Case Letter

The perils of prescribing second line anti-leprosy therapy for erythema nodosum leprosum ignoring resistance testing data

Dear Editor,

Leprosy is a chronic granulomatous disease caused by *Mycobacterium leprae and Mycobacterium lepromatosis*. The disease process can be complicated by reactional episodes (type 1 or type 2 reactions [T1R and T2R]).[1] Erythema nodosum leprosum (ENL)/T2R is an immune-mediated inflammatory condition which occurs in 50% of lepromatous leprosy and in 25% of borderline lepromatous cases.[1] Over the past few years, there has been a notable rise in resistance, observed in relapsed cases and in certain leprosy reactions (recurrent and late ENL, downgrading T1R).[2,3]

While studies have shown a rising trend of resistance across leprosy endemic nations, the use of second line therapy is only warranted for rifampicin resistance,[2] even though there is evidence for an increasing trend of ofloxacin resistance which may hamper the effectiveness of this drug.[4] We have encountered cases of leprosy where second-line anti-leprosy therapy (ALT) is prescribed in a bid to control ENL, without resistance testing, which is bereft of scientific logic. Herein, we report a case of lepromatous leprosy with T2R who was treated with conventional multi-bacillary multidrug therapy (MB MDT), oral steroids and a monthly single dose of ofloxacin and minocycline from a leprosy referral centre.

A 19-year-old man, diagnosed with a case of lepromatous leprosy, was administered MB MDT, one month after which he developed painful evanescent nodules associated with fever and bilateral claw hand. He was treated with oral prednisolone 40 mg, but due to inadequate control of reaction after one month of therapy, he was initiated on a monthly dose regimen of minocycline 100 mg and moxifloxacin 400 mg, in spite of drug resistance (DRS) testing indicating sensitivity to all drugs. This was continued for seven months with inadequate control of T2R and was referred to our centre with cutaneous and systemic features of ENL. On examination, he had multiple subcutaneous tender nodules on the face and extremities, bilateral inguinal lymphadenopathy, enlarged tender ulnar and supraorbital nerves. Erythema nodosum leprosum international study (ENLIST) score was 15 (severe ENL). His routine lab investigations were normal and no trigger factors (infective/non-infective) were noted. We stopped minocycline and moxifloxacin, continued conventional MB MDT, and initiated thalidomide 50 mg twice daily with oral prednisolone 40 mg/day, which resulted in marked improvement (ENLIST score = 2) within 14 days and the patient is controlled on this regimen with a plan to taper steroids.

Drug resistance in leprosy can be primary, due to infection with a resistant strain of *M. leprae* or secondary due to dapsone monotherapy, lack of adherence to treatment or indiscriminate use of antibiotics.[2,5] While the treatment regimen for drug resistant leprosy has been delineated in Table 1,[2] there is an increasing trend of clinicians prescribing second-line ALT in the mistaken belief that this therapy would control T2R which is not borne out by case-control studies.[3] A recent study revealed that second-line ALT administered to resistant cases in leprosy reactions could control only three of seven patients.[3] This is because the control of reactions is dependent on the host adaptive immune response (Th1/Th17/Treg cells) which is not markedly affected by ALT. A recent study has shown that low-dose thalidomide can effectively control T2R; thus, this should precede any other intervention for T2R.[6] Thalidomide has a multipronged action in ENL by inhibiting tumour necrosis factor-alpha (TNF-α), neutrophil infiltration; increasing the levels of Treg cells, IL-2, IL-10 and suppressing IL-1β.[6] The misuse of second line ALT, without resistance testing, would accelerate the chances of resistance to these reserve drugs and is against the policy of antibiotic stewardship apart from predisposing the patients to adverse effects. Also, we have not found any definitive data that substantiates the beneficial effect of second line ALT on ENL, which is an

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Table 1: Treatment recommendation for drug resistant leprosy

Resistance type	Treatment	
	First six months	Next 18 months
Rifampicin resistance	Ofloxacin 400 mg* + minocycline 100 mg + clofazimine 50 mg	Ofloxacin 400 mg* or minocycline 100 mg + clofazimine 50 mg
	Ofloxacin 400 mg* + clarithromycin 500 mg + clofazimine 50 mg	Ofloxacin 400 mg* + clofazimine 50 mg
Rifampicin and ofloxacin resistance	Clarithromycin 500 mg + minocycline 100 mg + clofazimine	Clarithromycin 500 mg or minocycline 100 mg + clofazimine 50 mg
Dapsone resistance	Rifampicin 600mg once a month + clofazimine 50mg (some prefer to add either ofloxacin/minocycline/clarithromycin once a month)	

* Ofloxacin 400mg can be replaced by moxifloxacin 400mg or levofloxacin 500mg

interplay of Th1/Th17/Treg cells with the bacillary antigens which persist long after successful chemotherapy.[1] A more important aspect is the cost of therapy and the economic burden on patients. Notably, the leprosy programme does not provide second line ALT and this adds to the cost of therapy, which is an understated concern in India as leprosy afflicts the financially deprived population.[7]

Our case red flags the twin issues of unwarranted use of second line ALT for T2R without DRS testing and burdening the patients with expensive drugs not provided by the programme. We reiterate the option of low-dose thalidomide 50-100 mg until disease control[6] with the option of tapering of steroids in T2R, which has the twin benefits of low cost and effects rapid reduction of oral steroids and should precede the use of reserve drugs in leprosy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of AI-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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