The utility of etanercept in chronic stable plaque psoriasis: Results from an open-label, prospective, single arm study

Sir,

The introduction of biologicals has greatly revolutionized the treatment options for psoriasis, with the advantages of good efficacy and a reasonable safety profile.

The recombinant tumor necrosis factor antagonist, etanercept is approved for use in India as monotherapy in adults and children (>6 years) with moderate to severe psoriasis. Extensive studies from around the world, in adults with moderate to severe plaque psoriasis, demonstrate its long-term benefits. However, Indian data is limited.

We conducted an open-label, non-randomized, single-arm, prospective, observational study in patients with chronic plaque-type psoriasis in order to observe the safety, efficacy and tolerability of subcutaneously injected etanercept (50 mg/week), at the Department of Dermatology, Government Stanley Medical College, Chennai. Data was collected between June 2012 and June 2013. The study was approved by the institutional ethics committee and informed consent was obtained from all patients.

A detailed medical history and physical examination findings were recorded at the initial visit. Twenty patients with chronic stable plaque type psoriasis satisfying the inclusion criteria [Table 1] were enrolled in this study. Baseline investigations were undertaken [Table 2].

Patients were hospitalized and administered weekly subcutaneous injections of etanercept 50 mg for 12 weeks and an additional 12-week safety follow-up was conducted. Assessment of the safety profile of etanercept was done using the National Cancer Institute's Common Toxicity Criteria, version 2.0, 1999.

Efficacy was assessed by monitoring the psoriasis area severity index score on a weekly basis throughout the duration of the study. Clinical improvement was graded as 'good' on achieving PASI 50 (50% or more reduction in psoriasis area severity index) and 'excellent' on achieving PASI 75 (75% or more reduction in psoriasis area severity index).

There were 10 men and 10 women with a mean age of 39.5 years and a mean duration of psoriasis of 9 years. The mean psoriasis area severity index score at baseline was 22.8. Eighteen patients had received prior systemic therapy or phototherapy.

Table 1: Inclusion and exclusion criteria for the enrolment of subjects in study

| Inclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|
| Male or female patient with stable chronic plaque psoriasis                       |
| Older than 18 years of age                                                        |
| PASI >10                                                                          |
| Adequate hematological (hemoglobin ≥10 g/dL, white blood cell count ≥3.5×10^9 cells/L, platelet count ≥125×10^9 cells/L), renal and hepatic (serum albumin >3.5 mg/dl, serum total bilirubin <1.5 mg/dl) functions |
| Patients willing to follow-up for the required duration                            |

| Exclusion criteria                                                                 |
|-----------------------------------------------------------------------------------|
| Pregnant or lactating women                                                        |
| Patients who received oral/parenteral treatment for psoriasis vulgaris during the 4 weeks before trial or topical treatment during the week before trial |
| Pustular, erythrodermic or active guttate psoriasis                                 |
| Active bacterial skin infections                                                   |
| Patient on immunosuppressants/patients with human immunodeficiency virus           |
| Active TB or history of TB                                                         |
| History of demyelinating neurological disease                                      |
| History of congestive heart failure                                                |
| History of liver diseases or renal disorders                                       |

TB: Tuberculosis, PASI: Psoriasis area severity index

Table 2: Baseline investigations

- Complete hemogram (HB, TC, DC, ESR)
- ENT and dental opinion to rule out focal sepsis
- Mantoux test
- Chest X-ray
- ECG
- Liver function test (SGOT, SGPT, serum alkaline phosphatase, serum bilirubin)
- Fasting blood glucose
- Serum creatinine
- Serum calcium, uric acid
- Human immunodeficiency virus ELISA, VDRL
- Ultrasound - abdomen and pelvis
- Skin biopsy

Table: Venereal disease research laboratory
At week 4, only 1 (5%) patient achieved PASI 25 (25% reduction in psoriasis area severity index) while the rest had less than 25% reduction in psoriasis area severity index. At week 8, 8 (40%) patients achieved PASI 50 (50% reduction in psoriasis area severity index), 9 (45%) patients achieved PASI 25 and 3 (15%) had patients less than 25% reduction.

At week 12, 13 (65%) patients had achieved PASI 75 (primary endpoint), 5 (25%) patient had achieved PASI 50, 1 (5%) patient had achieved PASI 25 and 1 patient had less than 25% reduction in psoriasis area severity index. Similarly, the mean psoriasis area severity index score was observed to decrease from 22.8 at baseline to 20.8 at the end of week 4, 12.8 at week 8 and 7.2 (68.4%) at the end of week 12 [Figures 1 and 2a-c].

No hematological, cutaneous or systemic adverse events were observed in this study. No specific adverse events leading to withdrawal occurred during this study after 12 weeks. In general, etanercept was well tolerated.

The mean duration of remission was 3 months (standard deviation = 2.35).

Our results correlated with the study conducted by Sterry et al. who reported that 62% of patients treated with injection etanercept 50 mg/week achieved PASI 75 (75% reduction in psoriasis area severity index) at week 12.[1] On the other hand, studies conducted by Leonardi et al. and Papp et al. showed that only around one-third of the patients receiving injection etanercept 50 mg/week achieved PASI 75 at week 12.[2,3] The mean time to relapse was 84 days which concurred with our results.[3] Another study by Papp et al. showed that etanercept was clinically beneficial to patients with chronic plaque psoriasis, with no apparent decrease in efficacy after dose reduction from 50 to 25 mg twice weekly.[4]

Even in the era of biologics, methotrexate remains the first-line drug in the treatment of moderate to severe psoriasis and psoriatic arthritis. Unfortunately, its dose-dependent risk of hepatotoxicity remains high.

Mazzotta et al. observed that patients who have not taken any biological therapy earlier have a better response to treatment with etanercept.[5] None of our patients had been exposed to biologics previously. A study conducted in Italy, by calculating quality adjusted life years, inferred that in patients with psoriasis area severity index >20, etanercept is a cost-effective treatment.

Numerous published psoriasis trials have shown that etanercept is well tolerated. In placebo-controlled trials, adverse events have been typically reported to be mild to moderate in intensity, and occurring with similar frequency in both groups. Psoriasis clinical trials have revealed no evidence of increased risk of
opportunistic infections, tuberculosis, or skin cancers during up to 60 weeks of etanercept treatment (Gottlieb et al., unpublished data, 2004).

The results from this study indicate that etanercept provided therapeutic improvement and was well tolerated in the treatment of stable chronic plaque psoriasis in our patients. Given the scarcity of available data, these findings from a small case series in an Indian tertiary level teaching hospital may be of value.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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REFERENCES
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Tuberculosis with atypical manifestations involving multiple sites of the oral cavity: A case study

Sir,

Oral tuberculosis is rarely observed; only 0.05–1.5% of tuberculosis cases present with oral manifestations.[1] Oral tuberculous lesions are characterized by atypical or persistent ulcers and are often misdiagnosed as malignancy, deep mycotic infection, syphilis and traumatic or aphthous ulcers.[2,3] Ulcers often appear as single lesions.[2]

A 52-year-old man with multiple oral ulcers visited our clinic in November 2014. While the initial lesion had developed 8 months earlier, there had been rapid progression of disease with multiple new ulcers over the previous 2 months. At presentation, he had a 2.5 cm × 1 cm sized irregular ulcer involving the buccal gingiva of the upper right second premolar and first and second molars with mild tenderness of the underlying bony surface at the ulcer base. The root of the upper right first molar was exposed with resorption of the underlying alveolar bone [Figure 1a]. Soft tissue defects, 2 and 5 mm in diameter, and extending as deep as the underlying bone were noted on the labial gingiva of the upper left lateral incisor and the palatal mucosa adjoining the upper left first molar, respectively [Figure 1b and 1c]. In addition, a 13-mm shallow erosion was noticed on the right hard palate [Figure 1d]. Shallow ulcers were present on the buccal gingival margin of the mandible adjacent to the lower right first and second molars [Figure 1e].

Eight months earlier, our patient's initial single gingival erosion located posteriorly in the right maxilla was diagnosed as osteoradionecrosis at a local hospital. Oral amoxicillin administered for 14 days was ineffective. Later, when multiple oral lesions appeared, there was difficulty in eating and speaking owing to pain. The patient also experienced considerable weight loss (approximately 10 kg), recurrent fever, as well as a decline in overall health. Medical histories included chemoradiotherapy for nasopharyngeal carcinoma 10 years previously and cure of chest cutaneous tuberculosis 8 years previously with standard treatment. In addition, he denied any family history of tuberculosis.

One month back, the patient had undergone a routine blood test that showed a normal complete blood count, blood glucose levels and liver and kidney functions. Laboratory investigations for human immunodeficiency virus and syphilis were negative; the tuberculosis-antibody assay was positive, purified protein derivative tuberculin skin test was negative and tuberculosis-interferon gamma release assay was positive (125.47; reference range: 0–14).

Computed tomography revealed right-sided partial maxillary alveolar resorption and swelling of the surrounding soft tissue. Chest radiography showed miliary nodular opacities in both the lungs. A biopsy taken from the maxillary right first molar vestibular groove revealed granulomatous inflammation suggesting the possibility of tuberculosis. Several acid-fast bacilli were identified on Ziehl–Nielsen staining [Figure 2]. DNA fragments of Mycobacterium tuberculosis were found on quantitative real-time polymerase chain reaction.