



Study

Primary cutaneous nocardiosis: A case study and review

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ABSTRACT

Background: Primary cutaneous nocardiosis is an uncommon entity. It usually occurs among immunocompetent but occupationally predisposed individuals. **Aim:** To study clinical profile of patients with primary cutaneous nocardiosis in a tertiary care hospital and to review the literature. **Methods:** The records of 10 cases of primary cutaneous nocardiosis were analyzed for clinical pattern, site of involvement with cultural study and response to treatment. **Results:** All the patients were agricultural workers (nine male) except one housewife. The commonest clinical type was mycetoma. Unusual sites like the scalp and back were involved in two cases. Culture was positive in six cases with *N. brasiliensis* being commonest organism. *N. nova* which was previously unreported cause of lymphocutaneous nocardiosis, was noted in one patient, who had associated HIV infection. All the patients responded to cotrimoxazole. **Conclusion:** Mycetoma is the commonest form of primary cutaneous nocardiosis and responds well to cotrimoxazole.

KEY WORDS: Primary cutaneous nocardiosis, Mycetoma, Lymphocutaneous nocardiosis

INTRODUCTION

Cutaneous nocardiosis presents either as a part of disseminated infection or as a primary infection resulting from inoculation. Primary cutaneous nocardiosis is relatively rare.¹ Three clinical variants have been identified: a superficial acute skin and soft tissue infection, a lymphocutaneous infection, and a deeper infection, mycetoma. Mycetoma is commoner than the other two clinical variants. None of these three types possess any characteristic feature that would make a definitive clinical diagnosis possible. Isolation of *Nocardia* from clinical specimens and species identification is difficult and need the expertise of a microbiologist. The incidence and prevalence of primary cutaneous nocardiosis have not been adequately documented even in areas where the

infection is prevalent. Many of the large series on nocardial infections mention the incidence of cutaneous nocardiosis without specifying whether the infection is primary or secondary. Indian reports of nocardial skin infections focus primarily on mycetoma. This may be attributed to a lack of awareness of primary cutaneous nocardiosis and its different clinical patterns other than mycetoma.

CASE REPORTS

Cases of primary cutaneous nocardiosis seen in a tertiary care hospital in South India over a period of ten years have been presented in Table 1. All the patients had a history of preceding injury to the affected area and were agricultural workers or laborers, except for a housewife. The commonest

How to cite this article: Inamadar AC, Palit A. Primary cutaneous nocardiosis: A case study and review. Indian J Dermatol Venereol Leprol 2003;69:386-91.

Received: November, 2003. **Accepted:** December, 2003. **Source of Support:** Nil.



Table 1: Clinical profile of patients with primary cutaneous nocardiosis

Sr. no.	Age/Sex	Occupation	Clinical pattern	Site of involvement	Gram & AFB stain	Culture	Underlying illness	Response to cotrimoxazole
1.	30/M	Agriculture	Mycetoma	Foot	+	<i>N. brasiliensis</i>	None	Complete
2.	35/M	Labourer	Mycetoma	Foot	+	<i>N. brasiliensis</i>	None	Complete
3.	16/M	Agriculture	Mycetoma	Scalp	+	<i>N. brasiliensis</i>	None	Complete
4.	23/M	Agriculture	Mycetoma	Back	+	—	None	Complete
5.	60/M	Agriculture	Abscess	Leg	+	—	None	Complete
6.	16/M	Agriculture	Lymphocutaneous	Leg	+	—	None	Complete
7.	60/F	Housewife	Mycetoma	Sole	+	<i>N. brasiliensis</i>	None	Complete
8.	25/M	Labourer	Abscess	Foot	+	—	None	Complete
9.	28/M	Agriculture	Abscess	Hand	+	<i>N. brasiliensis</i>	None	Complete
10.	30/M	Agriculture	Lymphocutaneous	Hand & forearm	+	<i>N. nova</i>	HIV	Complete

clinical presentation was mycetoma, including one on the sole. Unusual sites of involvement of mycetoma, like the scalp and back (Figures 1 and 2) were noted. There was a discharge of yellowish white granules from the overlying sinuses of the lesions. An acute abscess (Figure 3) was seen in 3 cases and a lymphocutaneous infection (Figure 4) in 2.

Organisms were demonstrable from clinical specimens like a granule or pus by Gram stain and modified Kinyoun stain in all the cases (Figure 5). Culture was positive in 6 cases (Figure 6), the commonest species being *N. brasiliensis*. Underlying HIV-1 infection was present in one patient (patient 10) with lymphocutaneous nocardiosis caused by *N. nova*, whose CD4+ T cell count was 550. None of the patients had systemic involvement. All our patients had complete clinical resolution in 2-3 months with cotrimoxazole DS twice daily, but treatment was continued for six months.

DISCUSSION AND REVIEW OF LITERATURE

Epidemiology

The genus *Nocardia* belongs to the order Actinomycetales, a group of aerobic, Gram positive, filamentous bacteria.² The organism is mainly geophilic, occurring in soil and decaying plant parts. This group of organisms can cause serious human and animal infections. The first description of *Nocardia* came from a French veterinarian, Edmond Nocard, in 1888 in relation to bovine farcy.² Subsequently, human nocardiosis was described by Eppinger (1890)² as a systemic infection.

The genus *Nocardia* comprises several species of clinical importance. Among these, *N. brasiliensis* is the main

pathogenic organism for primary cutaneous infection, followed by *N. asteroides*, which usually causes fulminant systemic infection.² Other pathogenic species like *N. ostitidis-caviarum*,³ *N. transvalensis*⁴ and the recently recognized species *N. farcinica*⁵ and *N. nova*⁶ are less common causative agents for primary cutaneous nocardiosis.

The exact incidence of primary cutaneous nocardiosis is not clear. In a series of nocardiosis patients,⁷ 7.8% of the patients had cutaneous disease, the commonest causative organism being *N. brasiliensis*. The number of cases with primary infection is not evident. Similarly, an unspecified 12% incidence of cutaneous nocardiosis was reported in a 24-year survey of nocardial infections in Spain.⁸ According to Palmer et al, the incidence of primary cutaneous nocardiosis reported in the English literature between 1961 and 1971 was 5%.⁹ In a Japanese survey, the incidence of primary cutaneous nocardiosis before 1984 was reported to be 91%.¹⁰ In a review of cases of pediatric *Nocardia asteroides* infection between 1895 and 1981, 8% children had cutaneous infection.¹¹ An incidence of 10% has been quoted by Uttamchandani et al¹² in patients with HIV infection. Data regarding the overall incidence of this infection in India is not available.

The mode of transmission is accidental inoculation. It is prevalent among the rural population where agriculture is the main way of livelihood. Adult males, especially bare-foot walkers, are the common sufferers of mycetoma. A history of thorn prick or splinter injury is common in patients with superficial cutaneous infection. Unusual modes of inoculation like animal scratch, burn injury and insect bite have been described.² A Japanese fish-handler suffering from



Figure 1: Resolving nocardial mycetoma on back



Figure 2: Scalp mycetoma due to nocardia



Figure 3: Acute nocardial abscess

primary cutaneous nocardiosis, without any preceding injury, has been reported.¹³ Pediatric cases can occur as early as three years of age.¹¹ Infection in



Figure 4: Lymphocutaneous nocardiosis

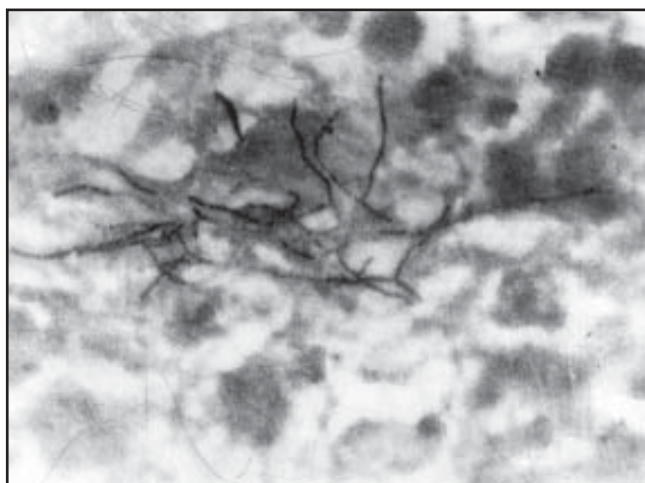


Figure 5: Thin beaded filaments of *Nocardia brasiliensis* (Kinyoun 1000X)



Figure 6: Whitish, dry, wrinkled colonies of *Nocardia nova*



immunosuppressed individuals is frequent, though there is no definite correlation with the degree of immunosuppression.

Clinical variants

Mycetoma is the commonest clinical pattern of primary cutaneous nocardiosis. *Nocardia* species are frequently isolated as the causative agents for mycetoma. The incidence of nocardial mycetoma in Indian reports varies from 5.2%-35%.^{14,15} In a study from Yemen, 8% of the 50 cases of mycetoma were caused by *Nocardia* species.¹⁶ The usual sites of involvement are the hands and feet. Other sites of occurrence like the scalp,¹⁷ shoulder and upper back,² which correspond to the usual sites of carrying loads by agricultural workers, have also been reported. Small, nodular lesions, termed as mini-mycetoma, can be the presenting feature.¹⁸

Unlike eumycetoma, these lesions are acute in onset, more inflammatory and associated with tenderness. The sinuses are usually surrounded by a raised border or are punched out. The granules discharged are less than 1 mm in size and yellowish-white. Mycetoma, especially when caused by *N. brasiliensis*, has a propensity to involve the underlying bone, and osteolytic changes are frequently observed radiologically. Compressive myelopathy has been reported as a sequel to bone involvement underlying a mycetoma caused by *N. brasiliensis*.¹⁹ Hematogenous dissemination from a mycetoma has been reported.²⁰

Superficial acute skin infections simulate those caused by common pyogenic organisms, occurring as a pustule, abscess, bulla, cellulitis or as a chronically draining ulcer. Unlike mycetoma, there is no granule formation.²¹ This type of infection constitutes 1% of the cases of primary cutaneous nocardiosis in Mexico.²¹ The lesions are rapidly progressive with intense pain, erythema and edema. One third of these cases may be transformed to lymphocutaneous disease.²¹ An intermediate form of the disease between mycetoma and superficial skin infection has been recently reported.⁷

The lymphocutaneous pattern of the disease is the rarest type and commonly occurs in otherwise healthy individuals.¹³ Clinically, it simulates sporotrichosis but

differs from this fungal infection by its acute onset, erythema of the overlying skin, tenderness and a highly inflammatory course. Rarely, granules may be observed in the discharge from noduloulcerative lesions.²² An atypical cervicofacial variant of the disease has been reported in children.²³ Two of the patients in this series had lymphocutaneous infection. One of them was HIV infected.^{24,25} He was infected with *Nocardia nova*, a previously unreported organism causing this pattern of infection.²⁵

Primary cutaneous infection caused by *N. brasiliensis* is more inflammatory, locally invasive and progressive rather than the self-limited course of the lesions caused by *N. asteroides*.² Mycetoma with double etiology, caused by both *N. brasiliensis* and *N. asteroides*, has been reported.²⁶

Primary cutaneous nocardiosis has been reported in patients with HIV infection, lymphoma, Cushing's syndrome or organ transplantation.^{2,12} The clinical severity and course of the disease seem to remain unaltered in this group of patients. The spectrum of causative organisms is similar to that in otherwise healthy individuals.

DIAGNOSIS

The initial clinical diagnosis may be difficult due to the non-specific clinical picture. Demonstration of the organism from clinical specimens like granules, pus or aspirated fluid from an unruptured nodule by Gram stain and modified Kinyoun stain is the mainstay of diagnosis. Gram positive and acid fast, thin, beaded, branching filaments are the characteristic appearance of the organism. Identification of the *Nocardia* species by culture is a tedious process. The organism is slow growing and it may take up to 2-3 weeks for isolation from a clinical specimen.² The small nocardial colonies are occasionally overgrown by other rapidly growing organisms, resulting in an initial negative culture report. Western blot assay, using monoclonal antibodies against 54-kDa circulating antigens of *Nocardia*, and species specific DNA probing help in the rapid and definitive diagnosis of nocardiosis.² ELISA for serodiagnosis of nocardial infection is also useful.²⁷

The commonest organism isolated from all the three



clinical types is *N. brasiliensis*. An antibiogram is suggested for all the species isolated because of the varied antibiotic sensitivity pattern. Radiological examination of the underlying bone or joint should be done in all cases of mycetoma to rule out bony involvement. Sclerotic lesions in the skull bone were observed in the X-ray of one of our patient with scalp mycetoma (patient 3). A thorough clinical examination and necessary investigations should be carried out to rule out systemic involvement, especially in immunosuppressed patients.

TREATMENT

Patients with primary cutaneous nocardiosis respond very well to medical therapy. Cotrimoxazole is the mainstay of therapy. Other effective drugs are dapsone, amikacin, amoxicillin, cephalosporins, minocycline, erythromycin, ciprofloxacin, clindamycin and imipenem.² *N. farcinica* shows multiple drug resistance to ampicillin, cephalosporins, erythromycin, amikacin and tobramycin.^{2,6} *N. nova* is highly sensitive to erythromycin.² Clinical response to therapy with cotrimoxazole is evident within a few weeks, but complete clearance may take up to three months. The drug has to be continued for a further three months to prevent recurrence. An excellent therapeutic response to cotrimoxazole was observed in all our patients.

Immunocompromised patients are similarly treated, except those who are HIV positive. They are particularly prone to develop adverse cutaneous drug reactions to sulphonamides and thus may need to be treated with alternative drugs. Some authors suggest prolonged treatment in patients with advanced HIV infection to prevent recurrence or systemic infection.¹² In our series the HIV-positive man infected with *N. nova* was treated with cotrimoxazole for 6 months and did not show any reaction to drug or recurrence on follow-up.

Minimal surgical intervention, in the form of draining an acute abscess, is sometimes needed.

Primary cutaneous nocardiosis remains a diagnostic challenge. The majority of acute nocardial abscesses and lymphocutaneous infections go unsuspected and undiagnosed because of the non-specific clinical

pictures and the difficulties involved in isolation of the organism. Rapid and reliable molecular techniques, though available, are beyond the reach of investigators in many countries. A high degree of clinical suspicion is needed for the diagnosis of the condition along with stringent efforts of the microbiologist to isolate the organism.

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