# Successful treatment of severe recalcitrant erythema nodosum leprosum with infliximab

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## Abstract

29 year old female presented with lepromatous leprosy with erythema nodosum leprosum (ENL) in January 2017 (bacillary index-5+, morphological index-20%) to National Hospital of Sri Lanka. Multidrug treatment (rifampicin, clofazimine and dapsone) was started but dapsone was replaced by ofloxacin due to anaemia. She developed seven episodes of severe recalcitrant ENL with five hospital admissions within one year despite high dose prednisolone, clofazimine, azathioprine and pentoxifylline.

Weekly rifampicin, minocycline and moxifloxacin were added in September 2017 to reduce the burden of high antigenaemia. She underwent one cycle of plasmapheresis and intravenous dexamethasone pulse. Despite all, her ENL reactions got worse while having overwhelming drug side effects.

Infliximab was started in March 2018 and five doses were given with successful outcome. Prednisolone, clofazimine and azathioprine were tailed off and discontinued. Most importantly she did not experience any ENL reactions for last 2 years after starting infliximab highlighting its success.

## Case report

A 29 year old female patient presented to National Hospital of Sri Lanka in January 2017 with fever and erythematous tender skin nodules on upper limbs, lower limbs and trunk. She did not have any hypopigmented patches, thickened nerves or sensory impairment. She was diagnosed with lepromatous leprosy with erythema nodosum leprosum (ENL). This was supported by skin biopsy and slit skin smear which showed a bacillary index of 5+ and morphological index of 20%.

She was started on multidrug treatment (MDT) in February 2017 consisting of monthly rifampicin 600 mg, monthly clofazimine 300 mg, daily dapsone 100 mg and daily clofazimine 50 mg along with prednisolone 40 mg /day. However, her treatment had to be modified by replacing dapsone with ofloxacin 400 mg daily due to refractory anaemia.

Over the next year she developed seven relapses of ENL including five hospital admissions.

She experienced two relapses in May 2017 initially while on prednisolone 10 mg/day and then on 30 mg/day requiring step back to 40 mg/day.

Four months later during her third relapse while on prednisolone 20 mg/day required a dose escalation of prednisolone to 50 mg/day and clofazimine to 100 mg /day with addition of pentoxifylline 400 mg three times a day.

Clofazimine was gradually increased to 300 mg/day during her fourth and fifth relapses.

Continued antigenaemia was suspected due to recurrent relapses and her high initial morphological index. As a counteracting measure weekly rifampicin 600 mg, minocycline 100 mg and moxifloxacin 400 mg were started.

Sixth relapse in November 2019 was severe with fever, vomiting and ENL nodules during which prednisolone was increased to 60 mg/day along with one cycle of plasmapheresis and one cycle of intravenous dexamethasone pulse (100 mg/day for 3 days). Azathioprine was started and gradually increased to 150 mg /day.

In spite of being on all these medications she went into a seventh relapse in February 2018.

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Additionally, overwhelming drug adverse effects were experienced by the patient including prednisolone induced osteopenia, diabetes mellitus and cushinoid features and clofazimine induced skin pigmentation without an improvement in ENL reactions.

She refused thalidomide being a female in reproductive age.

Infliximab was considered and first dose (5 mg/kg =300 mg) was administered in March 2018 followed by four more injections in 2, 6, 14 and 22 weeks.

Weekly rifampicin, minocycline and moxifloxacin were stopped after one year and MDT treatment was stopped in December 2018 after completing 24 cards. Prednisolone and high dose clofazimine were tailed off and discontinued in September and December 2018 respectively.

Azathioprine was also gradually tailed off and omitted in February 2020.

Most importantly after starting infliximab in March 2018 she did not experience any ENL reactions highlighting the success of the infliximab treatment.

## Discussion

ENL is considered an immune complex-mediated phenomenon with an accompanying vasculitis[1-3]. However, high levels of TNF-α and interleukin-6 are consistently found in patients with more severe disease, which suggests that a cell-mediated immune response also plays a role[4]. TNF-α production by peripheral-blood mononuclear cells after stimulation with cell-wall constituents of *M. leprae* was highest among those with ENL, as compared with patients who did not have a reaction[5].

The consistent over-expression of TNF-α in patients with severe ENL provided the rationale for the use of TNF-α inhibitory agents such as thalidomide and TNF-α inhibitory biologics.

Thalidomide improves the clinical condition of patients with ENL by inhibiting the production of TNF-α[6].

Ramien *et al*. in 2011 and Santos *et al*. in 2017 used etanercept and in 2006 Faber *et al*. used infliximab which are TNF-α inhibitors in patients with severe ENL reactions with successful outcomes.

Thus, TNF-α blockade using biologics are used as a therapeutic alternative in severe ENL not responding to standard therapies.

The severe nature of the disease and adverse effects of therapy experienced by this patient warranted a trial of TNF-α inhibitors.

For the first time in Sri Lanka a TNF-α inhibitor; infliximab was used to treat ENL while keeping a close watch on infections like tuberculosis because of the high risk of the reactivation of latent tuberculosis when using anti-TNF drugs (greater with infliximab when compared to etanercept).

Impressive improvement of this patient is a good example for successful use of TNF-α inhibitors for recalcitrant ENL reactions.

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