

CASE REPORT

Therapeutic effect of *Mercurius solubilis* on immune status of a borderline leprosy case

Dhruba Chakraborty, Amit Kumar Dinda¹, Utpal Sengupta, Pradeep Das²,
Tuhin Chakraborty³, Jogneshwar Sengupta

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ABSTRACT

A Borderline Lepromatous (BL) leprosy case was treated with *Mercurius solubilis*, a homoeopathic medicine for two years. The clinical, immunological and histological assessment of the patient before and after treatment was recorded. The patient showed appreciable improvement in clinical signs and symptoms. Lesions on the skin almost disappeared; no swelling of hand and feet was noted along with disappearance of infiltration on eye brows. Nodular lesions on both the ear lobes diminished remarkably. Regain of sensation to touch, pain and pressure were noted and their test responses were normal. Slit skin smears were negative from all sites with 0 Bacteriological Index [BI] which was positive for acid fast bacilli [AFB] with an average of 4+ BI before treatment. Histologic study revealed absence of granuloma in dermis except the presence of occasional clusters of lymphocytes. Lepromin reaction which was negative before treatment was positive with 14 mm after 2 years of treatment. Estimation of different cytokines after completion of treatment showed appreciable changes with remarkable reduction in the levels of proinflammatory cytokines (IFN and TNF).

Keywords: Bacterial index, Cytokines, Leprosy, *Mercurius solubilis*

Institute of Health Studies and Rehabilitation, Durgapur, West Bengal, ¹Department of Pathology, All India Institute of Medical Sciences, New Delhi, ²Rajendra Memorial Institute of Medical Sciences, Patna, Bihar, ³Specialist, Diagnostic Pathology, Regional Disease Diagnostic Laboratory (ER) IAH and VB, Government of West Bengal, Kolkata, West Bengal, India

Address for correspondence:

Dr. Dhruba Chakraborty, Institute of Health Studies and Rehabilitation, (Society for Welfare of the Handicapped Persons), 27 Tagore Avenue, Durgapur - 713 204, West Bengal, India.
E-mail: ihsrindia@gmail.com

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INTRODUCTION

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* (*M. leprae*) affecting the peripheral nerves leading to impairment of their motor, sensory or autonomic function.^[1,2] The disease is characterized by a spectrum of clinical manifestations determined by the host immune response to *M. leprae*.^[3] While at the Lepromatous (LL) pole, the hosts lack effective Cell-Mediated Immunity (CMI) to *M. leprae* allowing bacilli for unlimited proliferation, at the Tuberculoid (TT) pole, the hosts exhibit a strong CMI to *M. leprae* leading to elimination of mycobacteria. Borderline leprosy patients who lie between the tuberculoid and lepromatous poles are

immunologically unstable. At least 30% of borderline patients experience episodes of up-regulation of *M. leprae* specific CMI with acute inflammation of existing skin lesions and nerves, and is termed as Type 1 reaction (T1R) or reversal reaction.^[4] These episodes are often recurrent with increased CMI to *M. leprae* resulting in the elimination of bacilli leading to immunological upgradation of the patient towards a more tuberculoid type of disease. Most of the time, T1R is accompanied by local tissue damage, acute inflammation of pre-existing skin lesions and acute neuritis.^[5] The neuritis may often become rapid and severe leading to permanent nerve damage. World Health Organization (WHO) has recommended Multi Drug Therapy (MDT) regimen with combination of rifampicin, clofazimine

and dapsone for treatment of leprosy. If a reversal reaction is found to occur in the course of disease progression in borderline forms (Borderline Tuberculoid, BT; Borderline, BB; and Borderline Lepromatous, BL), steroid (prednisolone) is the only drug of choice along with MDT. Prednisolone, known to suppress CMI and inflammatory processes, leads to reduction in compression around the affected nerves, inhibiting scar formation in the nerve and thus helps in the recovery of nerve functions in T1R reaction. Thus, steroids and dapsone used for treatment of leprosy have no potential to up-regulate, rather these have the role to play in down-regulation of the immune status of the host.^[6] Levels of TNF- α and IFN- γ are significantly raised in paucibacillary cases, whereas IL-10 is found to be increased in multibacillary cases. In multibacillary cases, levels of IL-10 were found to decrease after one year of MDT. Thus, serum cytokine estimation may have a significant role in classifying various forms of leprosy and can be used to monitor therapy.^[7,8]

In this communication, a case of BL leprosy treated with *Mercurius solubilis* in 200 potency, with detailed follow up observations recorded after a period of two years has been presented.

CASE REPORT

A male patient of 56 years reported to the OPD of the Institute with multiple hypoaesthetic, hypopigmented macular lesions on the face [Figure 1a and b] and on other parts of the body.

Nodular type of lesions on the whole body and both the ear lobes were present. Swelling of both hands and feet with infiltration in eye brows was also noted along with complaint of pain in the nasal septum. As a whole, the signs and symptoms were expressed in the form of bilateral symmetrical presentation. Both ulnar nerves as well as peroneal and tibial nerves were thickened and tender.

On the day of registration, slit skin smears taken from both the ear lobes and both the hands and legs were positive for AFB with an average BI of 4+. Skin biopsies were taken from the edge of lesions before the onset and at the end of the treatment. The skin biopsies were fixed in 10% buffered formal-saline solution and processed for paraffin sectioning at 5/ μ thickness following standard techniques and stained with routine haematoxylin and eosin as well as

stained for AFB. Lepromin testing was carried out with standardized Dharmendra antigen which evokes both early (48 to 72 hours) and late (3 to 4 weeks) skin reaction.^[9] Venous blood sample (5 ml) was taken for estimation of interleukins (IL; IL-2, IL-4, IL-10) and other pro-inflammatory cytokines like Interferon-gamma (IFN- γ) and Tumour Necrosis Factor-alpha (TNF- α) employing standard enzyme-linked immunosorbent assay (ELISA) Kits.

The sensory nerve function testing of the palms of the hands and soles of the feet was carried out using ball-point pen as described by Jean Watson at twelve standard points on each palm and on eleven points on the soles.^[10] On the palm, five points were taken as supplied by the ulnar nerve and seven for the median nerve.

Touch sensation was tested using a standard set of coloured Semmes-Weinstein monofilaments. The monofilaments used were 200mg, 2g, 4g, 10g and 300g. Normal reference values were 200mg for hand and 10g for foot. The sensory test carried out on hands and feet showed complete loss of sensation to touch, pressure and pain.

Histopathological findings before treatment revealed normal epidermis. Dermis showed involvement of nerve bundles with perineuritis, endoneuritis and formation of granulomatous lesions in the nerves with foam cells. Multiple granulomas with foam cells were noted in the dermis. These features were suggestive of BL type of leprosy [Figure 2a]. The stain for AFB was positive.

Before treatment, lepromin testing showed negative reaction [Figure 3a]. On the basis of clinical signs and histopathology, the case was confirmed as a case of BL leprosy.

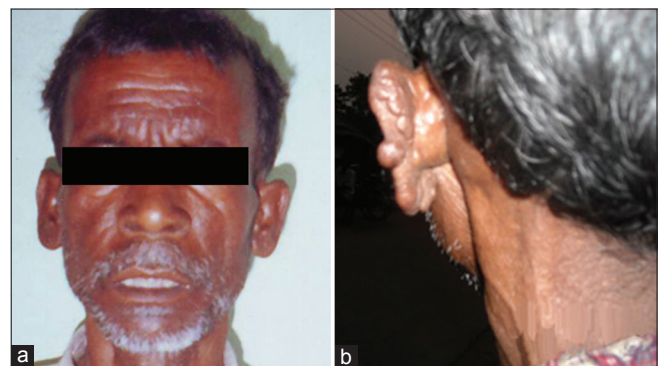


Figure 1: (a) Before treatment infiltration present on both eye brows and macular patch present on face; (b) Active nodules present on ear lobe

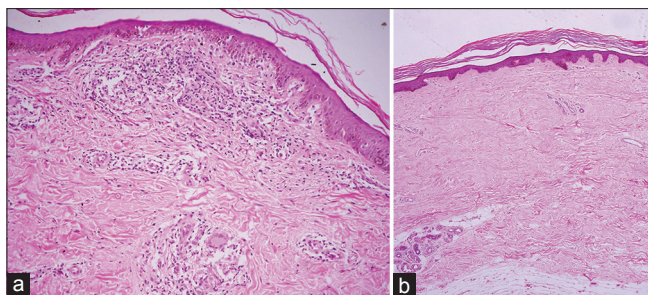


Figure 2: (a) Photomicrograph of the pretreatment skin biopsy showing normal epidermis, infiltration of dermis with histiocytes and lymphocytes. There is nerve involvement with perineuritis, endoneuritis and formation of granulomatous lesions in the nerve cell with foam cells. x400; (b) Photomicrograph of the post treatment skin biopsy showing unremarkable epidermis. There are few aggregates of lymphocytes in the dermis. No granuloma or foam cell is identified. x400



Figure 3: (a) Pretreatment lepromin (0mm) reaction after 3 weeks

The patient was subjected to detailed case taking which revealed,

A. Particular symptoms

Head - Headache of throbbing nature which aggravated in the heat, when exposed to sun and in a closed room

Eye - Low vision at night

Nose - Pain at the root of the nose with history of nasal bleeding

Mouth and Tongue - Moist, flabby, tendency of ulcer formation, profuse salivation, saliva was viscid and foetid, gums were painful with bleeding and with pain at night

Face - Swelling of face with reddish lesions on face and forehead

Stomach - Occasional colicky pain worse at night

Abdomen - Occasional pain in lower abdomen in summer with history of dysentery

Stool - Occasional dysenteric stool with occasional bleeding per rectum; slimy stool with mucus

Urine - Occasional burning during micturition.

Extremities (upper): Anaesthetic, hypopigmented macular patch present on hands, neuralgic pain in both ulnar nerves, swelling of both the hands with stiffness.

Extremities (lower): Swelling of both the feet with tendency of ulcer formation, neuralgic pain greater at night. Thickness of tibial and peroneal nerves was present.

Skin: Presence of anaesthesia in lesional areas. In general, skin was moist but dry in lesional areas without any sweating. Tendency of ulcer formation and little injury led to suppuration.

Nervous system: Both ulnar nerves as well as peroneal and tibial nerves were thickened and painful. Pain aggravated at night and during cold season, ameliorated by rest and pressure. Bones of hand and feet were very sensitive and painful and mild pressure led to pain.

B. General symptoms

Mental symptoms: Melancholy, hopelessness, lack of confidence, depression, anxiety at night. Anxious and fearful. Restlessness and weak memory. When asked a question, he was unable to reply properly.

Sleep - Complained of disturbed sleep, sleepless night.

Dreams: Bad and violent dreams at night, especially dreams of dead persons and murders.

Mouth: Moist mouth and salivation

Thirst: Profuse

Tongue: Thick, moist coating, flabby, teeth-indented. Ulceration of tongue

Sweat: Profuse sweating day and night without relief. The complaint increased when exposed to sun in summer. Offensive sweat caused discomfort < from least exertion

Appetite: Normal.

Liking: Nothing specific.

Response to heat and cold - High sensitivity to extreme heat and cold, all complaints aggravated in summer as well as in winter, preferred moderate climate and temperature, felt better under shade

General Agg. - All the complaints aggravated at night

Physical condition- Weak, lean, thin and emaciated.

The past history of the patient did not reveal any sexual illness or any drug or mercurial poisoning whereas skin disease with suppression was reported by the patient. It was also revealed further that the patient had close contact with other leprosy patients earlier.

The family history revealed that both the parents died long ago and father was suffering from leprosy. Four other family members were also found to be affected with leprosy.

Selection of Medicine

After thorough clinical examination and detailed case study, the selection of medicine was done according to William Boericke^[11] and Kent's repertory.^[12]

Based on Accumulated Similar Symptom (ASS), the selection of medicine, *Merc. sol.* in 200 potency was made and one dose weekly was given for two years as described by Chakraborty et al.^[13]

Post Treatment Evaluation

Clinical examination after six months (17.09.2008) revealed appreciable improvement in clinical signs and symptoms. Patches were found to have disappeared on both the extremities (upper and lower) and sensations were regained. The most remarkable sign was the disappearance of swelling of lower extremities and infiltration on eye brows [Figure 4a].

No signs of psychological depression was recorded in the appearance with complete absence of patches on the face. No swelling was recorded. The only particular symptom, low vision of the eye was reported by the patient.

Nodular lesions on both the ear lobes diminished remarkably [Figure 4b]. After two years on 23.03.2010,

clinical sign showed regain of sensation to touch, pain and pressure and their test responses were normal.

Pathological and Immunological Investigations

After one year of treatment, slit skin smears were positive for AFB and BI was 1.8, and after two years of treatment, slit skin smears were negative from all sites with 0 BI. After one year of treatment (18.03.2009), the numbers and sizes of granulomas reduced with lymphocytic infiltration. After two years of treatment (23.03.2010), no granuloma was noted in the dermis except for the presence of occasional clusters of lymphocytes [Figure 2b]. The stain for AFB was negative.

Estimation of different cytokines (IL2, IL4, IL10, IFN γ and TNF α) showed appreciable changes in post treated cases [Table 1].

At the end of two years, the only particular symptom, low vision of the eye was reported by the patient. No signs of psychological depression were recorded with complete absence of patches on the face. No swelling was noticed.

General symptoms as recorded:

- Mental symptoms: Very confident. No anxiety and depression was reported
- Thirst: Normal
- Sweat: Normal
- Appetite: Normal
- Liking and Aversion: No significant change
- Response to heat and cold: Normal response was noted
- Sleep and Dreams: No disturbed sleep was reported
- Physical condition: Good health.

During the period under treatment no acute illness was reported by the patient.

After completion of two years, the patient was subjected to follow up for another six months which did not reveal any significant change in clinical manifestation.

DISCUSSION

This case study reports successful treatment of a case of BL leprosy with two years of homoeopathic treatment. All lesions disappeared without any episode of reaction. The slit skin smears were negative with 0 BI. The nerve function impairment of hands and feet got reversed with complete regain of



Figure 4: (a) After treatment no infiltration and macular patch seen on face. Appearance of face looks normal; (b) After treatment ear lobe looks inactive, nodules are very small and dry

Table 1: Criteria for selection of medicine

Symptoms	Indicative medicine according to repertory	Remedies	Reference with page no
General symptoms			
Mental restlessness at night	Ars., Caust., Hyos., Kali-ar., Kreos., Lyc., Merc., Puls., Rhus-t., Sulph.	Merc.	(KR-73)
Anxiety at night	Ars., Merc., Puls.	Merc.	KR-5
Anxiety with fear	Anac., Ars., Caust., Ign., Merc., Sec.	Merc.	KR-6
Sleep-sleepless night	Ars., Cocc., Kali.c., Lyc., Merc., Bry., Coff., Con., Puls., Rhus-t., Sulph.	Merc.	(KR-1251)
Sleepless before midnight	Ars., Coff., Con., Kali.c., Lyc., Merc., Sulph.		(KR-1252)
Dreams of dead bodies	Anac., Calc., Merc., Thuja.	Merc.	(KR-1237)
Mouth- Profuse thirst with moist mouth and salivation.	Merc., Nat.m, Rhus-t.	Merc.	(KR-418) (WB-433)
General Agg. - All the complaints aggravated at night, heat and cold	Helleb., Hyos., Lyco., Kali. s, Merc., Phos., Puls., Sep., Syph.	Merc.	(WB-969)
Particular symptoms			
Skin- unhealthy skin, moist, every little injury suppurates	Graph., Hepar., Merc., Petr., Sil., Sulph.	Merc.	WB327,916
Skin -Perspiration	Hep., Merc., Samb.	Merc	(KR-1300)
Profuse sweating day and night without relief			
Ulceration of Tongue and mouth with salivation	Ars., Arum., Hep., Merc., Nit ac., Mur ac.	Merc.	WB 752
Disease symptoms			
Skin anaesthesia	Alum, Anac, Arg-n, Camph, Merc, Nux-v, OInd, Petr, Rhus-t.	Merc.	KR1303
Extremities-pain at night	Cham; Merc; Plb.	Merc.	KR-1044

sensation. The efficacy of the single homoeopathic medicine, *Mercurius solubilis* in this case is considered remarkable because of its ability to influence host immune response.

The immune system of the host gets adversely affected in leprosy posing major therapeutic challenge to the researchers. After completion of WHO recommended MDT for 6 months in paucibacillary leprosy and one year in multibacillary leprosy, clinically, most of the patients do not feel themselves as cured because of the existence of their lesions and loss of sensation even after completion of MDT. Even the immune status of the lepromatous type of leprosy remains unaltered. Furthermore, presence of viable *M. leprae* has been convincingly detected from such lesions after completion of MDT.^[14] Out of the three drugs included in MDT, dapsone and clofazimine are known bacteriostatic drugs, probably due to which the affected person does not get rid of the residual effects of the disease, and dapsone has also been found to lower the CMI status of the patients.^[15,16] However, rifampicin is known to kill 99.9% of *M. leprae* within a month's time.^[17] In spite of this, relapses are not uncommon among the treated cases.

Therefore, it may be concluded that the present homoeopathic treatment with *Merc. sol.* in leprosy

cases where neuritis has already developed, may save the patients from the grave consequences of nerve function impairment and development of deformity. The medicine in this case was found to be effective in reducing the load of *M. leprae* as was evident from the fall of BI from 4+ to 0 within two years. Whether this remarkable reduction in BI is due to the direct effect of the drug on *M. leprae* or due to the immunomodulation of the host, remains to be worked out. The lepromin response recorded after two years indicated that this medicine has up-regulated the immune status of the host which is not observed with MDT. This treatment specifically brought down the levels of proinflammatory cytokines (IFN γ and TNF α) and increased the levels of suppressive cytokine IL-10 and IL-4. IL-10 is known to down-regulate IFN γ and TNF α .^[18] IL-4 down-regulation appears to influence the B cells for reduced production of antibodies.^[19] The difference in cytokine levels of blood before and after treatment is also suggestive of some effect of the drug in modulating the mechanism on the host immune system, which needs to be studied. Studies revealed that treatment with multi drug has been found to cause a reduction in serum cytokines correlated with a reduction in the bacterial burden^[7,8] and the medicine used in

this case is equally effective in bringing down serum cytokines and bacterial burden.

CONCLUSION

MDT is used as an important instrument to reduce the burden of active cases of leprosy. However, affected people remain at risk of neuropathy resulting from immunological reactions caused by *M. leprae* antigens during and even after successful anti-leprosy treatment. In National Leprosy Eradication Programme (NLEP), there is no effective treatment suggested for prevention of disability caused by neuropathy, except the use of prednisolone for nerve function impairments that takes place during the period of MDT treatment.

Therefore, at this crucial juncture of leprosy elimination, this alternative therapeutic approach may be a justifiable proposition and would be of great help to treat the leprosy patients with nerve function impairments thus fulfilling the ultimate goal of WHO.^[20]

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मरक्यूरियस सोल्यूबिलिस द्वारा उपचारित सीमारेखीय लेप्रोमेटस लेप्रोसी केस

एक सीमारेखीय लेप्रोमेटस लेप्रोसी केस का उपचार, दो वर्षों तक मरक्यूरियस सोल्यूबिलिस नामक होम्योपैथिक दवा द्वारा किया गया। उपचार के पूर्व और पश्चात्, मरीज के चिकित्सीय, प्रतिरक्षणीय और ऊतक रोगी विज्ञानिक समीक्षा को दर्ज किया गया है। चिकित्सीय चिन्हों और रोग लक्षणों में मरीज में काफी सुधार देखा गया। त्वचा पर घाव और चोट के निशान लगभग गायब हो गए थे। भौहों के अंतःसरण के गायब होने के साथ-साथ हाथ और पैरों की सूजन भी चली गयी थी। दोनों कर्णपालियों पर घाव के निशान बहुत कम हो गए थे। स्पर्श, दर्द और दबाव के प्रति संवेदना के वापिस आने को भी देखा गया और जांच के परिणाम सामान्य थे। चिरी हुई खाल के निशान शून्य बैक्टीरियल इंडेक्स सहित सभी ओर से गायब थे जो चिकित्सा से पूर्व 4 जीवाणु सूचकांक सहित एसिड फास्ट बेसिली एएफबी, के लिए सकारात्मक थे। ऊतक रोगीय अध्ययन के अनुसार लिम्फोसाइट के गुच्छों की यदा-कदा उपस्थिति के अतिरिक्त त्वचा में ग्रेनुलोमा अनुपस्थित था। लेप्रोमिन अभिक्रिया, जो चिकित्सा पूर्व अनुपस्थित थी, चिकित्सा के दो वर्ष उपरान्त 14 मिमी के साथ उपस्थित थी। चिकित्सा के पश्चात् प्रोइनफ्लेमेट्री साइटोकिंस (आईएफएन और टीएनएफ) के स्तरों में आश्चर्यजनक कमी के साथ विभिन्न साइटोकिंस के अनुमान में काफी परिवर्तन दिखाई दिए।

