Case Report

Foot ulcer caused by multidrug-resistant *Mycobacterium tuberculosis* in a diabetic patient

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Osteoarticular tuberculosis is the fourth leading type of extrapulmonary tuberculosis. The disease has a progressive course and the diagnosis is often made in the later stages of bone destruction. We describe a case of a foot ulcer caused by drug-resistant *Mycobacterium tuberculosis* in a patient with known diabetes where the diagnosis was not suspected initially. Although tuberculous foot ulcers are rare, they should be included in the differential diagnosis of unknown foot ulcers. A greater awareness of this rare clinical entity may help in commencing specific evidence-based therapy quickly and preventing undue morbidity and mortality.

Case report

A 47-year-old female presented at the Lok Nayak Hospital, New Delhi, with the complaint of a non-healing wound on the left foot for over 3 years. The wound improved initially on antibiotic treatment; however, it had not shown any further improvement. She was illiterate, from a low socioeconomic background and was a resident of a village in Haryana, India. She was a housewife and frequently also worked in fields. She had admitted to having incurred frequent minor trauma while working on the field. She was a non-smoker and non-alcoholic. She was a known diabetic patient with known diabetes where the diagnosis was not suspected initially. Although she was aware of her diabetes, she did not have any other significant medical history. The family history was also not significant for tuberculosis.

On examination, the patient was obese, afebrile with a pallor. No other abnormality could be detected on performing systemic examination of the chest, cardiovascular system and central nervous system. Local physical examination showed a deformed left foot. A large ulcer was present over the lateral aspect of the foot and slough was present over the ulcer (Fig. 1). Past medical records showed that patient had already taken several course of antibiotics. The wound was dressed after debridement and the patient was asked to come for follow-up after 7 days with investigation reports which included complete blood count with erythrocyte sedimentation rate, blood sugar, pus culture sensitivity and wound edge biopsy. On follow-up it was observed that the haemoglobin was 8.2 mg dl−1, total leukocyte count was 8200 mm−3, and the differential leukocyte count was 67% polymorphs, 30% lymphocytes and 3% eosinophils. The erythrocyte sedimentation rate was 75 mm in the first hour. Blood sugar was abnormal with a fasting value of 120 mg dl−1 and post-prandial value of 210 mg dl−1; pus culture was sterile after 48 h of aerobic incubation. Edge biopsy revealed skin-covered tissue with focal ulceration which showed chronic inflammatory changes. No granuloma or caseation was seen. Human immunodeficiency virus serology was non-reactive.

The patient was started on diet control and oral hypoglycaemic agents. She was given augmentin 625 mg (amoxicillin 500 mg + clavulanic acid 125 mg) twice a day and was advised to carry out local wound care. Chest X-ray and X-ray of the left foot was advised. Chest X-ray was normal. A radiograph of the left foot showed mixed osteolytic and osteosclerotic changes in the metatarsals. There was no improvement in the wound with antibiotic treatment on follow-up.

Wound aspirate was sent for Ziehl–Neelsen staining, acid-fast bacilli culture using a BACTEC TB 460 instrument, and a PCR assay for *Mycobacterium tuberculosis*. Ziehl–Neelsen staining showed acid-fast bacilli, and BACTEC culture confirmed the same by isolating *M. tuberculosis* (by p-nitro-α-acetylamino-β-hydroxy-propiophenone test). A PCR assay targeting the MPB64 gene was done on the aspirate according to the method described elsewhere (Nguyen et al., 1996). PCR was positive for *M. tuberculosis* DNA.

Antitubercular therapy was started under supervision and after thorough counselling. The treatment included isoniazid, rifampicin, ethambutol and pyrazinamide with pyridoxine. The sensitivity report showed growth of *M. tuberculosis* resistant to isoniazid and rifampicin. The patient was started on an intensive phase of second-line antitubercular treatment, which included pyrazinamide, ethambutol, kanamycin, ofloxacin, ethionamide and p-aminosalicylic acid for 6 months. On follow-up after 4 months, the wound had clinically improved (Fig. 2). After the intensive phase of treatment, she was maintained on a continuation phase for 18 months with four drugs, i.e.
ofloxacin, ethionamide, ethambutol and p-aminosalicylic acid. On follow-up at 24 months, i.e. after the patient had taken a complete course of antitubercular therapy, the wound had completely healed.

**Discussion**

*M. tuberculosis* infects nearly one-third of the world's population. India contributes to one-third of the world's burden. The prevalence of multidrug-resistant tuberculosis has increased globally over the last decade. The incidence of multidrug-resistant tuberculosis in India in newly diagnosed cases varies between 1.1 and 5.3 % and in previously treated cases varies between 8 and 67 % (Prasad, 2005).

Skeletal tuberculosis can affect all the bones in the body, commonly the spine, femur, tibia and fibula. Tuberculosis involving the foot is seen in only 0.1–0.3 % of all patients with extrapulmonary disease (Davidson & Horowitz, 1970; Manzella *et al.*, 1979). Osteoarticular tuberculosis of the foot is usually secondary to a primary focus either in the chest or elsewhere. However, in the present case, no primary focus of infection was identifiable. In underdeveloped countries where people have a habit of walking barefoot, the chance of frequent minor trauma is common. This results in a relatively higher incidence of foot involvement because of tuberculosis (Tuli, 1977). This was seen in the present case, where no primary focus of tuberculosis could be identified but the patient had minor trauma of the foot on several occasions while working. This could have led to direct inoculation of tubercle bacilli. Foot infections in diabetics require co-ordinated management of both local and systemic (metabolic) issues as they cause substantial morbidity in such patients and can even lead to amputation of the lower limb. In such cases, there is a long list of differential diagnoses which includes infectious and non-infectious causes. The most common cause of foot ulceration in such patients is as a result of peripheral neuropathy with infection and other immunological disturbances playing a secondary role (Lipsky *et al.*, 2006). Tuberculous osteomyelitis as a cause of foot ulcer is rare (Yuen & Tung, 2001; Dhillon & Nagi, 2002). Since there is a lack of awareness about such an uncommon entity and it frequently mimics other conditions such as Madura foot, chronic pyogenic infection, Kaposi’s sarcoma, bone tumours and other inflammatory and neoplastic processes of the synovium, diagnosis is often delayed. Clinical signs and symptoms are very subtle. The typical radiological appearance of tuberculous osteomyelitis is uncommon and appears very late in the course (Choi *et al.*, 2008). Hence definitive diagnosis requires a strong clinical suspicion and edge biopsy or ulcer curettage/aspiration for mycobacteriological analysis. Usually osteoarticular tuberculosis follows a chronic insidious course and the patient usually presents with pain and swelling. Discharging sinus resulting in an ulcer is present very late in the course.

**Conclusions**

Tuberculous foot ulcers in particular are very difficult to treat as usually there is a diagnostic delay and the condition requires prolonged and adequate antitubercular therapy. It is difficult to monitor the success of therapy as radiological changes lag behind the biological process of repair. Hence if after 6–7 months of adequate chemotherapy there is no clinical improvement and/or imaging shows deteriorating lesions, a repeat biopsy is required to test drug sensitivity and rule out the presence of antitubercular drug resistance.
Therefore, the authors believe that in an endemic country like India, tuberculosis should be included in the differential diagnosis of a non-healing diabetic foot ulcer and sensitivity testing should be performed along with mycobacterial culture on the initial edge biopsy specimen for optimum management of the patient.

References


