Treatment of Recurrent Erythema Nodosum Leprosum with Infliximab

TO THE EDITOR: A 52-year-old woman with multibacillary (borderline lepromatous) leprosy, who had been treated intermittently with dapsone since 1965, presented to our department in 1996 with active skin lesions, a positive bacterial index (5+) on skin biopsy, and an elevated level of antibodies against *Mycobacterium leprae* specific to phenolic glycolipid I. She was treated with multidrug therapy (rifampin, dapsone, and clofazimine). One and a half years after treatment was started, disseminated painful erythematous nodules and plaques, or erythema nodosum leprosum, developed owing to an augmented immunologic response to mycobacterial antigens. These symptoms did not respond adequately to repeated courses of prednisolone (40 mg once daily), thalidomide (starting dose, 300 mg daily), and pentoxifylline (400 mg three times daily). It was not possible to discontinue the immunomodulating treatment because of the frequent reactivation of the erythema nodosum leprosum. Given the severity of the patient's symptoms despite the use of standard therapies, we considered alternative management strategies.

Various lines of evidence suggest that tumor necrosis factor α (TNF-α) may play an important role in the pathogenesis of erythema nodosum leprosum. Elevated levels have been found in patients with reactional leprosy, with the highest levels found in those with erythema nodosum leprosum.[1] Among patients with leprosy, TNF-α production by peripheral-blood mononuclear cells after stimulation with cell-wall constituents of *M. leprae* was highest among those with erythema nodosum leprosum, as compared with patients who did not have a reaction.[2] In another study, a spontaneous release of TNF-α by peripheral-blood mononuclear cells was found in patients with erythema nodosum leprosum, and this was enhanced after stimulation with *M. leprae*.[3] Thalidomide, which improves the clinical condition of these patients,[4] inhibits the production of TNF-α.[2,4] Therefore, treatment with infliximab to inhibit the production of TNF-α was considered in this patient.[5]

Her immunosuppressive medications were discontinued. One day later, painful red nodules appeared on her skin. On day 4, clinically significant symptoms associated with erythema nodosum leprosum (erythematous nodules confluent to plaques on the trunk and extremities, a thickened and tender ulnar nerve, and a tender axillary lymph node) were noted, and infliximab was given (5 mg per kilogram of body weight; total dose, 300 mg administered intravenously over a period of four hours), after premedication with 25 mg of intravenous prednisolone and 1000 mg of acetaminophen and 10 mg of cetirizine orally. The patient noticed improvement within hours after the treatment was started. The next day, the symptoms of erythema nodosum leprosum had greatly diminished. Infliximab infusions were repeated on weeks 2 and 6. No further treatment for erythema nodosum leprosum has been necessary. One year after the last infusion, the patient had no signs of erythema nodosum leprosum.

These data suggest that TNF-α contributes to the pathogenesis of erythema nodosum leprosum in humans and that TNF-α blockade may be considered as a therapeutic alternative in patients with severe erythema nodosum leprosum that has not responded to standard therapies. However, because TNF-α blockade carries an increased risk of *M. tuberculosis* and fungal infections, one needs to use infliximab in this setting with great care.

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