Variable response of hidradenitis suppurativa to infliximab in four patients

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We present a retrospective review of four patients treated with infliximab (5 mg/kg) for recalcitrant hidradenitis suppurativa (HS). Data including gender, age, previous treatments and therapeutic response are recorded in Table 1. All patients were screened beforehand with a chest X-ray and a Mantoux test to exclude concomitant TB.

Patients 1 and 2. Our first two patients were middle-aged women with long-standing severe HS of the axillae, abdomen and groin. Both had received a wide range of systemic treatments and extensive surgery. We treated them with three infusions of infliximab (0, 2 and 6 weeks). In patient 1, there was no evidence of significant clinical improvement after the final infusion. In contrast, patient 2 experienced a dramatic improvement in her skin after her third infusion, with resolution of all her inflammatory lesions. A further infusion of infliximab (5 mg/kg) was administered a month later in response to a mild flare, and she was subsequently listed for eight weekly infusions. Eleven months after her first infusion, she developed a positive antinuclear antibody titre (1/640; negative before infliximab), associated with a positive perinuclear neutrophil cytoplasmic antibody, and this, associated with arthralgia and diffuse alopecia, suggested an infliximab-induced lupus reaction. A double-stranded DNA and extractable nuclear antigen test were negative, with normal levels of complement. The infliximab was stopped immediately, and the patient’s clinical and serological markers improved.

Patient 3. This was a 48-year-old man with a 30-year history of extensive HS and associated pyoderma gangrenosum. On review 1 month after his third and final infusion of infliximab, his HS remained widespread. He currently remains on tacrolimus 5 mg twice daily and minocycline 100 mg twice daily.

Patient 4. Our final patient was a 27-year-old man with a long-standing history of HS affecting the axillae and groin, and concomitant perianal Crohn’s disease (CD). In December 2002, the patient was treated with two infusions of infliximab. His symptoms from both his conditions settled well. Unfortunately, his CD re-flared 2 years later, and a further course of infliximab was administered in 2004. During the first infusion of this new series, the patient developed facial swelling and shortness of breath within minutes of commencing the infusion, suggesting the development of antibodies to the infliximab. The infusion was stopped and his CD is currently maintained on azathioprine 50 mg three times daily. His HS is currently unmonitored, as he has since failed to attend his dermatology appointments.

HS is a chronic inflammatory condition in which successful medical treatment remains a therapeutic challenge. To date, several cases have been reported in the literature, which cite the success of infliximab in its treatment.1,2

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Table 1: Patient demographics, prior and current therapies and response to infliximab infusion (5 mg/kg).

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Age (years)</th>
<th>Duration of disease (years)</th>
<th>Aected areas</th>
<th>Prior therapy</th>
<th>Daily therapy before first infusion</th>
<th>Daily therapy after first infusion</th>
<th>Response to therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>47</td>
<td>30</td>
<td>Axillae, abdomen, groin</td>
<td>Surgery, topical treatments, corticosteroids</td>
<td>Prednisolone 10 mg, ciclosporin 3 mg/kg</td>
<td>Fusidic acid 500 mg twice daily, clarithromycin 500 mg, alternate weekly</td>
<td>Poor therapy</td>
</tr>
<tr>
<td>2</td>
<td>53</td>
<td>36</td>
<td>Groin, axillae</td>
<td>Ciclosporin, acetate, antibiotics, HRT, corticosteroids</td>
<td>Ciclosporin 3 mg/kg, etanercept</td>
<td>Fusidic acid 500 mg twice daily, clarithromycin 500 mg, alternate weekly</td>
<td>Poor response</td>
</tr>
<tr>
<td>3</td>
<td>48</td>
<td>30</td>
<td>Abdomen, buttocks, groin, thighs, axillae</td>
<td>Ciclosporin, antibiotics, steroids, metronidazole</td>
<td>Prednisolone 40 mg once daily</td>
<td>Tacrolimus 5 mg twice daily, minocin 100 mg twice daily</td>
<td>Good response</td>
</tr>
<tr>
<td>4</td>
<td>27</td>
<td>7</td>
<td>Axillae, groin</td>
<td>Minocin 100 mg once daily</td>
<td>Azathioprine 50 mg three times daily</td>
<td>Good response to first course of infusions. Second infusion led to allergic reaction.</td>
<td>Good response</td>
</tr>
</tbody>
</table>

HRT: hormone-replacement therapy; LE: lupus erythematosus; A/w: alternate weekly.
The largest study thus far investigated five patients with therapy-resistant HS and their response to infliximab. All patients experienced improvement clinically and in their self-reported disease, although three of the five patients continued on immunosuppressive medication while on infliximab, and two of these patients continued on some form of immunosuppression after the infliximab was stopped.

In conclusion, we present four patients with HS, whose outcome to infliximab was variable. One patient developed serological and clinical features of lupus, necessitating the cessation of treatment, although her HS had responded well to the previous infusions of infliximab. Another patient developed a hypersensitivity reaction to the infliximab, having had a course of it previously with some success. Although this side-effect is well-recognized, it is rare and has been reported in less than 1% in a series of 156 patients treated with infliximab for rheumatoid arthritis. However, in one of our patients it could also be attributed to the long time interval between infusions. In two other patients, both of whom had severe disease, the outcome was poor despite three infusions of infliximab.

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References

Intravenous immunoglobulin is effective as a sole immunomodulatory agent in pyoderma gangrenosum unresponsive to systemic corticosteroids
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An 83-year-old man presented with worsening painful ulceration on his feet. His medical history included a healed ulcer on his right ankle, a transurethral resection of the prostate for benign prostatic hyperplasia, and hypertension and atrial fibrillation. Medication included bendrofluazide and digoxin.

Examination revealed a full-thickness ulcer, 60 mm in diameter, on the right heel (Fig. 1b), more superficial ulceration on the left heel and the dorsa of the toes, and full-thickness ulcer, 40 mm in diameter, on the right calf. Neurological examination was normal. There was no evidence of venous hypertension. Arterial Doppler imaging was normal.

Biopsies were taken from the ulcer on the right heel. Histopathology revealed granulation tissue in the superficial dermis and a neutrophilic infiltrate in the dermis and subcutis (Fig. 1a). Investigations revealed haemoglobin of 8.8 g/dL (normal range 12.5–17.5), an albumin of 19 g/L (normal range 35–55) and erythrocyte sedimentation rate of 129 mm/h. Serum electrophoresis showed an IgM-k paraprotein band without immune paresis. A diagnosis of monoclonal gammopathy of unknown significance was made. No bacteria were cultured. An X-ray of the patient’s right foot showed osteopenia but no evidence of osteomyelitis. A final diagnosis of pyoderma gangrenosum (PG) was made.

The patient had no response to topical Dermovate and 4 weeks of oral prednisolone at a dose of 40 mg/day. Minocycline 100 mg twice daily was commenced, and the prednisolone dose was increased to 60 mg/day for a further 4 weeks. The patient received 3 units of blood. Because of progressive deterioration in his ulceration and clinical condition, intravenous immunoglobulin (IVIg) (Vigam®/Flebogamma®) was commenced at 0.4 g/kg/day for 5 days, repeated at monthly intervals.

The prednisolone dose was gradually tapered and stopped over the next 4 months. The ulcer on the patient’s right heel showed significant re-epithelialization after two cycles of IVIg (Fig. 1c) and complete healing after five cycles (Fig. 1d). The remaining ulcers had healed after two cycles of IVIg. The patient’s blood parameters and clinical condition returned to normal, as did his serum electrophoresis. He is currently maintained on IVIg 0.4 g/kg/day for 5 days, repeated every 8 weeks, without any adverse effects. He has had a total of 10 cycles of IVIg at the time of writing, and his ulcers remain healed.

PG is a clinical diagnosis, often made by exclusion. The majority (50–70%) of cases are associated with systemic conditions including inflammatory bowel disease, rheumatoid arthritis, myeloma and haematological malignancy. IgM-k paraproteinaemia has previously been reported in association with PG. First-line therapy usually comprises systemic corticosteroids and ciclosporin. Our patient failed to respond to oral prednisolone 60 mg/day, and his age, plus concurrent anaemia, osteopenia and hypertension, prompted us to use IVIg instead of higher doses of prednisolone and ciclosporin.

IVIg has successfully been used in a few cases of PG, although there are also some reports of its lack of efficacy in