Case report

Efficacy of adalimumab in Behçet’s disease. Description of 6 cases

Javier Calvo Catalá,a,* Cristina Campos Fernandez,a Amalia Rueda Cid,a Maria Isabel Gonzalez-Cruz Cervellera,a Aurelio Baixauli Rubio,b Maria Dolores Pastor Cubilloa

a Servicio de Reumatología y Metabolismo Óseo, Consorcio Hospital General Universitario, Valencia, Spain
b Servicio de Medicina Interna, Hospital de Manises, Valencia, Spain

Introduction

Behçet disease (BD) is a systemic vasculitis. Its most common manifestations are oral-genital ulcers, polyarthritis, ocular involvement (uveitis) and skin involvement (erythema nodosum, folliculitis and pathergy).1,2 The use of antagonists of tumor necrosis factor alpha (anti-TNF) biological agents as part of a therapeutic strategy for the management of systemic vasculitis is increasingly frequent.3

Adalimumab (Humira®) is a human anti-TNF-alpha that, in most cases, is self-administered subcutaneously every 14 days.

The medical literature there are some described cases of BD treated with adalimumab, with a good clinical response.4-12 We present our experience with 6 BD patients treated with adalimumab.

Clinical observation

6 Spanish patients (Caucasian), meeting international criteria for BD15 are described, 4 being women. The mean age was 42.5±2.8 years (range 38-46). Average time of disease 14.1±6.5 years (range 5-22). All patients had involvement of mucous membranes (mouth ulcers and / or genitals). Five patients had ocular involvement, 3 skin lesions and one woman had neurological disease (inflammatory leuкоencephalopathy) (Table 1). All patients had negative autoantibodies and normal complement levels (C3, C4, factor B).
The patients had received conventional treatment: steroids, azathioprine, cyclosporine, anti-inflammatory drugs, colchicine and 2 received infliximab (Table 1).

We conducted a review of the literature, identifying 9 items, a total of EB 20 patients who received adalimumab (Table 2). The mean age of patients was 39.5 (range 21-55) years, 9 were women, and the median time since the onset of disease (n=8 patients) was 6.75 (range 1-10) years.

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Gender, Age, years</th>
<th>BD Motive</th>
<th>BD duration, for use of Adalimumab</th>
<th>Prior medication</th>
<th>Concomitant treatment</th>
<th>Evolution medication</th>
<th>Adverse effects</th>
<th>Adalimumab Follow up, months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (38)</td>
<td>Bipolar ulcers*</td>
<td>22</td>
<td>Aza, Ste Colchi, Cyclo</td>
<td>None</td>
<td>Asymptomatic</td>
<td>No</td>
<td>40</td>
</tr>
<tr>
<td>Female (41)</td>
<td>Erythema nodosum</td>
<td>5</td>
<td>Cyclo, Ste Infli</td>
<td>Colchi, Ste</td>
<td>Improvement (Oral Ulcers Back pain)</td>
<td>No</td>
<td>23</td>
</tr>
<tr>
<td>Female (42)</td>
<td>Oral ulcers Inflammatory leukoencephalopathy</td>
<td>10</td>
<td>Aza, Ste Cyclo</td>
<td>Aza</td>
<td>Asymptomatic</td>
<td>No</td>
<td>30</td>
</tr>
<tr>
<td>Female (44)</td>
<td>Uveitísa 11</td>
<td>Ste</td>
<td>Ste, NSAID</td>
<td>Ste</td>
<td>Improvement (Oral ulcers Heel pain/low back pain)</td>
<td>No</td>
<td>15</td>
</tr>
<tr>
<td>Male (46)</td>
<td>Female (44)</td>
<td>Bilateral panuveitísa 17</td>
<td>Ste, NSAID</td>
<td>Ste</td>
<td>Asymptomatic</td>
<td>No</td>
<td>12</td>
</tr>
<tr>
<td>Male (44)</td>
<td>Uveitísa 20</td>
<td>Ste</td>
<td>Ste, NSAID</td>
<td>Ste</td>
<td>Improvement (Oral ulcers Heel pain/low back pain)</td>
<td>No</td>
<td>15</td>
</tr>
</tbody>
</table>

Aza indicates azathioprine; BD, Behçet’s disease; Colchi, colchicine; Cyclo, cyclosporin; Infli, infliximab; NSAID, non steroidal anti-inflammatory drugs; Para: paracetamol; Ste, steroids.

\*Motive for use of adalimumab.

Discussion

The indication of anti-TNF drugs as part of a therapeutic strategy for the management of systemic vasculitis is increasingly frequent. As BD is a vasculitis with a chronic course and relapses, where further treatment options are limited and not without side effects, the use of anti-TNF is a possibility in order to control symptoms in these patients.

We have presented 6 patients who received adalimumab for BD, observing a good clinical response and tolerance (mean follow up of 26.8 months).
In the recommendations by EULAR,\textsuperscript{19,20} the authors confirmed the lack of solid evidence (randomized, double-blind trials) on the efficacy of drugs in BD, but recommended, given the systemic involvement of disease, the use of immunosuppressants (cyclosporin A, azathioprine, interferon alpha and anti-TNF).

All reported cases responded to this drug, showing a good safety profile: there were only 4 adverse events described (one allergy\textsuperscript{5} and 3 lichenoid skin lesions at the site of injection\textsuperscript{12}). The mean follow-up time with adalimumab was 17 months (range 1-36).

Compared with our patients we observed that the most common indication was ocular involvement, as well as a patient with inflammatory leukoencephalopathy. Two had received infliximab with relapse of symptoms (eye inflammation and neurological disease). Our patients showed no adverse events at the time of publication.

Adalimumab appears to be a useful treatment for BD. Although published evidence to date is limited and is based exclusively on small case series showing good efficacy and tolerability in patients with this type of vasculitis, resistant to other immunosuppressive agents, although further studies are needed to determine the dose and optimal and safe treatment regimens with anti-TNF for the management of BD.

### Conclusions

According to our study and prior published data in the medical literature, we believe that anti-TNF therapy, especially adalimumab, is a good option for patients with BD who are resistant to conventional therapy. We found no adverse effects in patients treated with adalimumab, which coincides with the few cases reported in the reviewed literature.

### Conflict of interest

The authors have no conflict of interest.
References


