapy has ranged from 6 weeks for minor infections to 1 year for severe systemic diseases. Recurrence is not uncommon. There was one report of a relapse in a patient with nocardial pneumonia after 15 months of therapy with TMP-SMX<sup>9</sup>.

In some textbooks, nocardiosis is classified as a transition form between bacteria and fungus or as a fungal disease. Itraconazole is known to be a useful, efficient agent for almost all fungal diseases and it can also be effective for nocardiosis, according to the Janssen laboratory (from Basic Medical Information Brochure, published at May 1986, Swiss), which reports its MIC for nocardiosis (i.e., *N. asteroides*: 100 µg/ml; steady state serum level with daily 100 mg itraconazole, *N. brasiliensis*: 10 µg/ml). Although our MIC result (between 100 and 125 µg/ml: *N. asteroides*) was slightly higher than that of the Janssen laboratory and despite some unknown laboratory bias, if any, itraconazole is assumed to have played a beneficial role in the treatment of our patient, because of the absence of any other combination treatment in the first episode. A controlled clinical study to evaluate the effectiveness of itraconazole would seem worthwhile. It is likely that the frequency of nocardiosis will increase in the future, due to the wide spread of HIV-infection and the increasing use of immunosuppressive agents, for example in organ transplantation. Therefore, physicians should be aware of nocardiosis and its treatment.

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