Multidrug Resistant *M. tuberculosis* from Multiple Cutaneous Abscesses in a Patient with Polymyositis: Response to treatment

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Abstract

Background
It is a case of pyomyositis in a HIV negative patient complicated with miliary tuberculosis of non-reactive type and cutaneous abscesses all over the body. From every abscess site and from sputum, multidrug resistant *M. tuberculosis* was isolated.

Methods
The isolated organism was confirmed as M. tuberculosis with Niacin test, FAST plaque assay and molecular method. The sensitivity of the organism was done by BACTEC 460TB system as well as with Loewenstein Jensen media, incorporated with 9 antitubercular drugs in different concentrations.

Result
The isolated *M. tuberculosis* was resistant to nine antitubercular drugs. The patient was treated successfully for 1.5 years with 6 antitubercular drugs, 5 conventional and 1 newer.

Conclusion
Early diagnosis of multiple cutaneous abscesses and miliary tuberculosis with multidrug resistant *M. tuberculosis* along with prompt management and strict follow up are necessary for successful treatment in case of a highly susceptible immunocompromised patients.
Background

Global Tuberculosis Control Report 2003 issued by World Health Organisation on World Tuberculosis (TB) day ranks India as number one in the world by estimated number of tuberculosis cases. There are about 0.9 million incident smear positive cases of pulmonary TB in India every year whereas the incidence of extrapulmonary TB cases estimated at about 0.2 million involving brain and spinal cord, bone, kidney, endometrium and fallopian tubes, abdomen, pleura, pericardium, lymph nodes, bone marrow and skin mainly. However, cutaneous tuberculosis is a rare manifestation as reported to be 0.1% of dermatology patients, Lupus vulgaris being most frequent manifestation (55%) in a tertiary-care hospital in northern India (1975-95). Retrospective survey detected the incidence of 0.07% and 0.14% of cutaneous TB in Hong Kong (1983-1992) and 1980-1993 in Madrid (1980-1993) respectively. With the rapid spread of HIV/AIDS as an epidemic, cutaneous tuberculosis has become a resurgent disease. Atypical mycobacteria like M. kansasii, M. scrofulaceum are the most common etiological agents for cutaneous tuberculosis in HIV/AIDS and other immunocompromised patients but M. tuberculosis is still rare.

The pathogenesis of cutaneous involvement is either due to true bacterial invasion of the skin or tuberculid (hypersensitivity reaction) associated with primary focus elsewhere. Primary resistance of a strain is mainly seen in a patient, who was not treated with antitubercular drugs early, whereas acquired resistance develops during treatment with an inappropriate regimen or due to early discontinuation of therapy. Multidrug resistance (MDR) is higher among
HIV-infected patients. WHO working group ("DOTS-Plus for multidrug-resistant tuberculosis") reported more cases in low-income and middle-income countries.5 Here we are reporting a case of multiple cutaneous abscesses with MDR *M. tuberculosis* in a case of polymyositis where the presentation of clinical signs of tuberculosis is unique and resistant pattern to nine antitubercular drugs is rare. The most important event is that the patient responded to treatment.
Case Report

A 23-year-old male was diagnosed as a case of polymyositis on the basis of presenting symptoms, muscle biopsy, enzyme assay, needle electromyography (EMG) and nerve conduction velocity test (NCV). He was HIV negative, chest x-ray was normal and sputum was AFB negative. He was treated with immunosuppressive drugs like corticosteroid (1 mg/kg per day for 3 to 4 weeks, tapered slowly over a period of 10 weeks to 1 mg/kg every other day) and methotrexate (7.5 mg weekly for the first 3 weeks with gradual dose escalation by 2.5 mg per week to a total of 25 mg weekly for 1.5 years). During this period, his muscle power improved slightly. After 6 months, he was readmitted with a single cutaneous abscess in the right side of the neck with no sinus formation along with cervical and axillary lymphadenopathy. Chest x-ray was normal. Aspirated pus from cutaneous abscess showed AFB. Biopsy taken from the axillary lymph node showed nonspecific necrosis with disintegrating polymorphs and enormous number of tubercle bacilli. There were very few granulomatous cells and no epithelioid cells. The organism grew in culture after 5 weeks. Niacin test was positive. Molecular identification of *M. tuberculosis* was done by using species specific primers for devR (Differentially expressed Virulent gene) (Singh *et al.*, 1999) (Figure 1). Rapid bacteriophage assay by FAST Plaque Tuberculosis kit (BIOTEC Laboratories Ltd, UK) was performed. Chest x-ray showed miliary mottling. USG of kidney, liver or spleen revealed no abscess. The patient was treated with 4-drugs regimen [isoniazide (H) 300mg/d, rifampicin (R) 450mg/d, ethambutol (E) 800mg/d and pyrazinamide (Z) 1.5 g/d] for 8 months.
All the 4 drugs were found to be sensitive with BACTEC 460TB system. The patient was however improved. However, the patient revisited only after 6 months with cutaneous abscesses all over the body, especially in the back, left thigh and left arm, all being highly positive for *M. tuberculosis* though there was no history of irregular intake of antitubercular drugs. There was miliary mottling all over the chest x-ray. The isolated *M. tuberculosis* was resistant to the all the 4 first-line drugs by BACTEC 460TB system and to the following nine drug concentrations incorporated into Loewenstein Jensen media [Hi-media, Mumbai, India]: H (1µg/ml), H (1µg/ml), R (20µg/ml), R (50µg/ml), E (2µg/ml), E (10µg/ml), Z (50µg/ml, at pH 5.5), streptomycin (5µg/ml), streptomycin (50µg/ml), para-amino salicylate (2.5µg/ml), cycloserine (30µg/ml), amikacin (700µg/ml) and ciprofloxacin (12.5µg/ml). The patient was started treatment with H (5mg/kg/d) and R (10mg/kg/d), pyrazinamide (30mg/kg/d), ethambutol (15mg/kg/d), kanamycin (15mg/kg IM 5 times weekly) and sparfloxacin (500mg/d). For the first two months he was treated under direct observation and then, the same treatment was followed for upto 1.5 years. The patient responded to the therapy slowly and by the end of 1.5 years, he was cured clinically, microbiologically and radiologically.
Discussion

Isolation of MDR *M. tuberculosis* from multiple cutaneous abscesses and sputum of an immunosuppressed but HIV-negative patient of polymyositis and miliary tuberculosis showed that the lesions of the skin were not a tuberculid type. There was true bacterial invasion of the skin. The cutaneous abscesses were of various sizes both over the flexor and the extensor surfaces of the limbs and the trunk with no muscle involvement and no sinus formation. It was a rare case of miliary tuberculosis of non-reactive type involving the cutaneous tissue, as evident by the biopsy picture of the axillary lymph node. A similar case study has been documented in a patient with dermatomyositis under immunosuppressive therapy. Our patient had an additional pulmonary involvement.

The rapid clinical progression of the skin infection indicated the poor cellular immune response due to immunosuppressive therapy with corticosteroid and methotrexate, which was reported earlier also. Resistance is higher and more rapidly acquired in HIV-infected patients. The patient was not HIV-positive but developed MDR tuberculosis rapidly within 6 months, involving lungs as well as skin due to the immunosuppressed condition. It was not a ‘primarily-resistant’ strain as evident from the initial sensitivity pattern. Inadequate treatment may give rise to acquired resistance. In this case, the treatment was adequate but the development of new skin with initial regression of disease suggests that the tubercle bacilli in the cutaneous and subcutaneous tissue were somehow protected from the action of the antituberculous drugs. This could be the ‘paradoxical expansion of disease during therapy’ where the drugs could not
penetrate well in these areas probably due to polymyositis as reported in a case of dermatomyositis-associated subcutaneous calcification, or the large mass of bacilli present during the acute dissemination phase of the infection might have lodged in the small arterial vessels and caused obstruction to these vessels, which might led to necrosis and abscess formation in the surrounding areas. 

Fast plaque assay as well as molecular identification was done to confirm that the strain was *M. tuberculosis* and not any atypical mycobacteria, like *M. kansasii* and *M. scrofulaceum* which are the most common organisms causing cutaneous involvement in immunosuppressed patients.

This is probably the first case reported where the entire first and most of the second line drugs with a total of 9 antitubercular drugs were found to be resistant and yet the patient was treated successfully. The patient was treated with 6 antitubercular drugs, 5 conventional and 1 newer ie. sparfloxacin for 1.5 years. The clinical progress of the patient during therapy was slow and the patient was microbiologically cured for the first time only after 1 year. The treatment was continued for another 6 months. The active lesions in chest x-ray diminished gradually only after 10 months.
Conclusions

It is important to recognize the development of multiple cutaneous abscesses and miliary tuberculosis due to MDR *M. tuberculosis* at the earliest in the patients with immunosuppressive therapy. Early diagnosis, prompt management and strict follow up under constant vigilance are necessary for treating successfully the highly susceptible immunocompromised patients.
Competing interests

- We did not receive any reimbursement, fee, funding, or salary from an organization that may in any way gain or lose financially from the publication of this paper in the past five years, or is such an organization financing the article-processing charge for this article.

- We did not hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this paper.

- We do not have any other financial competing interests.

- There is no non-financial competing interest to declare in relation to this paper.
Authors’ contributions

CM carried out the case study and follow-up, clinical as well as microbiological, study plan, sensitivity of the organism, participated in the FAST plaque assay and molecular identification method and drafted the manuscript.

AG carried out FAST plaque assay and molecular identification method.

AA conceived of the study, participated in the design of the study and acted as an overall supervisor.

All authors read and approved the final manuscript.
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References


Figure 1

Sample figure title

PCR for devR gene (513 bps) of *M. tuberculosis*.

Figure legend text

(From left to right) Lane M; 100bp ladder Banglore Genei (India), Lane 1; Negative control, Lane 2; *M. tuberculosis* H37Rv Lanes 3-4; Patient isolate, Lane 5; *M. kansasii*, Lane 6; *M. scrofulaceum*. 