BRIEF REPORT

Partial Response to Etanercept in the Treatment of Hidradenitis Suppurativa

C. López-Martín,* B. Tortajada Goitia, V. Faus Felipe, A. Gómez Sánchez, F. Ferrer Soler, M. Garrido Siles

Servicio de Farmacia, Agencia Sanitaria Pública Hospital Costa del Sol, Marbella, Spain

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Etanercept; Hidradenitis suppurativa; Indication not included in the summary of product characteristics; Biological tumour necrosis factor (TNF) inhibitors

Abstract
Objective: To review the treatment of hidradenitis suppurativa and the role of etanercept in terms of efficacy and safety.
Methods: Descriptive, cross-sectional and retrospective study. Patients diagnosed with hidradenitis suppurativa who were treated with etanercept (indication not on its Summary of Product Characteristics) until June 2009 were included in the study. The study variables were: age, sex, treatments before and after etanercept, response, adverse effects, duration and reason for stopping treatment.
Results: Antibiotics, contraceptives, corticosteroids, isotretinoin or oral sulfones were used as the first-line treatment. When patients no longer responded to these treatments, the use of etanercept was requested. It was well tolerated but it only led to an initial improvement. It was, therefore, suspended. The options employed included the following: corticosteroids, antibiotics, isotretinoin, contraceptives, immunosuppressive drugs and antiandrogens. Patients who were treated with adalimumab and infliximab as an alternative treatment found that their lesions flared up. Surgery was considered as a last option. At present, the majority of patients are undergoing maintenance therapy with oral treatments.
Conclusions: The treatment of hidradenitis suppurativa is based on antibiotics, corticosteroids or contraceptives. These are able to control the disease temporarily. Etanercept is well tolerated but it only results in an initial improvement. Similar results have been found with infliximab and adalimumab. The affected areas can be controlled with surgery. Therefore, the role of TNF inhibitors in the treatment of hidradenitis suppurativa is controversial.
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Introduction

Hidradenitis suppurativa (HS) is a chronic and recurrent inflammatory disorder of the apocrine sweat glands characterised by the presence of deep and painful follicular nodules, papules, pustules and abscesses, located mainly in the armpits, groin and perianal region. The disease course is variable, and lesions frequently progress to fibrosis, suppuration, deformation and hypertrophy. The prevalence of HS is around 1%-4%. It affects more women than men, with a ratio of 3:1, and generally occurs between puberty and 40 years with a mean age-of-onset of 23 years.

The aetiology and pathogenesis of HS are unknown. It is believed that the disease develops after occlusion of the hair follicle as a result of a defect in the maturation of these cells that prevents the shedding of follicular epithelium. The occlusive folliculitis triggers an inflammatory reaction resulting in tissue destruction and epithelial damage. The situation is frequently aggravated by bacterial infections.

Treatment of HS is complex, as there are no specific indications by the dermatologist's outpatient dispensing program. A search was made of hidradenitis suppurativa treated with etanercept (indicación fuera de ficha técnica) until June 2009. The variables studied were: age, sex, treatments before and after to etanercept, response, adverse effects, duration and reason for suspension.

Methods

It was a retrospective cross-sectional study in a level 2 hospital. The territorial scope of the hospital is the Costa del Sol health district comprising 358,433 inhabitants (according to the census of January 2008).

Patients were selected through the pharmacy department’s outpatient dispensing program. A search was made for etanercept prescriptions assigned to the dermatology service up to June 2009 for use in unapproved indications by the *Agencia Española de Medicamentos y Productos Sanitarios* (Spanish Agency of Medicines and Health Products). The diagnosis of these patients was confirmed from the medical records, and 6 patients who received etanercept for the treatment of HS were identified.

The variables recorded were age, sex, previous surgical and pharmacological treatments and those following the use of etanercept, doses of etanercept, therapeutic response, time to response assessment, adverse effects, treatment period, and reasons for suspension.
Results

There were 6 patients treated and followed up for HS in the dermatology department of the Hospital Costa del Sol, Marbella (Table 1).

Etanercept was not used as a first-line treatment in any of the patients. It was used as a second-line treatment in 1 patient, as a third-line treatment in 3 patients, a fifth-line treatment in 1 patient, and a sixth-line treatment in 1 patient.

The first-line treatments included antibiotics, steroids, contraceptives, isotretinoin and oral sulfones. None of the patients could control the disease and prevent new lesions with these conventional drugs. However, some improvement was made in the treatment of exacerbations and they led to an initial transient improvement in some cases. Fig. 1 has a list of patients, previous treatments to etanercept and response, which is defined as acute infection control in the case of oral antibiotics and initial improvement in the rest of the treatments.

In the absence of sustained response to previous alternatives, treatment with a modulating factor of the inflammatory response was suggested. Etanercept was administered at a starting dose of 100 mg/week subcutaneously. In 2 patients, the dose was reduced to 50 mg/week after an initial improvement assessed at 16 and 20 weeks, respectively. One of these 2 patients, after a week with a dose of 50 mg/week, presented with an exacerbation of the disease and returned to the initial dose of 100 mg/week.

An initial improvement was seen in 4 patients, with new lesions appearing in a time ranging between 3 and 8 months. The other 2 patients experienced no improvement whatsoever, and so were considered as non-responders.

Discussion

The results obtained show that there is no effective therapy for the treatment of HS. All patients followed a similar treatment with similar results.
As a first-line treatment, the use of antibiotics, contraceptives, steroids, isotretinoin and/or oral sulfones showed some initial transient improvement in the lesions. No case achieved adequate control or could prevent the occurrence of new lesions. Oral antibiotics are effective in the treatment of acute infection.

Etanercept was used for the treatment of HS after at least one other treatment option had been used. It was well tolerated, but only yielded an initial improvement in the lesions, which prompted the discontinuation of the treatment after a variable period that depended on the patient.

After treatment failure, subsequent treatments were administered according to each patient. Some of the cases were treated with other TNF inhibitors, like infliximab and adalimumab, with a similar response to that obtained with etanercept.

Currently, most patients are receiving the treatment they had prior to the use of etanercept: antibiotics, steroids or oral contraceptives.

Surgery is an alternative in patients with HS who gain no control of their disease with drug therapy. However, the efficacy of this procedure is restricted to the treated area.

In view of these results and those reported in the literature, the role of etanercept in the treatment of HS is controversial. Authors such as Trent et al.6 and Cusack et al.14 demonstrate the efficacy of etanercept in patients with HS. Other authors have shown limited efficacy in treatment with etanercept. Lee et al.5 conclude their study stating that there is minimum clinically significant evidence for the efficacy of etanercept. In the study by Pelekanou et al.,11 there was a lack of response in 1/3 of the patients (n = 10), and all those who had an initial response required retreatting. Giamarellos et al.1F obtained a good response in the initial control of the disease in a phase II open trial on the safety and efficacy of etanercept in HS, and mentioned the need to develop controlled trials to determine the efficacy of etanercept in HS.

A limitation of the study was the lack of use of indices to objectively appraise the response to treatment, which made it very difficult to expand the sample size with results from other hospitals.

**Conflict of Interest**

The authors affirm they have no conflicts of interest.

**References**