

Multidrug-resistant tuberculosis and leprosy: An unsolved mystery

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ABSTRACT

Tuberculosis (TB) and leprosy are two age-old infections, which we are facing even today. With drug-resistant TB on the rise, we report a case of multidrug-resistant TB with leprosy, which has never been reported previously. The peculiar course of this case forces us to rethink about the upcoming challenges due to their cooccurrence.

KEY WORDS: Coinfection, leprosy, tuberculosis

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INTRODUCTION

Mycobacterium tuberculosis and *Mycobacterium leprae* are known to infect human race since 9000^[1] and 4000^[2] years, respectively. Occurrence of these two diseases in a single individual is infrequent, with only sporadic case reports.^[3] This rarity of cooccurrence may be due to their transmission dynamics, variable growth rate of mycobacteria, and cross-immunity between them.

In the present era of multidrug-resistant tuberculosis (MDR-TB), we report a case of MDR-TB with leprosy and Type I lepra reaction warning us regarding upcoming challenges of their management. Even after extensive search of available literature, we could not find any case report of drug-resistant TB and leprosy coinfection.

CASE REPORT

A 19-year-old male, on treatment for MDR-TB, presented with complaints of localized swelling over face, reddish

discoloration of limbs, and hypopigmented patches over body since 1 month. He was on Category IV directly observed treatment, short-course chemotherapy for the last 5½ months on the basis of sputum line probe assay report from Revised National Tuberculosis Control Program (RNTCP) accredited laboratory, which showed *M. tuberculosis* isolates, resistant to drugs isoniazid and rifampicin. The patient was taking kanamycin, ethionamide, pyrazinamide, ethambutol, levofloxacin, and cycloserine regularly. There was a history of leprosy 6 years back, for which the patient was treated for 6 months. The patient had a history of TB 5 years back which was treated with 9 months of daily regimen antitubercular therapy. Clinical examination revealed hypopigmented, dry, scaly plaque over upper arms [Figure 1], hypoanesthetic plaque over right palm [Figure 2], and erythematous plaque over right side cheek and nose [Figure 3]. Respiratory system examination revealed bilateral infraclavicular crepts.

Routine investigations were normal. Chest radiograph was suggestive of fibrotic lesions, bilateral upper lobes [Figure 4].

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Figure 1: Dry, scaly, hypopigmented, anesthetic plaque over left upper arm



Figure 2: Hypoanesthetic plaque over the right palm extending to the wrist



Figure 3: Erythematous raised plaque over the right cheek extending to the nose



Figure 4: Chest radiograph (posteroanterior view) showing bilateral upper lobe fibrotic lesions

Sputum culture from RNTCP accredited laboratory at 4th month was positive for growth of *M. tuberculosis*.

Dermatology review was taken for skin lesions. The patient was diagnosed as multibacillary (MB) leprosy and started on multidrug therapy regimen (MB-MDT) consisting of rifampicin 600 mg once monthly, dapsone 100 mg daily, and clofazimine 300 mg once monthly and 50 mg daily. Biopsy of skin lesions was suggestive of mid-borderline leprosy. Two weeks later, the patient presented with increased erythema and pain over the skin lesions and appearance of new lesions [Figure 5]. The patient was diagnosed with Type I lepra reaction and started on analgesics and steroids (prednisolone). Prednisolone was given in the dose of 30 mg/day orally for the first 2 weeks and then gradually tapered over the next 4 weeks. It was thus stopped after a total duration of 6 weeks. MB-MDT was continued as per the National Leprosy Eradication Programme guidelines.

Thus, final diagnosis of MDR-TB with mid-borderline leprosy and Type I lepra reaction was made. Skin lesions markedly improved with treatment [Figure 6]. Patient's subsequent sputum cultures were negative and MDR-TB was thereafter managed as per the RNTCP guidelines.

DISCUSSION

In concurrent infections, weakening of immune system by one organism makes patient more susceptible to other virulent infections. Concomitant infection of TB and leprosy is not a recently reported phenomenon.^[4] However, MDR-TB with leprosy has never been reported previously. Some authors have implicated that decreased cellular immunity in MB leprosy patients coupled with social impact led to either reactivation or superinfection with TB.^[5] However, contrary studies hypothesize that previous exposure to TB provides some degree of protection against leprosy, thus proposing cross-immunity hypothesis.^[3] Furthermore, vaccination by *Bacillus Calmette-Guerin* might also provide immunity against leprosy.^[6] Thus, the literature has evidence supporting both coinfection and cross-immunity theories, but none can individually explain all the interactions.

The point to be highlighted in this case is that the patient suffered from MDR-TB along with leprosy, the evidence of which is lacking in the literature. The patient was



Figure 5: Dry, scaly anesthetic plaque over the right upper arm. Two new erythematous lesions near the elbow (black arrows)

treated for leprosy with adequate dosage and duration 6 years back as per the guidelines and was thus cured. This time, the patient developed leprosy during active TB which can be labeled as a relapse of leprosy. This observation questions the cross-immunity theory according to which one disease provides immunity from the other.

This case also questions the rifampicin use in leprosy patients. There are concerns in literature about avoiding monotherapy with rifampicin for any undetected TB in the form of once-monthly dose in MDT for leprosy as it may promote MDR-TB in concomitantly infected patients.^[7] Whether rifampicin monotherapy played a contributory role in the development of MDR-TB in this patient or not remains a query.

The patient developed lepra reaction on starting antileprosy drugs, for which steroids had to be given. However, studies suggest that immune suppression due to steroids may lead to TB. This patient already had MDR-TB, for which he was receiving adequate treatment. It is again doubtful that whether use of steroids can have some negative repercussions over long-term.

The interplay between the two infections is further complicated in the present case by daily use of clofazimine in leprosy regimen, which has antitubercular activity as well. Its dosage for leprosy treatment (50 mg once daily) is half the dosage recommended for MDR-TB.^[8] Whether sputum culture conversion to negative after a positive culture is because of addition of clofazimine and its antitubercular effects or due to recovery of the patient owing to his continuing category IV regimen is debatable. Furthermore, whether this low dose of clofazimine can precipitate further drug resistance in tubercle bacilli may only be inferred after long-term follow-up of multiple patients.

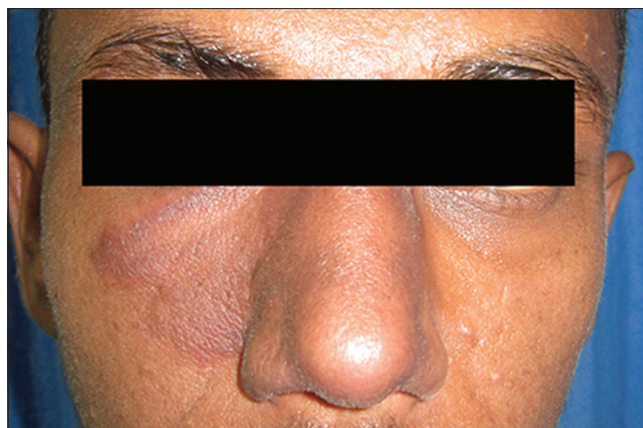


Figure 6: Lesion over the face showing decreased swelling and dusky erythema

This patient is responding well to treatment. However, in view of the multiple aspects highlighted and discussed above, the management of concomitant leprosy and TB disease, especially MDR-TB, and its repercussions on each other needs further elicitation.

CONCLUSION

MDR-TB and leprosy coinfection poses new challenges to clinicians in their management, with various questions remaining unanswered. First, in leprosy patients with undiagnosed TB, there is a rising concern for rifampicin usage as a part of leprosy treatment. However, screening of every leprosy patient for undetected TB will burden the health-care resources. Second, use of steroids for lepra reactions may flare underlying TB. Third, use of drugs such as clofazimine may complicate the management of drug-resistant TB. Fourth, this case also questions cross-immunity theory, as this patient, with active TB developed leprosy.

Concrete answers to the above-focused issues are needed to solve the mystery of this coinfection, especially when associated with drug-resistant TB.

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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Conflicts of interest

There are no conflicts of interest.

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