Infliximab for severe hidradenitis suppurativa: Transient clinical efficacy in 7 consecutive patients

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Background: Hidradenitis suppurativa (HS) is a chronic and debilitating disorder. Despite its significant prevalence, few reports of therapeutic studies are available. Recent case studies have reported the efficacy of antitumor necrosis factor monoclonal antibodies in treating the condition. In the study presented here, we assessed the safety and efficacy of infliximab in a series of patients with severe HS.

Methods: We reviewed all consecutive patients with severe HS and treated with infliximab between October 2004 and December 2005. They were evaluated using the Sartorius severity score, a physician and patient overall assessment, and the Skindex-29 quality-of-life index. A substantive response was defined as marked or moderate overall improvement assessed by both physician and patient.

Results: Seven patients were reviewed. All received at least 3 infusions of infliximab (5 mg/kg) in weeks 0, 2, and 6, and 5 patients received a fourth infusion at week 10. At week 6, a substantive improvement was seen in 5 patients. With the other 2 patients, any improvement was minimal or nonexistent. At week 10, there was a substantive response in 2 of the 5 patients. Adverse events occurred in 3 patients: abdominal pain caused by colon cancer, a multifocal motor neuropathy with conduction block, and a severe allergic reaction.

Limitations: We have reported on only 7 patients. All had severe and chronic disease.

Conclusion: The efficacy of infliximab in patients with severe HS seems transient and is associated with significant toxicity. Prospective randomized studies are required to better assess the benefit-risk ratio of antitumor necrosis factor agents for this indication. (J Am Acad Dermatol 2006;55:602-605.)

Hidradenitis suppurativa (HS) is a chronic, suppurative, and cicatricial disorder that affects skin areas rich in apocrine glands, such as perineum and axillae. It is very debilitating, both physically and psychologically. Patients experience recurrent painful abscesses and malodorous discharges requiring regular dressing and leading to social isolation. Because of these consequences, and because of a prevalence of 0.3% to 4% in industrialized countries, HS presents a therapeutic challenge to dermatologists. However, there is little evidence of effective treatment in the medical literature, because the results of only 3 prospective randomized controlled trials are currently available. A modest clinical effect was observed with topical clindamycin when compared with topical placebo whereas no better results were obtained when systemic tetracycline was compared with topical clindamycin. The improvement induced by antiandrogen therapy mostly concerned acne, which may be associated with HS. Complete surgical excision of affected areas is the best treatment available so far, but is associated with a significant morbidity with extensive scarring, particularly in the extra-axillary areas. Moreover, operation does not prevent distant recurrence. In this context, recent case reports on the efficacy of infliximab (Remicade) in treating HS, whether or not associated with Crohn’s disease, are encouraging. However, because the data from
isolated reports are difficult to interpret because of selection bias, we treated with infliximab all consecutive patients with severe HS, not limited to axillae, who were resistant to usual medical therapies and reluctant to undergo operation.

**METHODS**

We reviewed the files of all patients with severe HS and treated with infliximab in our department between October 2004 and December 2005. All had: (1) a HS resistant to usual medical therapies, such as systemic or local antibiotherapy; and (2) HS that could not be easily cured by operation (HS not limited to the axillae, operation refused by patient). No other medication was introduced for 2 months before infliximab. No patient had a history of Crohn’s disease, neoplasia, tuberculosis, HIV, or hepatitis B or C.

All were treated with intravenous infliximab (5 mg/kg) without corticosteroid or antihistamine premedication. Clinical evaluation was routinely performed at weeks 0, 6, and 10. Clinical features were assessed using the Sartorius score, which evaluates the number of regions involved and the state of the disease (Table I). Quality of life was assessed using Skindex-29 France, an index taking account of emotion, symptoms, and function. Moreover, to assess the evolution under treatment, one physician and each patient evaluated the overall evolution (marked improvement, moderate improvement, minor improvement, no improvement, worsening) before the third and fourth infusions. A substantive response was defined as an overall improvement rated as “marked” or “moderate” by both physician and patient.

Lastly, any adverse effects of infliximab were reported according to the Common Terminology Criteria for Adverse Events v3.0. We did not test for antibodies to infliximab.

**RESULTS**

Seven patients with severe HS (mean Sartorius score: 82 [SD:30]) were treated. At the initial administration, all were free of known acute or chronic infections and had a negative chest radiograph result and a negative purified derived protein test result. Their characteristics are summarized in Table II.

All patients received at least 3 infusions (weeks 0, 2, and 6). Five received a fourth infusion in week 10. The tolerance was poor. Three patients developed severe side effects. A grade 3 allergic reaction (symptomatic bronchospasm with urticaria; parenteral medication indicated) occurred in patient 3 at the beginning of the third infusion and the treatment was stopped. This patient was not evaluated at week 10. After the third infusion, patient 7 developed severe abdominal pain related to a colon cancer. This patient was not evaluated at week 10. Lastly, patient 6 developed a grade 3 multifocal motor neuropathy with conduction block (motor weakness interfering with daily living; assistance indicated). This appeared 4 weeks after the fourth infusion, which was then definitively contraindicated. This patient did not have a history of neurologic disease.

At week 6, a substantive improvement was seen in 5 patients (patients 1, 2, 3, 5, and 6) (Table III). The Sartorius score decreased by at least 40% in 5 patients (Fig 1) and the efficacy of infliximab was minimal or nonexistent for 2 patients. At week 10, a clinical response was observed in 2 of the 5 evaluated patients (patients 1 and 2). One developed adverse

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**Table I. The Sartorius score**

| 1 - Anatomic region involved (axilla, groin, gluteal or other region, or inframammary region left and/or right): | 3 points per region involved |
| 2 - Number and scores of lesions (abscesses, nodules, fistulas, scars): points per lesion of all regions involved | Nodules = 2 points; fistulas = 4 points; scars = 1 point; others = 1 point |
| 3 - The longest distance between two relevant lesions (ie, nodules and fistulas) in each region, or size if only one lesion | <5 cm = 2 points; <10 cm = 4 points; >10 cm = 8 points |
| 4 - Are all lesions clearly separated by normal skin? In each region yes = 0 points; no = 6 points |

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**Table II. Baseline characteristics of patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>Disease duration, y</th>
<th>Prior therapy</th>
<th>Affected areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>31/F</td>
<td>1</td>
<td>Systemic ATBT R/L inguinal Operation Perianal</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>26/F</td>
<td>10</td>
<td>Systemic ATBT R/L inguinal Local ATBT Isotretinoin Operation L inguinal</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>24/F</td>
<td>8</td>
<td>Systemic ATBT R/L inguinal Local ATBT Isotretinoin Operation L axillary</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>51/M</td>
<td>20</td>
<td>Systemic ATBT R/L inguinal Operation Perianal</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>64/M</td>
<td>40</td>
<td>Systemic ATBT R/L inguinal Operation Perianal</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>39/M</td>
<td>15</td>
<td>Systemic ATBT R/L inguinal Local ATBT Isotretinoin Operation R/L axillary</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>76/M</td>
<td>45</td>
<td>Systemic ATBT Operation Perianal</td>
<td></td>
</tr>
</tbody>
</table>

ATBT, Antibiotherapy; L, left; R, right.
effects and infliximab was then contraindicated. Treatment of the other patient was stopped after 4 infusions and there was marked recurrence of HS 10 weeks later. Infliximab was then reintroduced, leading to clinical improvement until infusion 8. Thereafter the disease worsened, despite two more infliximab infusions.

**DISCUSSION**

Even though the pathogenesis of HS is poorly understood, there is a rationale for using anti-tumor necrosis factor (TNF-α). On the one hand, the primary lesion in HS is an occluding spongiform infundibulo-folliculitis leading to dilatation of the follicle followed by its rupture and leakage of contents (including keratin and bacteria) into the surrounding dermis. This induces a vigorous chemotactic response with an inflammatory cell infiltrate of neutrophils, lymphocytes, and histiocytes. Moreover, in the chronic phase of the disease, granuloma with giant cells may be seen. TNF-α, which induces proinflammatory cytokines and activates neutrophils and lymphocytes, also recruits inflammatory cells to sites of inflammation and, thus, contributes to granuloma formation. It may, therefore, play an important role in HS. Hence, TNF inhibition by infliximab may be beneficial. On the other hand, the value of infliximab is suggested by anecdotal evidence from cases of HS associated or not with Crohn’s disease and from 5 patients with severe HS without Crohn’s disease. More recently a marked improvement was reported with etanercept in a retrospective study of 6 patients with severe HS but without Crohn’s disease. An initial response was seen within 2 to 3 weeks.

In our study, clinical improvement occurred within the first month. This is similar to that seen in patients with psoriasis or Crohn’s disease. Although the very short-term responses were encouraging, at week 10, with 5 patients under treatment, only two were still responding. In the literature, long-lasting responses have been reported with anti-TNF therapy in HS. Three possible reasons can be advanced for such discrepancy. First, we have reported on all severe HS cases presenting in our department that were treated consecutively with infliximab, thereby avoiding the selection bias of previous published studies. Second, we excluded those patients with HS associated with Crohn’s disease, whose skin disease might have had a different pathogenesis. Third, in our study, a poor response to infliximab occurred mainly in those patients with long-standing disease characterized by chronic inflammation, multiple sinus formation, and “bridged” scarring. These patients may have been in too advanced a state to respond to a treatment that mainly affects the early acute phase of inflammation. Furthermore, we can also postulate that these patients had particularly resistant form of the disease.

Infliximab toxicity in our study appeared greater than that reported in previous trials (ie, the treatment...
of psoriasis or Crohn’s disease). The absence of corticosteroid premedication in our patients may be the explanation, even if the value of corticosteroids in preventing infusion reaction remains relevant. Unexpectedly, we encountered both neoplastic and severe adverse neurologic disease. Because of the rapidity of onset and the severity of symptoms soon after the initiation of anti-TNF (the patient was free of intestinal symptoms before treatment), we suspect that infliximab may have exacerbated a pre-existing colon cancer in patient 7. Motor neuropathy has been observed with infliximab. Other neurologic side effects, such as optic neuropathy, chronic inflammatory demyelinating polyneuropathy, or new-onset multiple sclerosis/demyelination have also been reported.

In conclusion, although efficacy was not as impressive as that described in other case reports, our results confirm that infliximab may induce a short-term response in severe HS. Because predictive response factors are still not clear, some patients may have benefited from higher doses, more frequent infusions, or both. Moreover, our study was remarkable for the high number of severe adverse events. Such findings highlight the need for further prospective randomized studies to better assess the predictive factors for response and whether or not some patients might benefit from higher doses, more frequent infusions, or both. Future studies will be important to define the benefit-risk ratio of anti-TNF agents in severe HS.

REFERENCES


