

Case Series

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A case series on immunotherapy for leprosy reactions

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ABSTRACT

Leprosy is a chronic granulomatous disease caused by *mycobacterium leprae*. As a result of immunological alterations evoked by organism, patients suffer from acute inflammatory episodes known as leprosy reactions, which can continue to occur before, during and after stoppage of therapy and are a cause of concern for the resulting morbidity. Understanding the beneficial effects of immunotherapy with chemotherapy will help in reducing reactions as well the duration of treatment. Five untreated patients of middle age with MI=0 was enrolled in our study who were presented with lepra reactions started on Multi-drug therapy (MDT) and then sent for BCG vaccination. Patients were evaluated monthly for clinical improvement 60% of patients showed improvement within 3 to 4 months whereas 40% patient showed improvement in 7 to 8 months of immunotherapy. Despite of available effective MDT, persisting viable organisms as well as persisting clinical activity are significant problems in leprosy patients. Immunotherapy combined with chemotherapy is good and more promising options to overcome these problems.

Keywords: Lepra reactions, Multidrug therapy, Immunotherapy

INTRODUCTION

Leprosy is a chronic granulomatous disease caused by *mycobacterium leprae* and *mycobacterium lepromatosis*, which has a long and variable incubation period.¹ The disease manifestation depends to a large extent on immune response of the host. As a result of immunological alterations evoked by organism, patients suffer from acute inflammatory episodes known as leprosy reactions, which can continue to occur before, during and after stoppage of therapy and are a cause of concern for the resulting morbidity.² Immunotherapy aims to modify the defective cell-mediated immune response in a section of leprosy cases. This presentation reviews the various immunomodulators developed/investigated for this purpose. Among the various mycobacterial agents, Bacillus Calmette–Guérin (BCG), BCG + M.leprae, Mycobacterium w, ICRC bacillus and M. vaccae have been tried in leprosy patients and varying degree of beneficial effects on bacterial killing and

clearance have been observed. Studies carried out at Central Jalma Institute of Leprosy (CJIL), Agra and elsewhere suggest an important role for these mycobacteria as immunotherapeutic agents.³ Despite the variable efficacy, BCG vaccination is still widely recommended for use in leprosy-endemic countries.⁴ Although the BCG vaccine was initially developed for protection against *M. tuberculosis*, but it was found to be protective against *M. leprae* as well.⁵ The protective efficacy of the first dose of BCG vaccine was found to be 14 percent in the general population and 80 per cent in household contacts of leprosy cases in India.⁶ So, by knowing the beneficial effects of immunotherapy with chemotherapy which will help in reducing reactions as well the duration of treatment.

CASE SERIES

Five untreated patients of middle age with MI=0 was enrolled in our study who was presented with

erythematous, tender papules, nodules or plaques variable in size. Routine laboratory investigations including chest X-ray were normal. Serology for HIV, HBsAG, HCV, VDRL, tuberculin skin tests were negative. All patients were screened for any immunocompromised states started on multi-drug therapy (MDT) and then sent for BCG vaccination. 0.1 ml intradermal BCG injections were given in immunisation centre of our hospital, every month for 12 months. Patients were evaluated monthly for a minimum period of one year and disease activity is

clinically assessed every 3 months oral steroids was tapered to half doses in between these durations and at the end of 6 month, no relapses were seen and hence oral steroids stopped thereafter. Clinical improvement was measured by resolution of lesions and fewer incidences of relapses. Out of five patients, 60% of patients show improvement within 3 to 4 months of immunotherapy whereas 40% patient shown improvement on 7-8 months of immunotherapy this shows as follows (Table 1).

Table 1: Cases series.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5
Age/sex	46/M	30/M	26/F	38/F	24/M
Morphology of lesions	Erythematous papules and nodules	Painful erythematous nodules and plaques	Painful erythematous nodules and plaques	Erythematous papules and nodules	Painful erythematous nodules and plaques
Prodromal symptoms	Fever, malaise, arthralgia	Fever, malaise, arthralgia, peripheral edema	Fever, malaise, arthralgia	Fever, malaise	Fever, malaise, arthralgia, peripheral edema
Therapy prior to Immunotherapy	Thalidomide steroids	Thalidomide steroids	Thalidomide steroids	Thalidomide steroids	Thalidomide steroids
Time for symptoms to subside after Immunotherapy	7-8 months	3-4 months	6-7 months	3-4 months	3-4 months



Figure 1: (A) Before immunotherapy and (B) after immunotherapy.

DISCUSSION

Leprosy is a chronic granulomatous disease involving skin and nerves and treated by MDT. Immunological alteration occurs as a result of this acute inflammatory episodes occurs in the form of lepra reactions during or after stoppage of MDT which is concerning morbidity. Antireactional treatment may helpful in so many cases, but very few does not responds and recurrent lepra reactions occurs. So, there is need of immunotherapy in the form leprosy vaccines.

There are so many obstacles for preparation of leprosy vaccines, as *Mycobacterium leprae* unable to culture on artificial media and long incubation period and precise immunology of leprosy still not understood.

Due to shared antigenicity of *M. Leprae* with *Mycobacterium tuberculosis*, BCG vaccine has been shown to protect against leprosy⁷. *Mycobacterium bovis* (BCG) is a live vaccine and Fernandez in 1939 demonstrated lepromin conversion in 30% to 100% individuals vaccinated with BCG.⁸ Convit et al showed the immunogenicity of *M. leprae* was enhanced by the addition of BCG and mixed vaccine containing *BCG + heat killed M.leprae*, and observed that both BCG as well as the combination provided protection, but the combination did not provide significant additive effect as compared to BCG alone.^{9,10} In a South India comparative vaccine study by Gupte et al, the protective efficacies of *BCG+HKML*, *ICRC bacillus* (killed vaccine), *Mycobacterium w/M. indicuspranii* (MIP), *BCG*, and employed normal saline as placebo were 64%, 65.5%, 25.7%, 34.1%.¹¹

Our study population is identified as one of few remaining endemic provinces for leprosy elimination in India.

Despite effective MDT and anti-reactional treatments, reactions were not resolving, leading to further comorbidities, thus immunotherapy (BCG vaccine) is good and more promising options to overcome these problems.

As BCG vaccine is readily available in all health-care facilities and it is safe, efficient, well tolerated and cost-effective vaccine used against leprosy reactions.

CONCLUSION

As leprosy is endemic in our area, we came across chronic and recurrent lepra reactions usually not responding to conventional treatment. Understanding the beneficial effects of immunotherapy in reducing the recurrent lepra reactions as well as duration of treatments.

Henceforth we conclude that immunotherapy may be helpful in leprosy patients with recurrent reactions.

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