Long-term Successful Adalimumab Therapy in Severe Hidradenitis Suppurativa

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**Background:** Several studies report the use of tumor necrosis factor α (TNF-α) inhibitors in refractory hidradenitis suppurativa (HS), particularly infliximab and etanercept. However, very limited data have been reported for HS, particularly infliximab and etanercept. We evaluated the long-term efficacy and safety of adalimumab therapy in 6 patients with refractory HS. In the case of positive culture findings from any draining lesion, antibiotic therapy was administered for at least 2 weeks before initiating adalimumab therapy. Adalimumab (in 40-mg subcutaneous injections) was prescribed every other week. If the disease was inadequately controlled, the dosage was increased to 40 mg/wk. If HS was in persistent clinical remission, adalimumab therapy was gradually decreased to 40 mg every 3 weeks. Quality of life was assessed using the Dermatology Life Quality Index.

**Observations:** Six patients (mean [SD] age, 39.3 [12.9] years) with severe HS (mean [SD] duration, 22.5 [11.7] years) were treated with adalimumab. Significant improvements after 1 month of treatment were seen in the Dermatology Life Quality Index; in the number of affected regions, nodules, and fistulas; and in the basic laboratory findings. Improvements were maintained for a mean (SD) follow-up of 21.5 (7.1) (range, 13-29) months. Adalimumab was well tolerated.

**Conclusion:** Adalimumab appears to be an effective and safe treatment for refractory HS.

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**HIDRADENITIS SUPPURATIVA (HS) is a chronic relapsing skin disorder characterized by recurrent inflammatory lesions leading in later stages to sclerosis, sinus tract formation, and fistula formation.** A number of treatment options are available for HS, including antibiotics, retinoids, immunosuppressants, and surgery. Despite such treatments, HS causes significant morbidity. The etiopathogenesis of HS remains incompletely understood. The most relevant pathological finding in HS is an inflammatory process with or without overlapping infection. Tumor necrosis factor α (TNF-α) is a potent and central proinflammatory cytokine involved in many conditions, including rheumatic, gastrointestinal tract, and skin diseases. The following 3 TNF-α inhibitors are currently being used in dermatology: etanercept, infliximab, and adalimumab.

An increasing number of reports have been published on the use of TNF-α antagonists in refractory HS. Most of them have reported the effects of infliximab on HS, whereas some reported the effects of etanercept. To our knowledge, however, only 2 patients with HS treated with adalimumab have been described. Unfortunately, the lengths of follow-up of most reported cases of HS that were treated with anti-TNF-α agents were short, and negative results were reported in other cases because of limited efficacy or unacceptable adverse effects. Six patients treated with adalimumab for refractory HS were reviewed in this study. Most of them had successful control of the disease during a long-term follow-up.

**Methods**

We reviewed findings from 6 patients treated with adalimumab for refractory HS. They all fulfilled the following criteria: (1) HS resistant to standard medical treatments; (2) lack of response to at least 1 systemic immunosuppressive/immunomodulating drug; (3) multifocal active HS; and (4) at least 1 year of follow-up. In all cases, written informed consent and approval of the National Health Institute, Madrid, Spain, were obtained before adalimumab therapy was started. Chest radiography and a purified protein derivative test were performed to rule out concomitant tuberculosis (TB). In the event of latent TB, adequate prophylaxis was administered. Basic laboratory tests (a complete blood cell count and chemistry panel) and cultures of every draining lesion were also performed. If positive culture...
results were found, adequate antibiotic therapy was started at least 2 weeks before starting adalimumab therapy. Antibiotic therapy was maintained for at least 2 additional weeks after adalimumab therapy was started.

Adalimumab (Humira; Abbott Laboratories, Abbott Park, Illinois) therapy consisted of 40-mg subcutaneous injections. The initial dosage was 40 mg every other week. When relapse occurred or the HS was inadequately controlled, the adalimumab dosage was increased up to 40 mg/wk. If the HS was in persistent clinical remission, adalimumab therapy was gradually decreased to a minimum dosage of 40 mg every 3 weeks.

All patients were closely monitored throughout the treatment period for signs of infection and other possible adverse effects. A complete clinical evaluation was routinely performed in all patients. Dermatologists performed a more specific dermatological examination, including an assessment of the number of regions involved and their state. In all patients, involvement of the following anatomic regions was evaluated, and the numbers of nodules and fistulas were expressed as the median value for the whole series of patients at each clinical visit.

Dermatologists and rheumatologists from our institution agreed to collaborate in the treatment of patients with refractory HS. Dermatologists focused mainly on the evolution of clinical efficacy. Because of their more extensive clinical experience with anti–TNF-α drugs, rheumatologists focused mainly on the assessment of possible adverse effects.

Our patients were provided the translated, validated Spanish version of the original English Dermatology Life Quality Index (DLQI) questionnaire.14,15 Differences in DLQI scores, numbers of affected regions and lesions, and basic laboratory findings at each visit compared with baseline were assessed using a Wilcoxon rank sum test. \( P < .05 \) was considered statistically significant. Unless otherwise indicated, data are expressed as mean (SD).

### RESULTS

Six patients with severe HS (mean age, 39.3 [12.9] years [range, 22-56 years]) were treated with adalimumab (Table). The mean disease duration was 22.5 (11.7) (range, 8-38) years. Systemic lupus erythematosus had also been diagnosed in patients 5 and 6. All patients had been treated previously with oral antibiotics and systemic corticosteroids, and some of them had received isotretinoin or oral contraceptives. Four patients had undergone repeated surgery (excision with or without grafting). Patient 6 had been adequately treated for TB 11 years before adalimumab therapy was started. In this patient, HS was initially treated with etanercept (50 mg/wk subcutaneously) for 3 months. However, the therapy was switched to adalimumab because of etanercept inefficacy.

Before the initial administration of adalimumab (baseline), suppurative exudates from 5 patients were positive for bacterial infection in at least 1 culture. Based on susceptibility testing results, antibiotics were administered for at least 2 weeks in these cases before adalimumab therapy was started. Two weeks after antibiotic therapy was initiated, a new drainage culture was performed, and results were negative. Adalimumab therapy was then started (baseline).

At the onset of adalimumab therapy, all patients had multifocal involvement with marked tenderness, induration, and sinus drainage. The mean baseline DLQI score was 23.7 (5.9). Laboratory tests showed leukocytosis (white blood cell count, \( \geq 11 \times 10^9 \) cells/L [to convert to cells \( \times 10^9 \) per liter, multiply by 0.001]) in 3 patients and an increased erythrocyte sedimentation rate in 4. The Table gives the changes in the main basic laboratory findings and the DLQI at each visit. The DLQI decreased at 1 month and 1 year compared with baseline (\( P = .03 \) for both). The white blood cell count was not statistically significantly reduced. The erythrocyte sedimentation rate decreased at 1 month (\( P = .03 \)) but not at 1 year (\( P = .34 \)). All patients experienced a marked reduction in the numbers of affected regions, fistulas, and nodules during dermatologic examination (Figure 1). The number of affected regions decreased at 1 month (\( P = .02 \)) and 1 year (\( P = .01 \)) compared with baseline. The number of nodules also decreased at 1 month and 1 year (\( P = .03 \) for both), as did the number of fistulas at 1 month and 1 year (\( P = .03 \) for both). Most patients reported a progressive response after the first subcutaneous injection (Table and Figure 1).

A gallium citrate Ga 67–labeled scan was performed in patients 1 and 2, and showed complete resolution of pathologic features after 2 months of adalimumab therapy. Magnetic resonance imaging was performed in patient 1

### Table. Main Demographic Data and Outcome Measures in 6 Patients Diagnosed as Having Refractory HS

<table>
<thead>
<tr>
<th>Patient No./Sex/ Age, y</th>
<th>HS Duration, y</th>
<th>Baseline</th>
<th>1 mo</th>
<th>1 y</th>
<th>Baseline</th>
<th>1 mo</th>
<th>1 y</th>
<th>Follow-up, mo</th>
<th>Relapse</th>
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<tr>
<td>1/M/56</td>
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<td>5</td>
<td>4</td>
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<td>6.8</td>
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<td>10</td>
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<td>10.6</td>
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<td>15</td>
<td>2</td>
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<td>8</td>
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</table>

**Abbreviations:** DLQI, Dermatology Life Quality Index; ESR, erythrocyte sedimentation rate; HS, hidradenitis suppurativa; WBC, white blood cell.

\( \text{SI conversion factor: To convert WBC count to number of cells } \times 10^9 \text{ per liter, multiply by 0.001.} \)

\( ^a \) These were usually mild and transient.

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and also showed a clear improvement (Figure 2) parallel to clinical improvement (Figure 3).

The mean follow-up was 21.5 (7.1) months (range, 13-29 months), but was longer than 2 years in 3 patients. Five patients experienced mild relapses that consisted of increasing pain and occasionally draining lesions (Table). In these cases, a drainage culture was usually repeated and, if the results were found to be sterile, the adalimumab dose was increased up to a maximum of 40 mg/wk. However, if the culture was positive for bacterial infection, specific oral antibiotic therapy was prescribed for 2 to 4 weeks, with the length of therapy based on the results of susceptibility tests. Paradoxically, patient 5, who had HS and systemic lupus erythematosus, experienced a transient worsening of arthritis, with no other evidence indicative of active systemic lupus erythematosus, 3 months after adalimumab therapy was started. Arthritis spontaneously resolved without specific treatment.

Because of sustained HS improvement, the adalimumab dosage could be decreased to 40 mg every 3 weeks in 2 patients. Among the 3 patients receiving prednisone at baseline, the drug therapy was tapered and finally withdrawn in patient 2.

Adalimumab therapy was well tolerated. The most common adverse effect was mild to moderate pain at the injection site. Severe facial cellulitis occurred in patient 1 but resolved without sequelae after 2 weeks of intravenous ceftriaxone sodium therapy. In this patient, adalimumab therapy was discontinued for 1 month.

**COMMENT**

We studied 6 patients who were treated with adalimumab for refractory HS. All of them showed a successful course after a relatively long-term follow-up.

The initial pathological event in HS is a follicular hyperkeratosis with plugging and dilatation of the hair fol-
licle that causes inflammation. This persistent inflammation appears to be the main mechanism leading to HS chronicity, progression, and irreversible structural damage. A key therapeutic target may therefore be the control of the underlying inflammatory process before significant and irreversible structural damage occurs. As expected, in a recent study a poor therapeutic response mainly occurred in patients with long-standing disease characterized by chronic inflammation, multiple sinus formation, and "bridged" scarring.

Tumor necrosis factor-α is a potent and central ubiquitous proinflammatory cytokine. Adalimumab is a fully human monoclonal IgG1 antibody specific for TNF-α that is administered subcutaneously. By contrast, infliximab is a murine-human chimeric antibody that is administered intravenously. Encouraging results were seen in the first patients with HS treated with infliximab, but the follow-up was usually short. Infliximab use was also reported in patients with HS associated with Crohn disease. We did not include patients with HS associated with Crohn disease in our study, owing to a possibly different pathogenetic mechanism. Two recent studies with infliximab reported a poor efficacy and significant adverse effects. Another study with a single course of infliximab therapy showed recurrence in most patients. Other reports found encouraging results with etanercept therapy, but the follow-up was only 24 weeks. To our knowledge, efficacy with adalimumab has been reported in only 2 patients. Hidradenitis suppurativa was probably not severe enough in one of the patients, whereas the other was followed up for only 4 months.

We described herein 6 patients with severe, multifocal HS treated with adalimumab for a long-term follow-up (>2 years in 3 patients). In this series, most adverse effects were usually minor, in particular mild to moderate pain at the adalimumab injection site. Despite the relatively long follow-up of our patients, only 1 severe adverse effect (facial infectious cellulitis) was seen. Moreover, we included patients with HS and severe comorbidities. One patient had been treated previously for lymph node TB, 1 had latent TB, 2 had systemic lupus erythematosus, and 1 had experienced an acute myocardial infarction 3 years before.

Anti-TNF-α therapy is associated with an increased risk of serious skin and soft-tissue infections. Severe infections have also been reported in association with HS, regardless of anti–TNF-α therapy. Local superinfection in HS may also spread, leading to septicemia. In this regard, a case of lumbosacral epidural abscess has been re-

Figure 3. Photographs of patient 1. A, Before the initial administration of adalimumab (baseline), erythema, nodules, and draining fistulas were observed in the intergluteal area. B, Six months after the initiation of adalimumab therapy, important improvement consisting of decreased erythema and healing of the fistulas is observed.
ported.23 Based on these considerations, the significance of obtaining culture specimens from every draining lesion before starting anti–TNF-α therapy should be emphasized. We recommend prescribing of specific antibiotics for at least 2 weeks before starting anti–TNF-α therapy. During the follow-up period, we also suggest that the adalimumab dosage be adjusted according to the clinical response.

In conclusion, this is, to our knowledge, the largest study assessing patients with refractory HS and their response to adalimumab. All patients experienced a rapid, significant, and sustained clinical improvement. Four of them remained in complete clinical remission at the last follow-up visit. Adverse effects were exceptional. However, further controlled studies analyzing the efficacy and safety of adalimumab for HS are warranted.

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Author Contributions: Dr Blanco had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Blanco, Martínez-Taboada, González-Vela, and González-López. Acquisition of data: Blanco, Villa, González-Vela, Fernández-Llaca, Agudo, and González-López. Analysis and interpretation of data: Blanco, Martínez-Taboada, and Villa. Drafting of the manuscript: Blanco, Villa, González-Vela, Agudo, and González-López. Critical revision of the manuscript for important intellectual content: Blanco, Martínez-Taboada, Fernández-Llaca, and González-López. Administrative, technical, and material support: Villa, González-Vela, and Agudo. Study supervision: Blanco, Martínez-Taboada, Fernández-Llaca, and González-López.

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