Mycetoma due to *Nocardia Africana/Nova* Treated Successfully with Cotrimoxazole and Moxifloxacin

Abstract

Nocardia africana is a recently identified organism and has rarely been reported to cause mycetoma. Here we report the case of a 40-year-old woman who presented with discharging sinuses and nodules for the past 7 years along with few discrete axillary lymph nodes. Cultures and Maldi-TOF MS (Matrix-assisted laser desorption/ionization–time of flight mass spectrometry) method identified the causative organism as *Nocardia africana/nova.* The organism was acid-fast positive on modified Ziehl-Neelsen stain and Gram's stain revealed branched filamentous beaded gram-positive bacilli, while histopathology showed granulation tissue along with few ill-defined epithelioid cell granulomas, with giant cells. Based on the sensitivity report, the patient was started on tablet moxifloxacin and cotrimoxazole, and has shown considerable improvement at 2.5 months of follow-up.

Keywords: *Cutaneous nocardiosis, mycetoma, Nocardia africana/nova, treatment*

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Introduction

The *Nocardia* sp. are aerobic, gram-positive, filamentous bacteria found in soil and decaying organic plant matter. They cause infection in humans following traumatic implantation in the skin by a thorn or stick injury or scratch by animal claws.[1] Cutaneous nocardiosis presents as *acute superficial skin infection* with abscesses or cellulitis, *mycetoma*, *lymphocutaneous (sporotrichoid) infection*, or *disseminated infection* in an immune-compromised host.[2-4] Actinomycetoma is the most common form and presents typically as triad of swelling, discharging sinuses, and grains.[5] Differentiating actinomycetoma from eumycetoma can be difficult clinically and cultures are needed for a definite diagnosis, but actinomycetoma is rapidly progressive and more destructive with early bone invasion.[6] An early diagnosis for actinomycetoma is particularly important to avoid unnecessary drastic surgical deep tissue debridement or amputation as it responds well to antibiotics. We discuss the diagnosis and treatment of a case of actinomycetoma caused by the rare *N. africana/nova.*

Case Report

A 35-year-old-female presented with painful, skin-colored nodules on the left arm with few sinuses discharging yellowish pus intermittently for the past 7 years. [Figure 1] Seven years back, she had a single painful nodule that was operated but it reappeared after a year. Since then, there had been a gradual increase in similar nodules and sinuses. There was no history of grains, fever, systemic symptoms, trauma, or injections, however, the patient frequently fed stray cats who visited her house. Six months ago, she was treated with itraconazole 200 mg twice daily and potassium iodide 25 drops thrice daily for 1.5 months with no improvement. On cutaneous examination, an ill-defined, indurated, firm swelling was present on the left upper arm with multiple tender subcutaneous nodules of size 1–2 cm and few discharging sinuses. Few discrete, tender, mobile left medial axillary lymph nodes ranging in size from 1 × 1 cm to 2 × 2 cm were present. Systemic examination was within normal limits.

Smear from pus showed acid-fast filamentous bacilli on modified Ziehl-Neelsen stain (1% sulphuric acid) [Figure 2a] and branched

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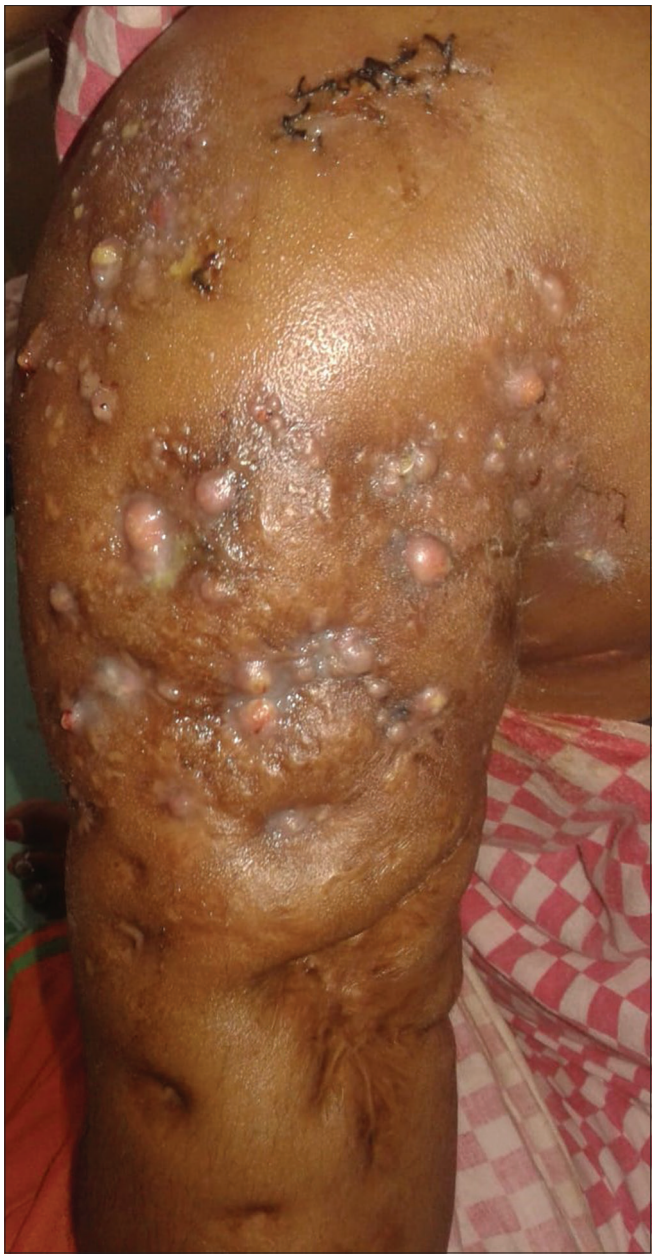

Figure 1: Multiple erythematous nodules and discharging sinuses on the arm

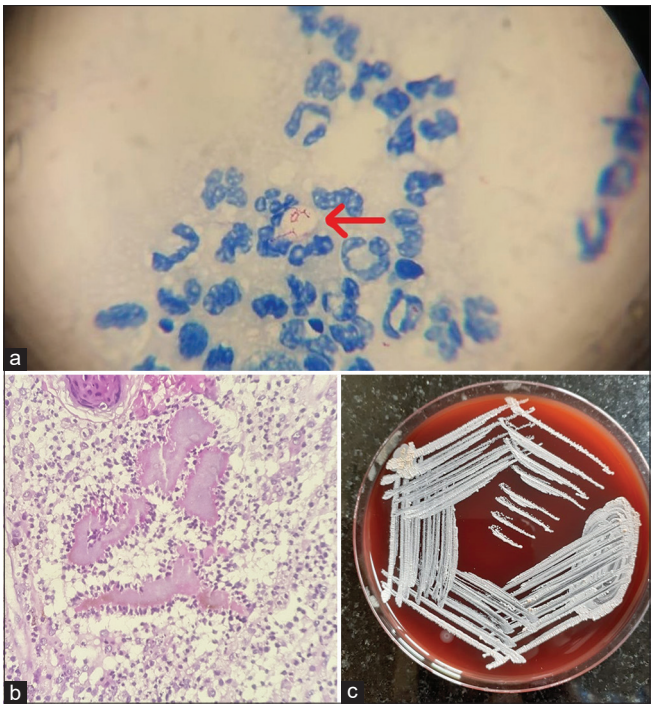

Figure 2: (a) Modified Ziehl-Neelson stain showing filamentous acid-fast bacilli (Modified Ziehl-Neelson stain, ×100). (b) Photomicrograph shows partially basophilic granules surrounded by an amorphous, eosinophilic, radially arranged material on the periphery surrounded by neutrophils revealing a Splendore-Hoeppli phenomenon (hematoxylin and eosin, ×200). (c) Growth of *Nocardia* from soiled gauze on 5% sheep blood agar on the fifth day

filamentous beaded gram-positive bacilli on Gram's stain. On histopathology, epidermis showed focal ulceration, dermis showed granulation tissue with dense acute on chronic infiltrate and few ill-defined epithelioid cell granulomas, with giant cells. Few organisms arranged in clusters were seen with basophilic radiating filaments, the Splendore-Hoeppli phenomenon [Figure 2b]. On investigations, hemoglobin was low, peripheral smear revealed microcytic hypochromic anemia and ESR was 52 mm/h by Westergren method (normal = 0–20 mm/h). Chest X-ray, ultrasound abdomen, viral markers, HIV were negative and Mantoux test using 5 Tuberculin units showed an induration of 12 × 10 mm at 48 h. Fine needle aspiration and cytology of left medial axillary lymph node showed reactive lymphadenitis. The X-ray revealed minor bony irregularities but the non-contrast computed tomography (NCCT) showed lytic lesions in the humeral head and adjacent scapula with features of myositis and sinus tracts in the overlying skin. MRI also revealed lytic lesions with enhancing marrow edema suggestive of chronic osteomyelitis. Other investigations like 10% potassium hydroxide mount of pus, microscopy for AFB, tissue for anaerobic culture (Robertson's cooked meat agar), tissue for fungal culture (Sabouraud's dextrose agar) and tissue for *Mycobacterium tuberculosis culture (MGIT)* were negative. Repeated cultures of pus after keeping a gauze overnight over the lesions yielded chalky white colonies with musty/earthy odor of *Nocardia spp* on 5% sheep blood agar on the fifth day on the third attempt [Figure 2c]. The organism was identified as *Nocardia sp.* by Vitek2 compact system (Biomerieux). Using Matrix-assisted laser desorption/ionization–time of flight mass spectrometry (Maldi-TOF MS), the causative organism was found to be *Nocardia africana/nova.* On doing an antimicrobial susceptibility testing by Epsilometer test (E-strips), it was sensitive to ampicillin, meropenem, imipenem, moxifloxacin, cotrimoxazole, ceftriaxone, amikacin, and piperacillin-tazobactam, while resistance to ciprofloxacin and amoxyclav was found.

Based on the antibiotic susceptibility testing, she was started on tablet cotrimoxazole-DS (160/800) BD and tablet moxifloxacin 400 mg OD. At 2.5 months of follow-up, the

pus has dried up, edema has decreased and the sinuses are healing with deep scarring [Figure 3]. No side effects of the treatment were seen. The patient is under follow up and we intend to treat the patient till 3 months after complete clinical and radiological recovery.

Discussion

Nocardia spp. includes over 50 species, of which *N. brasiliensis*, *N. asteroides* complex, and *N. farcinica/N. nova* are commonly implicated in various human infections.[7] Majority of cutaneous nocardioses, worldwide and in India, are caused by either *N. brasiliensis* or *N. asteroides*.[5] Bone involvement such as periosteal thickening, osteolysis, and osteoporosis in longstanding cases is infrequent in nocardial mycetoma, but progressive fibrosis, mutilation, and dysfunction is rapid.[8] In our patient, bone involvement was not visualized on X-ray but was evident on NCCT and MRI highlighting the importance of higher resolution imaging. CT has the maximum sensitivity for early detection of bone involvement, while MRI is the most comprehensive method for assessment of bone and soft tissue involvement.[6] The bony lesions also provide an objective assessment for monitoring response to treatment, hence need to be repeated 6 monthly.

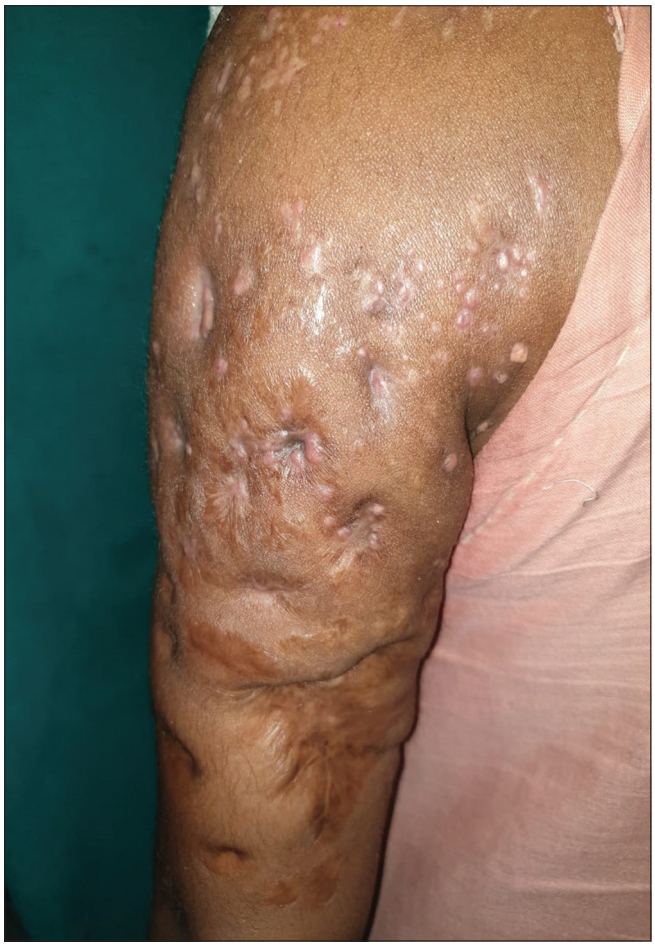

Figure 3: Resolution of nodules and sinuses after treatment

N. africana/nova identified as the aetiological agent in our case is a rare organism causing mycetoma. Species identification of *Nocardia* is done by a combination of antibiotic susceptibility patterns, molecular methods like gene sequencing of 16SrRNA and hsp65PRA patterns and Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). MALDI-TOF MS has accurate species-level identification in 94–95.9% in *Nocardia* isolates[9,10] and 97.9% in *N. africana*. Previously, *N. africana* has been reported in few select case reports to cause cauliflower-like verrucous plaque resembling squamous cell carcinoma,[11] fulminant disseminated nocardiosis leading to death in a 12-year-old immunocompetent boy,[12] feline mycetoma,[13] bovine mastitis,[14] and feline mandibular osteomyelitis.[15] Nocardiosis has been recorded to be transmitted from bites and scratches of seemingly asymptomatic animals like cats.[1] In our case, the patient had a history of feeding many stray cats who visited her house and may have acquired infection through them. Identification of subspecies of *Nocardia* is important as it adds to the epidemiology and geographical distribution; helps to correlate species to a particular clinical presentation and deciding the antibiotics for successful treatment. It is known that common cause of cutaneous nocardiosis, *N. brasiliensis* is susceptible to amoxicillin-clavulanic acid whereas *N. nova/africana* which was the causative organism in our case is susceptible to ampicillin but resistant to amoxicillin-clavulanic acid. Hence, it should be attempted to narrow down speciation to the complex such as *N. nova* complex.

In conclusion, *N. africana/nova* is a rare organism causing actinomycetoma. NCCT or MRI is better for evaluating bone involvement. Multiple attempts must be made to culture the organism and identify its subspecies so that treatment can be offered according to the antibiotic susceptibility pattern.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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