

Twenty-year cervicothoracic *Nocardia* mycetoma with advanced thoracic cavity infiltration



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INTRODUCTION

Nocardia is a soil-dwelling, aerobic, facultative intracellular bacteria with a challenging growth pattern to discern when sampled from cutaneous infections.^{1,2} This difficulty is partly attributed to similarity with the *Actinomyces* species, slow growth rate, and low incidence.³ Although considered opportunistic, immunocompetent hosts may become infected with a primary cutaneous infection following penetrative trauma.⁴ *Nocardia* causes localized destruction or systemic infection, with a particular affinity for the pulmonary and central nervous systems once disseminated. More prevalent in tropical countries, *Nocardia* has various cutaneous presentations, belonging with differential diagnoses including *Actinomyces*, sporotrichosis, and tuberculosis because of similarity in presentation.² Cutaneous infections left untreated can progress into a mycetoma, a chronic subcutaneous, granulomatous infection with fistulous tracts leading to invasion of the musculoskeletal system, lymphatics, or the central nervous system.^{3,5}

CASE REPORT

This patient is an immunocompetent 56-year-old Hispanic man with no significant medical history, presenting with painful posterior cervicothoracic skin lesions (Fig 1).

Abbreviations used:

MRI: magnetic resonance imaging
 TMP-SMX: trimethoprim-sulfamethoxazole

Onset was estimated to be 20 years ago; however, in the last 6 months, pain and purulent drainage from fistulous tracts had progressively increased. Evaluations and laboratory analysis by previous institutions' dermatology and infectious disease departments were nonrevealing. Earlier differential diagnoses including acne conglobata, *Actinomyces*, and eumycetoma were addressed; however, a definitive diagnosis was never established because of persistently negative tissue biopsies, blood cultures, or response to treatment.

Three months before presentation, the patient had motor and sensory deficits in bilateral lower extremities with resultant gait disturbances. Magnetic resonance imaging (MRI) found epidural abscesses, fistulous tracts, vertebral osteomyelitis, and lower cervical/upper thoracic spinal cord compression. He subsequently underwent laminectomy of C7 and T1-4, removal of phlegmon, and osseous biopsies. Tissue biopsies found neutrophilic clusters that failed to culture. Suspicion was maintained for *Actinomyces* infection due to a single Gram stain demonstrating its branching formation. The patient

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Fig 1. Prior to laminectomy.

was discharged empirically on ceftriaxone, metronidazole, and daptomycin thereafter. Lack of improvement 1 month postoperatively prompted regimen alteration to 8 weeks of metronidazole with 3 weeks of penicillin V and doxycycline. Despite this extensive course, symptoms persisted, and a suspicion for an infectious etiology remained.

At presentation to our service, lesions had expanded with increased drainage and worsening pain. New symptoms included right-sided rib pain, cough, low-grade fever, fatigue, and an unintentional 25-pound weight loss. Immunocompetence was assessed via negative rapid plasma reagin, p24 HIV, coccidioides antigen, QuantiFERON, hepatitis panels, and HgA1C (5.8%). MRI and computed tomography of the thorax found that the spinal cord remained preserved; however, there was contiguous advancement of abscesses and fistulous tracts into the thoracic cavity with osteomyelitis of the vertebral column and rib cage (Fig 2).

Abscess fluid and tissue were obtained for repeat culture. Because of failure of prior *Actinomyces* sp therapies and culture techniques, the differential diagnosis broadened to include *Nocardia*. Clinical suspicion prompted treatment despite lacking confirmation from molecular techniques, culture, or staining (Gram, acid-fast bacilli, Fite, periodic acid–Schiff, or Gomori methenamine–silver nitrate stain). Specific consideration to *Nocardia*'s particular growth pattern showed eventual growth of *Nocardia* with preliminary confirmation per microbiology and pathology report (Fig 3). With a successful culture, a reference laboratory performed gene sequencing further classifying the sample as *Nocardia vulneris*.

Clinical suspicion was imperative, as culture necessitated 27 days for identifiable growth. Trimethoprim-sulfamethoxazole (TMP-SMX) and meropenem were initiated, resulting in substantial

improvement of leukocytosis, from 17.3 to 12.2 in 2 days, alongside subjective improvement in pain and drainage. Responsiveness to *Nocardia* therapy encouraged the addition of amikacin on day 3 of treatment, further accelerating his improvement. Appearance of his fistulous tracts markedly improved over the lengthy inpatient antibiotic administration: 3 months of TMP-SMX and meropenem, with 4 weeks of amikacin, with frequent metabolic panels. The patient was discharged home on 6 months of daily oral moxifloxacin and lifetime oral TMP-SMX. Primary care provided follow-up and monitored for nephrotoxic effects of associated therapies.

DISCUSSION

Mycetomas are considered a neglected tropical disease and rare within developed nations.⁶ Creating extensive disfigurement, they are defined by chronic, destructive granulomas, tumefaction, and draining tracts from subcutaneous nodules.^{3,4,6} Requiring extensive time for growth, *Nocardia* cultures rarely develop before 48 hours, which further complicates the diagnosis.¹ Because of this constraint, clinical suspicion remains imperative for prompt therapy initiation. Suspicion for a Nocardial mycetoma should ideally involve consulting a tropical identification team if available. Prior antibiotic application reduces the sensitivity of microbial cultures producing additional diagnostic difficulties. Serologic or other molecular techniques such as the B-cell P61 marker, 16S rRNA polymerase chain reaction–based assay, or 54-kDa antigen, are more expedient diagnostic options for laboratories with molecular capabilities.⁷ These techniques may require referral to reference laboratories outside of an institution's standard referral. Reference laboratories may provide specific susceptibilities furthering patient safety and response to therapies.⁷ Molecular options and tropical identification teams were unavailable at this patient's institutions, exemplifying this report as an educational reminder of these options and emphasis on clinical suspicion.

Nocardia resides within the soil, which facilitates primary cutaneous infections from penetrative injury to predominantly involve the foot.^{4-6,8} Large-scale studies of *Nocardia* mycetoma, 400 to 3,000 cases, report affecting the back at only 7.88% compared with the foot at 60.29% to 62.44%.^{3,5,8} In this patient's native country of Mexico, *Nocardia brasiliensis* is the most common etiologic agent of bacterial mycetoma (65.58%-78.21%).^{5,8} *N vulneris* species in this case, is closely related to *N brasiliensis* phylogenetically at 99.37%.⁹

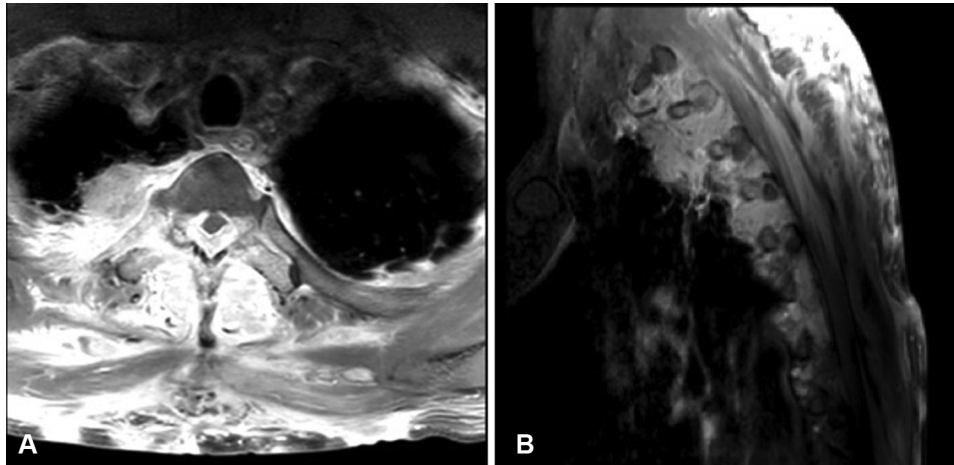


Fig 2. **A**, MRI, T1 weighted with contrast axial view. Shows anterior advancement of phlegmon into right thoracic cavity. **B**, MRI, T1 weighted with contrast sagittal view. Shows anterior advancement of phlegmon into right thoracic cavity.

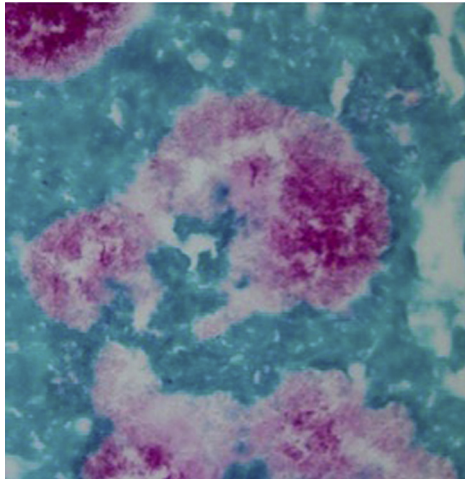


Fig 3. Fite stain shows weakly acid-fast organisms. (Original magnification: $\times 100$.)

Primary cutaneous nocardiosis has multiple presentations, mimicking other diseases including tuberculosis, neoplasms, or lymphocutaneous infections such as *Sporotrichosis*.^{1,6} Diagnosis may be further complicated by seeding of a disseminated infection precipitating distal cutaneous infectious sites.³ The presence of pain does not distinguish an origin; however, it may provide additional clinical suspicion for a nocardial agent. Differentials such as *Sporotrichosis* and leishmaniasis typically manifest as painless ulcers.²

Treatments using sulfonamides are highly effective in simple cutaneous infections; however, alternatives exist in minocycline, imipenem, and moxifloxacin.¹⁰ Complicated cases involving dissemination, neural tissue, or bone may require

combination therapy with amikacin and meropenem as in this case.¹⁰ Combination therapy, such as TMP-SMX and amikacin, has been successful when used for several months.^{9,10} Aggressive therapy lends concern for nephrotoxic effects; therefore, strict monitoring of electrolytes and kidney function remain an additional cause for inpatient treatment beyond that of intravenous application.

Understanding of serologic laboratory confirmation techniques in combination with clinical suspicion may aid in proper treatment of recalcitrant cutaneous *Nocardia* infections. Treatments may need to be aggressive while awaiting serologic or culture confirmation, exemplified by the exorbitant timeframe necessitated for growth and definitive diagnosis. Although mycetomas are rare within developed nations, cognizance of the possible introductions and apparent difficulties in standard confirmation is necessary. This finding is especially pertinent within communities possessing increasing transient populations from endemic countries.

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