Multiple nontuberculous scrofulodermas showing dramatic response to clarithromycin

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ABSTRACT

Atypical mycobacteria are distinct from the *Mycobacterium tuberculosis*. *Mycobacterium chelonae*, a non-pigment producing rapid grower, can be found in many cutaneous sites; infection occurs most commonly after skin trauma from surgery, injections, or minor injuries. In immune competent patients, the infection is more frequently localized as a cellulitis or a nodule, whereas, in the immunocompromised patient, dissemination (more than five lesions) can occur. Because the organism is resistant to antituberculous therapy, abscess can develop and follow a chronic, indolent course. We report a case of multiple scrofuloderma due to nontuberculous infection caused by *M. chelonae* showing dramatic response to clarithromycin.

Key words: Clarithromycin, *Mycobacterium chelonae*, nontuberculous infection, scrofuloderma

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INTRODUCTION

Scrofuloderma due to nontuberculous infection (NTI) was first described in 1951. It is now recognized that scrofuloderma due NTI far outnumbers tuberculous scrofuloderma.[1] *Mycobacterium chelonae* is an uncommon cause of infection in humans, mostly reported in immune compromised patients. *M. chelonae* infections respond well to clarithromycin. There should be a high index of suspicion for diagnosing atypical pathogens in patients with suspected cutaneous tuberculosis, who do not respond to standard antimicrobial therapy.

CASE REPORT

A 23-year-old female patient presented to the skin department with a large ulcer over the left side of her neck. She also had ulcers over the left axilla and chest wall with a discharging sinus. There was a history of loss of weight, appetite, and on and off fever. She had developed neck swellings two years ago for which she was treated with category II antituberculous therapy (ATT) for 6 months. However, the swellings did not subside, rather she noticed a subsequent increase in their size. She was diagnosed as Rosai–Dorfman syndrome, and was administered systemic steroids for three months. When she presented to us in the skin department, she was ill-looking, malnourished and anemic. She had matted cervical lymphadenopathy on the right side of her neck. There was an irregular ulcer 5 inch × 3 inch, the floor covered with slough over the region of left sternomastoid muscle. The base was indurated and formed by matted lymph nodes. There were two irregular ulcers over the left axilla and chest wall, one of which had a discharging sinus. The ulcers were tethered to the underlying indurated tissue [Figure 1]. Clinically, multidrug-resistant tuberculosis (TB), NTI, and immunodeficiency were considered as differentials. Hemogram revealed anemia and elevated erythrocyte sedimentation rate. There was no leukocytosis. Touch smear and sputum were negative for tuberculous bacilli. Mantoux test was negative. Chest radiograph was normal. She was negative for HIV I and II. Pus culture grew *Staphylococcus aureus*. Her biochemical parameters were normal. Histology showed lympho histiocytic infiltrate in the dermis. She was empirically re-started on ATT category II along with cotrimoxazole. There was very little clinical response to the above treatment and hence culture was repeated. There was no growth from the discharge on blood agar, MacConkey agar and thioglycollate broth after 48 h of incubation. To establish the cause, culture was repeated, which this time grew non pigmented, smooth colonies on Lowenstein–Jensen medium on 7th day of inoculation at 37°C [Figures 2a and b].

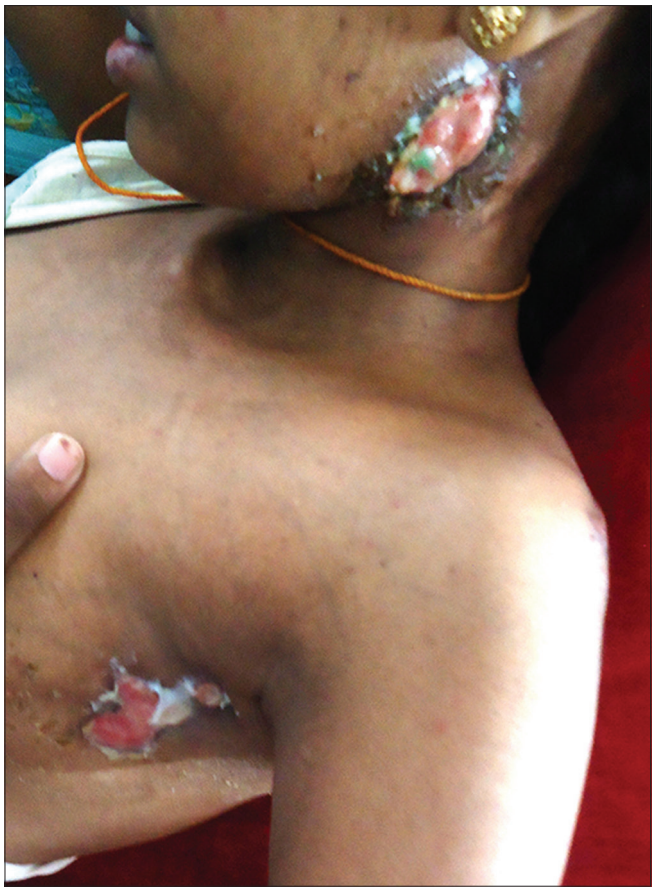

Figure 1: Ulcers covered with pus and slough seen over the left side of the neck, left axilla and lateral chest wall

The isolate reduced nitrate was urease positive and sensitive to amikacin and patient was started on injection amikacin. The colonies were confirmed as *M. chelonae*-abscessus by molecular diagnostic method (DNA sequencing). Since she could not tolerate amikacin, she was started on clarithromycin 500 mg orally. Within 2 weeks of institution of clarithromycin, the axillary ulcer and sinus healed. The ulcer over the neck showed a slow response. At the end of 40 days of clarithromycin, the ulcer over the neck, completely healed [Figure 3]. The patient gained wait, and her appetite improved. Clarithromycin was continued for one more month and withdrawn.

DISCUSSION

Cutaneous disease due to *M. chelonae* is typically associated with injury to the skin as a result of trauma, injection, or surgery. The disease can be recognized when a wound fails to heal, or a previously healed wound breaks down.[2] Causes of *M. chelonae* infection include **t**rauma or injection such as accidental or surgical trauma, particularly puncture wounds (e.g., tattoos, acupuncture, injection sites), catheters, prosthetic valves, stents, and breast implants. Disseminated disease is seen in immune suppression, immune defects, and during cytotoxic chemotherapy.[3]

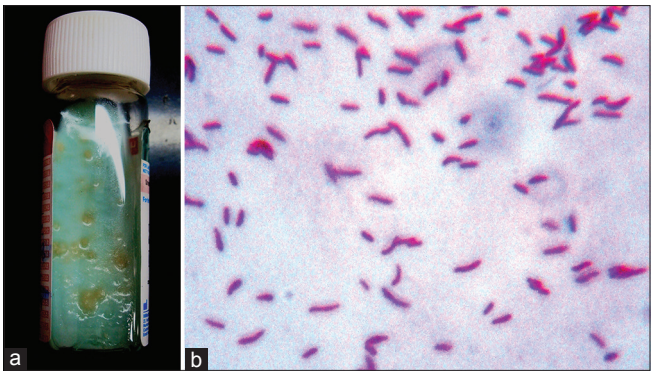

Figure 2: (a) Non pigmented, smooth colonies on Lowenstein–Jensen medium on 7th day of inoculation at 37°C (b) Ziehl–Neelsen stain of the culture showing acid fast *bacilli*

In purely cutaneous disease, *M. chelonae* is introduced by trauma to the skin.[4] The organism can also cause various clinical syndromes such as isolated lymphadenitis, osteomyelitis, joint infections, ocular disease and pulmonary disease. Lesions characteristically commence as red-to-violaceous subcutaneous nodules that may be painful and sometimes progress to cellulitis, abscesses or ulcers. Regional lymphadenopathy may be present.[5] Constitutional symptoms are typically absent. Disseminated disease, usually originating from primary skin and soft tissue lesions, occurs almost exclusively in immune compromised patients, such as those having solid organ transplants.[6] *M. chelonae* infection has been reported in systemic lupus erythematosus and other collagen vascular diseases, most of whom were on immunosuppressive therapy such as oral corticosteroids.[7] Scrofuloderma due to nontuberculous mycobacteria (NTM) has been described as early as 1951. These lesions clinically and histologically mimic tuberculous scrofuloderma involving the cervical group of nodes.[1] Species identification of the NTM as well as susceptibility studies are important steps when evaluating all forms of NTM, since their clinical presentation and manifestations, as well as their response to therapy, can be quite different. However one must also remember that *in vitro* susceptibility testing may not correlate with *in vivo* results and vice versa.[3] In an Indian study, where a total of 619 clinical specimens from cases of pulmonary and extrapulmonary TB were processed, 15.35% of samples yielded positive growth of which atypical Mycobacteria constituted 1.73%. However, no isolate of *M. chelonae* was made.[8]

Clarithromycin, a macrolide antibiotic having excellent absorption in the dose of 500 mg twice a day was found to be extremely effective against *M. chelonae*. However, there are rare reports of cases of *M. chelonae* showing resistance to clarithromycin. Terry *et al*. have reported a case of leg ulcer caused by *M. chelonae* infection that was successfully treated with clarithromycin.[9] In disseminated disease the duration of treatment should be at least six months or until all symptoms and signs resolve. In our case, the immune suppression

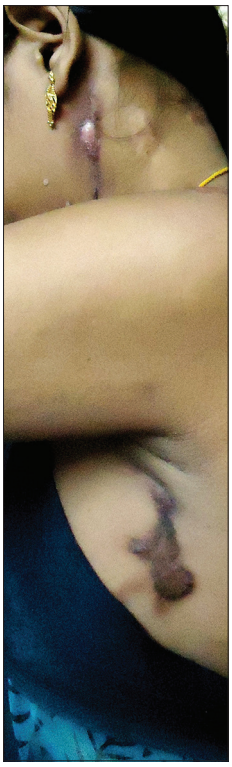

Figure 3: Complete healing of the ulcers, 2 months after treatment

induced by systemic corticosteroid therapy had worsened the infection leading to ulceration and sinus formation. Demonstration of the organism helped in the specific treatment of the disease that was otherwise was unresponsive to ATT. Cutaneous TB is a common problem in India. With the changing trend in the causative pathogens, one must keep in mind the possibility of NTM infection whenever the lab tests fail to prove *Mycobacterium tuberculosis* or when the clinical response is inadequate to standard ATT. In all such cases, culture should be done for NTM along with antimicrobial sensitivity.

Scrofuloderma due to NTI caused by *Mycobacterium scrofulaceum*, *Mycobacterium kansasii* and *Mycobacterium intracellulare* are already reported in Indian literature. To the best of the authors' knowledge, multiple scrofuloderma due to *M. chelonae* responding completely to clarithromycin has so far not been reported from India.

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