# MANAGEMENT OF LARGE FACIAL PATCH WITH RECURRING REVERSAL REACTION: A CASE REPORT

Delwar Hossain<sup>1</sup> Rezina Yasmin<sup>2</sup> Alvin Saha<sup>3</sup>

## **Summary**

Inflamed large facial patch, being compromising the appearance and beauty of a patient, is a source of embarrassment and distress, and affects anti-leprosy drive adversely in many ways in the field situation. Its management with oral prednisolone alone, the mainstay of treatment for reversal reaction, proved disappointing. To see whether topical tacrolimus will be helpful in managing those patients. We treated a patient with recurring reversal reaction in large facial patch with tacrolimus 0.1% ointment, twice daily and lower dose oral prednisolone for twelve months during March, 2012-February, 2013. Complete remission was achieved. No side effects of whatsoever was seen. No recurrence of reaction is seen till to date. Tacrolimus ointment and lower dose prednisolone was found helpful in managing patient with recurring reversal reaction in large facial patch.

# **Key words**

Leprosy; Reversal Reaction; Reacting Facial Patch; Management; Tacrolimus and Prednisolone.

## Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae. The disease may be complicated by immunological adverse reactions called reversal reaction and erythema nodosum leprosum reaction. Reversal reaction is a cell mediated immunological reaction directed against M. leprae in the dermal macrophages and Schwann cells leading to inflammation of skin and nerve lesions.

- Professor of Dermatology & Venereology (Retired)
  University of Science & Technology, Chittagong (USTC)
- 2. Lecturer of Community Medicine Sir Salimullah Medical College, Dhaka.
- 3. Associate Professor of Dermatology & Venereology BGC Trust Medical College, Chittagong

Correspondence: Dr. Alvin Saha

Email: samar@actl\_bd.com Cell : 01819 078842 Reversal reaction predominantly occurs in borderline leprosy [1]. Its frequency varies from 8.8% to 47% [2,3]. It may be recurrent in one-third of cases [4].

Facial patch is self-expressive. It easily attracts others attention and incurs harm to the patient in the form of embarrassment, anxiety and mental distress. Moreover, reacting angry looking patch affects anti-leprosy drive in many ways in the field situation particularly where the disease is associated with intense psychosocial stigma like ours.

Oral prednisolone is the mainstay of treatment of reversal reaction. However, its management with only prednisolone may be disappointing. In that case, methotrexate, cyclosporine and azathioprine were also tried. Gilles Safa et al reported a case managed by topical tacrolimus with oral prednisolone [5,6,7,8]. Here we report the outcome of a patient with recurring reversal reaction in large facial patch treated with topical tacrolimus and lower dose prednisolone for twelve months.

# **Case Report**

A male of 28 years attended a local leprosy clinic with the complaint of burning/ tingling pink swollen hot large facial plaque on left half of face involving forehead, eye lids, cheek, nose and auricle. Some areas of the plaque were anesthetic to cotton touch. His forceful eye closure was weak (4+ in Quick Muscle Test). He had multiple anesthetic pale patches over limbs and trunk and both common peroneal nerves enlarged and tender. His slit skin smear test from ear lobes and face lesion was negative. He was diagnosed as BT leprosy with reversal reaction.

He was put on MDT (MB), adult dose, for 12 months and oral prednisolone for six months with an initial dose of 40 mg/day. Unfortunately he experienced inflammation in patch at an attempt to reduce prednisolone from 20 mg/day to 15 mg/day at fourth month of his prednisolone therapy. His pednisolone dose was increased again to 20 mg/day and continued for next 15 months with several failed attempts to reduce it.

With this prolonged steroid he got remission of his neuritis and reaction in skin patches elsewhere and got back lid muscle power but facial patch remained quiescent as long as oral prednisolone maintained 20 mg/day. At this stage, he was referred to us in February, 2012 for further management.

We treated him in a leprosy clinic during March, 2012-February, 2013. At the outset, a health education talk was arranged to identify the problem and to discuss the action plan of management. He was on prednisolone maintenance dose (20 mg/day) and facial patch was at quiescent. At this stage we asked him to taper prednisolone, 5 mg weekly to end the course within next four weeks and report to clinic again.

One month later (March, 2012) he returned back with full blown reversal reaction on his facial lesion. It was pink in color, swollen, shiny and angry looking with impaired cotton touch sensation. After thorough clinical evaluation, we did sensation test of facial patch and eyes with the wisp of cotton and routine sensory test for hands and feet with the help of monofilament nylon as designed for field practice by the World Health Organization (WHO). We did quick muscle test (QMT) of eyes, hands and feet as per WHO guidelines, routine blood, urine and stool test and a baseline record was made.

We put him on tacrolimus (0.1%) ointment, twice daily for twelve months and oral prednisolone for twelve months (20 mg/day for first three months, 15 mg/day for next three months, 10 mg/day for next three months and 5 mg/day for last three months and then stop) and asked him to report to clinic monthly.

With our treatment, heat, swelling and redness took three months to go, and tingling and firmness took six months to go. Soft supple normal looking skin with normal sensation appeared by twelve months of treatment (Fig-1 & 2). No side effects of whatsoever from topical tacrolimus and lower dose prednisolone was seen. At the end of twelve months treatment, there was no recurrence of reversal reaction on facial lesion. He is fine and enjoying happy life even today (April, 2014).



Fig 1: Facial appearence after treatment. Pink swollen hot plaque over left half of the face involving forehead, eye lids, cheek, nose and auricle.



Fig 2: Facial appearence before treatment. Normal looking face at the end of twelve months treatment.

### Discussion

A patient had been suffering from borderline tuberculoid leprosy with recurring reversal reaction on his large facial patch. He was on prednisolone (maintenance dose) for 15 months. We treated him with topical tacrolimus and lower dose prednisolone for twelve months. At the end of the course, we achieved complete remission of the reaction and successful waning of prednisolone. He remained free from reaction for last 14 months after stoppage of our treatment.

Frequency of large facial patch with recurring reversal reaction is 1.36% (in one of our centers, occurrence of reversal reaction in new registered cases is 50.68%. Of them 15.06% occurs in only skin lesions, 23.28% in only nerve, 10.95% in both skin and nerve, and 1.36% occur in large facial patch.). Numerically it is insignificant. However, being self-expressive and having potential for affecting the anti-leprosy drive in many ways, it becomes an issue of great concern in the field situation. Prednisolone is the treatment of choice for reversal reaction. Generally BT patients require prednisolone for 4-9 months [9]. However, our patients were on it for 15 months. With this prolonged prednisolone, he got remission of reversal reaction that occurred in nerves and skin lesions elsewhere but for unknown reason did not get relief of reversal reaction in facial patch. However, reportedly facial patch is one of the risk factors for recurrent reversal reactions [10].

Methotrexate has mechanism based action against reversal reaction [11]. It is found fairly safe and effective in managing a severe reversal reaction developed in a BL patient who was intolerant to prednisolone [5]. However we did not consider systemic use of methotrexate to manage a single patch reversal reaction in our case.

Cyclosporine is also found effective in managing severe reversal reaction. However it is prohibitively expensive and associated with considerable side-effects [6]. Azathioprine was also found effective in managing reversal reaction with multiple skin and nerve lesions [7]. It is also a steroid-sparing agent. However its potential for bone-marrow suppression, increase infection risk and gastrointestinal disturbances deterred us to use it in our case.

Topical tacrolimus along with oral prednisolone was found effective in managing a very complicated leprosy patient with many reacting skin lesions [8]. Having been given due consideration in its availability in the market and amenability of our patient, its safety and efficacy, we preferred it for our patient having single reacting lesion.

Reversal reaction is a cell mediated immunity directed against M. leprae in the skin and nerve lesions. Infection of the skin macrophages and Schwann cells of the nerve by M. leprae causes expression of adhesion molecules on their surfaces. This may give rise to antigen presentation which triggers cell mediated immunity that result in localized inflammation and edema [12]. It is a complex immunological mechanism involving release of pro-inflammatory cytokines and mediators, namely, IL-1, IL-2, IL-4, IL-8, IL-10, IL-12, INF- and TNF- [13-14]. Tacrolimus is a macrolide calcineurin inhibitor agent. It inhibits T-lymphocytes activation by inhibition of transcription and release of proinflammatory cytokines and mediators [15]. On the other hand prednisolone suppresses Tlymphocytes during inflammatory process and reduces tissue edema [16]. Thus both the drugs might have worked synergistically to bring complete resolution and permanent remission of the reaction in our case. But the exact mechanism by which tacrolimus helped in waning prednisolone is yet to be elucidated.

In conclusion, topical tacrolimus together with lower dose prednisolone was found helpful in aborting recurring reversal reaction on large facial patch. Further formal study is welcomed.

## Acknowledgements

We thank Sultan Mohammed Elias Uddin, Leprosy Control Officer (LCO), the Leprosy Mission International-Chittagong program, for referring the patient.

# Disclosure

All the authors declared no competing interest.

### References

- **1.** Job CK. Pathology of leprosy. In: Hastings RC (ed). Leprosy, 2<sup>nd</sup> edn. Churchill Livingstone, Edinburgh, 1994; 193-234.
- **2.** Richardus JH, Finlay K, Croft RP and Smith WCS. Nerve function impairment in leprosy at diagnosis and completion of MDT: a retrospective cohort study of 786 patients in Bangladesh. Lepr Rev. 1996; 67: 297-305.
- **3.** Lockwood DNJ. Clinical features and outcome of reversal (type 1) reactions in Hyderabad, India. J Int Lepr. 1993; 61: 8-15.
- **4.** Becx-Bleumink M, Berhe D. Occurrence of reactions, their diagnosis and management in leprosy patients treated with multidrug therapy: experience in the leprosy control program of the All Africa Leprosy and Rehabilitation Training Center (ALERT) in Ethiopia. Int J Lepr. 1992; 60: 173-184.
- **5.** Guillermo Biosca, Sonia Casallo and Rogelio Lopez-Velez. Methotrexate treatment for type 1 (reversal) leprosy reactions. Clin Infect Dis, 2007; 45 (1): e7-e9. Doi: 10.1086/518699.
- **6.** Frankel RI, Mita RT, Kim R and Dann FJ. Resolution of type 1 reaction in multibacillary Hensen's disease as a result of treatment with cyclosporine. Int J Lepr Other Mycobact Dis. 1992; 60: 8-12.
- 7. Marlowe SN, Hawksworth RA, Butlin CR, Nicholls PG and Loockwood DN. Clinical outcomes in a randomized controlled study comparing azathioprine and prednisolone versus prednisolone alone in the treatment of severe leprosy type 1 reactions in Nepal.Trans R Soc Trop Med Hyg. 2004; 98: 602-609.

- **8.** Gilles Safa, Laure Darrieux, Alain Coic, Laurent Tisseau. Type 1 leprosy reversal reaction treated with topical tacrolimus along with systemic corticosteroids. Indian J Med Sci, 2009; 63 (8): 359-362.
- **9.** Rose P, Waters MFR. Reversal reactions in leprosy and their management. Lepr Rev. 1991; 62: 113-121.
- **10.** Roche PW, LeMaster J, Butlin CR. Risk factors for type 1 reactions in leprosy. Int J Lepr, 1997; 65: 450-455.
- **11.** Swierkot J, Szechinski J. Methotrexate in rheumatoid arthritis. Pharmacol Rep, 2006; 58: 473-492.
- **12.** Ochoa MT, Stenger S, Sieling PA et al. T-cell release of granulysin contributes to host defense in leprosy. Nat Med. 2001; 7: 174-179.
- **13.** Cooper RL, Mueller C, Sinchaisri T-A et al. Analysis of naturally occurring delayed type hypersensitivity reactions in leprosy by in situ hybridization. J Exp Immunol. 1989; 169: 1565-1581.
- **14.** Sullivan L, Sano S, Pirmez C et at. Expression of adhesion molecules in leprosy lesions. Infect Immun. 1991; 59: 4154-4160.
- **15.** Gupta AK, Adamiak A, Chow M. Tacrolimus: A review of its use for the management of dermatoses. J Eur Acad Dermatol Venereol. 2002; 16: 100-114.
- **16.** Naafs B. Treatment of reactions and nerve damage. Int J Lepr, 1996; 64: S21-28.