

Ocular inflammatory signs observed in a cohort of Spanish patients with Behçet disease and ocular inflammation

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PURPOSE. *To study the clinical characteristics of a cohort of Spanish patients diagnosed with Behçet disease and who also presented ocular inflammation.*

METHODS. *Thirty cases of Behçet disease were studied retrospectively. The authors studied age distribution, distribution by sex, clinical course, laterality, type of uveitis, secondary glaucoma, corneal involvement, hypopyon, iris-lens synechiae, secondary cataract, cystoid macular edema (CME), and papillitis (optic neuritis).*

RESULTS. *Fourteen of the patients were men and 16 were women (ratio 0.875:1). The mean age of the patients was 35.24 years (± 10.917 ; 21–61 years). In 23 patients, the disease course was recurrent. In 9 patients, the disease manifested unilaterally. In 5 patients showing unilateral onset, the contralateral eye became affected. In 2 of the 30 patients, uveitis exclusively affected the anterior segment. In 8 patients, uveitis was solely posterior. There was one case of intermediate uveitis. The remaining 19 patients showed panuveitis. Three had focal chorioretinitis. One had diffuse chorioretinitis. Fifteen showed signs of diffuse vasculitis. Eight patients showed focal vasculitis.*

CONCLUSIONS. *Women were slightly more affected than men, although the authors found no significant correlation between sex and the clinical variables examined. Apart from one unexpected case of intermediate uveitis, the observations are similar to those reported for other patient series. (Eur J Ophthalmol 2008; 18: 563-6)*

KEY WORDS. *Behçet disease, Uveitis, Spanish population*

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INTRODUCTION

Behçet disease is a chronic, multisystem disorder characterized by recurrent flares of inflammatory symptoms. Although its etiology is unclear, it is thought that autoimmune reactions may be involved. The disease affects persons throughout the world although it is most prevalent in countries connected by the silk trading route such as Turkey, Iraq, Saudi Arabia, Iran, Afghanistan, Pakistan, China, North Korea, South Korea, and Japan (1-10).

Ocular involvement occurs in 70% of cases of Behçet disease; the most typical form is recurrent panuveitis, al-

though isolated anterior, intermediate, or posterior uveitis is also common (1-4). Conjunctivitis, episcleritis, and scleritis are less frequent (1-3).

The present study retrospectively analyzes the clinical features of the ophthalmologic component of the disease in a cohort of 30 patients diagnosed with Behçet disease.

METHODS

The study design is a retrospective descriptive analysis of a case series.

Inclusion criteria

Patients diagnosed with the complete or incomplete form of Behçet disease who also presented any form of ocular inflammation between 1990 and 2002 were included. Criteria for diagnosis of Behçet disease were used (1-6). The patients were followed from diagnosis to at least 2 years post-diagnosis. Patients with the suspect or possible form were excluded as diagnosis of Behçet disease in these patients is uncertain. We also excluded patients who could not be followed for at least 2 years after diagnosis. In patients in whom the disease started unilaterally but progressed to bilateral involvement, the eye studied was the first to manifest. In patients with bilateral disease onset, the eye studied was that with the worst visual acuity at presentation.

Clinical characteristics

The following characteristics were analyzed: age distribution at onset, distribution by sex, clinical course, laterality, type of uveitis, secondary glaucoma, corneal involvement, hypopyon, iris-lens synechiae, secondary cataract, cystoid macular edema (CME), and papillitis (optic neuritis).

Standardization of uveitis nomenclature (SUN) was used to classify and describe the clinical characteristics analyzed (8).

Possible correlations between sex and the clinical characteristics examined were also evaluated.

To assess the age at onset, we stratified the population into groups of 5 years (i.e., 20–24, 25–29).

The variable “laterality” refers to whether the clinical signs at disease onset affected one or both eyes; when only one eye was initially affected, we also recorded whether the contralateral eye developed symptoms during the follow-up. For patients in whom disease was unilateral at onset and then bilateral, the time (in months) elapsed from diagnosis to bilateralization was also recorded.

The clinical course of disease was described as recurrent, when there was remission of inflammatory symptoms between flares, or chronic, when inflammation persisted at some degree between flares.

Uveitis was recorded as anterior, posterior, or panuveitis. When the posterior segment was affected, the form of uveitis was described as focal chorioretinitis, diffuse chorioretinitis, focal vasculitis, or diffuse vasculitis.

RESULTS

The series examined contained 30 consecutive patients of native Spanish descent diagnosed with the complete or incomplete form of Behçet disease accompanied by some form of ocular inflammation over the period 1990 to 2002.

Fourteen of the patients were men and 16 women (ratio 0.875:1). Tugal-Tutkun et al (5) published a series of 880 patients with Behçet disease showing a ratio of 1:2.1; our results were compared with those of Tugal-Tutkun et al's finding that a statistically significant difference indeed exists ($p=0.014$).

The mean age at onset was 35.24 years (± 10.917 ; 21–61 years). The distribution by age group was as follows: 2 patients aged between 20 and 24 years (6.7%); 11 between 25 and 29 years (36.7%); 4 between 30 and 34 years (13.3%); 5 between 35 and 39 years (16.7%); 2 between 40 and 44 years (6.7%); 2 between 45 and 49 years (6.7%); 2 between 50 and 54 years (6.7%); 1 between 55 and 59 years (3.3%); and 1 between 60 and 64 years (3.3%). We did not observe any case under 21 years; this finding was also compared with Tugal-Tutkun et al's (5) results (in which series, 68 cases of the 880 were under 21 years), but in this case, the difference was not statistically significant ($p=0.52$).

In 23 patients, the disease course was recurrent. This course involved inflammation that presented abruptly but on remission there was no evidence of inflammatory activity whatsoever in the eye. In the rest of the patients the course was described as chronic, in which the same abrupt attacks were observed but the eye did not remain completely free of inflammation between flares. It should be noted that in patients showing a recurrent disease course, ocular inflammation between flares could be controlled with treatment, although inflammation returned when treatment was reduced or withdrawn.

In 9 patients, the disease manifested unilaterally, while in the remaining 21, clinical onset was bilateral.

In 5 of the 9 patients showing unilateral onset, the contralateral eye became affected within 2 years of diagnosis such that at the end of the study, both eyes were affected in 26 patients while in 4 patients, ocular involvement remained unilateral.

Of the 5 patients who underwent bilateralization, one did so at 4 months, another one at 6 months, two at 10 months, and a further one at 20 months. The mean time to bilateralization was 10 months, with a standard deviation of 7.12 months.

In 2 of the 30 patients, uveitis exclusively affected the anterior segment. In 8 patients, uveitis was solely posterior. There was one case of intermediate uveitis. The remaining 19 patients showed panuveitis.

The 21 patients in whom uveitis affected the anterior segment (those with anterior uveitis plus those with panuveitis) exhibited iridocyclitis with nongranulomatous persisting keratic precipitates (KPs) and Tyndall effect in the anterior chamber (grading from 1+ to 4+). All these patients had KPs and 1 of the 21 patients had a band keratopathy. Six of the 21 patients also displayed posterior iris-lens synechiae.

We observed a single case of intermediate uveitis. The clinical features of uveitis in this patient were as follows: a normal cornea, anterior Tyndall 0.5+, no synechiae, marked anterior vitreous Tyndall, and snowballs and sheathing of the outermost peripheral venules of the retina.

Of the 27 patients with posterior segment involvement, 3 had focal chorioretinitis, characterized by whitish infiltrates associated or not with intraretinal inflammation and with or without hemorrhages. Only one of the patients with posterior uveitis had a clinical picture of diffuse choroiditis. Among the patients with posterior involvement, 15 showed signs of diffuse vasculitis due to periphlebitis related to vascular exudates. Eight further patients showed the same form of vasculitis but of a focal nature.

During the course of the disease, three of our patients had a hypopyon. All three affected patients had panuveitis including vasculitis.

Five patients in the series had cataract. One of these patients was in the age group 25–29 years, 2 were in the 30–34-year-old group, 1 in the 35–39-year-old group, and 1 in the 50–54-year-old group.

In three of the patients, snowbank deposits were observed. One of these patients was the only case of intermediate uveitis recorded, and the remaining two patients had panuveitis, with diffuse vasculitis in one and focal vasculitis the other.

Ten patients had cystoid macular edema (CME) at some point during follow-up. One case was that of the patient with intermediate uveitis, and two affected patients had posterior uveitis with one diffuse and another focal vasculitis. The remaining patients with CME had panuveitis although with different posterior involvement: five with diffuse vasculitis, one with focal vasculitis, and one with diffuse chorioretinitis.

Seven patients had optic neuritis (optic disc edema or hyperemia). All but one of these patients had panuveitis with

varying posterior involvement (five diffuse and one focal vasculitis). The remaining patient had posterior uveitis with focal vasculitis.

One of the patient series had chronic episcleritis with acute exacerbations.

No significant correlation was observed between the sex of the patients and the clinical characteristics analyzed (the χ^2 test was used to compare proportions between sexes; p value > 0.05 in all cases).

DISCUSSION

Mamo calculated that if left untreated, Behçet disease leads to blindness 3.36 years after the presentation of ocular symptoms. This justifies research work on this disease (1). The disease affects persons throughout the world although it is most prevalent in countries connected by the silk trading route such as Turkey, Iraq, Saudi Arabia, Iran, Afghanistan, Pakistan, China, North and South Korea, and Japan (1–3). The prevalence in Spain seems moderately high with estimates by González-Gay *et al* for the northeast region being 0.66 cases per 100,000 persons (4). We were unable to estimate the incidence in our area because the Uveitis Department of the Hospital Clínico San Carlos of Madrid attends patients referred from the whole country when specialized care cannot be provided in their region.

Contrary to published data, we noted a slight predilection of the disease for women; this difference was statistically significant with regard to larger series (5). Also in contrast with previous findings, none of our affected patients was under the age of 21 years, but this observation was not statistically significant when compared with larger series (5).

Nine patients started unilateral disease and by end of follow-up, the disease remained unilateral in 4 of these (1, 3–10).

A further finding of significance was the single case of intermediate uveitis observed here. As far as we are aware, there are no descriptions in the literature of intermediate uveitis associated with Behçet disease. Our patient presented with typical intermediate uveitis: white eye, anterior chamber Tyndall 0.5+, anterior vitreous Tyndall (2+/3+), snowbank deposits, retinal periphlebitis in the extreme periphery, and lack of posterior involvement. According to Nussenblatt *et al* and Kanski (1, 2), the clinical picture of intermediate uveitis indicates one of three uveal syndromes: namely, pars planitis, chronic cyclitis, and senile

vitritis. Given its features (patient age 35 years, snowball deposits, and CME), the disease in our patient looks like pars planitis. However, despite this diagnosis, it is not clear whether this intermediate uveitis may be considered a manifestation of ocular Behçet syndrome. If we consider intermediate uveitis as an atypical form of uveitis in Behçet disease and therefore not a major diagnostic feature, then our patient can be described as having the incomplete form of the disease. The fact that in this patient ocular inflammation was aggravated during exacerbations of systemic clinical symptoms suggests an association between the uveitis process and Behçet disease (1-6).

No unexpected clinical findings were observed in the patient series examined.

No significant correlation was detected between patient sex and the clinical characteristics examined, contrary to the findings of most studies involving larger patient series (5). The most likely explanation is our reduced population size, which although *a priori* seem limited, we must not forget that we included every patient referred to our hospital with the complete or incomplete form of Behçet

disease with ocular inflammation between 1990 and 2002.

Ocular involvement in Behçet disease warrants careful attention since it is a chronic disease characterized by sudden bouts of ocular inflammation that may cause significant damage to several eye structures, with the consequent functional repercussions. Epidemiologic studies would help improve our understanding of the nature of this entity. Here, we present a descriptive study of 30 patients with Behçet disease and ocular inflammation. Future studies should address the therapeutic management of these patients along with their genetic characteristics and possible clinical and prognostic implications, as undertaken in other countries (7-10).

Proprietary interest: None.

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