Use of ultrasound biomicroscopy, indocyanine green angiography and HLA-B51 testing as adjunct methods in the appraisal of Behçet’s uveitis

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Abstract

Purpose: Behçet’s uveitis is not common in western Europe and the disease presentation is less obvious than in “endemic” countries such as Turkey and Japan. This makes the diagnosis more difficult. Early diagnosis is important, as the prognosis is better if therapy is started early. New methods such as ultrasound biomicroscopy (UBM) and indocyanine green angiography (ICGA) can improve the characterisation and diagnosis of uveitis. Our purpose was to present our experience with these new methods as well as HLA-B51 testing in the appraisal of patients with Behçet’s uveitis. Patients and Methods: Patients seen by the authors between 1997 and 2001 with Behçet’s uveitis or suspected Behçet’s uveitis and who underwent ICG angiography or UBM were included. Symptoms and signs, results of laboratory work-up including HLA-B51 antigen testing and the delay to diagnosis, were analysed. Fluorescein and ICG angiography and UBM testing were performed according to standard protocols used for uveitis patients and their contribution towards diagnosis and management were analysed. Results: Uveitis was non granulomatous in all patients. Fluorescein angiography showed moderate to severe diffuse retinal vasculitis compatible with Behçet’s uveitis in all cases. HLA-B51 testing was positive in 5 of 7 tested cases, being useful to orient the diagnosis. UBM contributed to the diagnosis in all five tested cases, being the determining element in 3 patients. It allowed redirection of the diagnosis from pars planitis to Behçet’s in 2 patients with poorly transparent media because it failed to show the typical pars planitis deposits. In a case originally diagnosed as Behçet’s it allowed correction of the diagnosis to pars planitis because of the presence of the typical UBM pars plana deposits. ICG angiography allowed detection of choroidal vasculitis in all five tested cases. Conclusions: In Behçet’s patients who did not present with a full-blown clinical picture, as they are often seen in non-endemic areas, UBM examination and HLA-B51 testing were valuable additional diagnostic elements helping to redirect the diagnosis correctly and to reduce the diagnostic delay in these patients. The hitherto unknown choroidal vasculitis shown by ICG angiography in all five investigated patients indicates that choroidal involvement probably occurs in most newly diagnosed Behçet’s patients.

Introduction

Behçet’s uveitis is relatively uncommon in Switzerland and in other western European Countries [1]. It is also less common to have the full-blown clinical picture in patients in these countries, as compared to countries where the disease is endemic. Because of a milder presentation and because our clinicians tend not to include Behçet’s uveitis in the differential diagnosis, diagnostic delay often occurs in these cases. However, early diagnosis is important as the prognosis is better when adequately dosed therapy is started early.

In the last years new diagnostic tools such as ultrasound biomicroscopy and indocyanine green angiography (ICGA) have become available for the appraisal of uveitis cases [2–5]. Firstly ultrasound biomicroscopy (UBM) is a high-frequency ultrasound
device allowing analysis of the retro-iridal space and the pars plana, areas that are mostly not accessible to clinical examination [6]. UBM examination of these areas is especially useful in inflammatory cases where the inflammatory process is suspected to be principally located in these structures. The yield of essential information obtained by UBM examination was maximal in cases with opacified media [6]. Secondly, indocyanine green (ICG) angiography is another major contribution to improve investigation of uveitis cases [7]. By giving imaging access to the choroidal compartment it allows the precise assessment of choroidal inflammatory involvement. Little is known so far about the involvement of choroidal vessels in Behçet’s uveitis. Thirdly, the use of HLA-B51 antigen testing in Behçet’s uveitis is controversial as the correlation with disease is much weaker than the association of HLA-A29 antigen with birdshot chorioretinopathy and the association of HLA-B27 antigen with acute anterior non-granulomatous uveitis. However in non-endemic Behçet-poor areas this test might present an additional diagnostic help to orient the diagnosis.

When necessary we routinely use these investigational modalities. The aim of this work was to analyse a group of consecutive Behçet patients for whom these tests were available and present our experience on their use in the appraisal of Behçet’s uveitis.

Patients and methods

Among all the new uveitis patients seen by the authors between 1997 and 2001, nine patients with Behçet’s uveitis or suspected Behçet’s uveitis underwent ICG angiography or UBM and were included in this study. In all patients fluorescein angiography was performed. In order to limit our study to primary inflammatory events and to avoid secondary non specific ICG angiographic signs, only patients with active untreated or inadequately treated disease were included. The symptoms and signs, association with HLA-B51, ICG and fluorescein angiographic signs, UBM features, latency to the diagnosis, therapy and the follow-up were analysed. The diagnosis was based on the criteria of the International Study Group for Behçet’s disease [8].

ICG angiography was performed according to a standard protocol as described earlier [7]. To exclude autofluorescence, preinjection fluorescence was looked for with the highest flash intensity used for ICG angiography. Frames of the posterior pole were taken at the early phase for up to 2 min. One posterior pole and 8 panoramic frames of the periphery were taken at the intermediate phase (10 ± 2 min) and late phase 40 ± 10 min) of the angiography. A Topcon TRC 50I/A® camera coupled to an ImageNet® image digitalizing system was used. ICG angiographic signs were analyzed and correlated with fundus findings and fluorescein angiographic signs at presentation and after introduction of therapy.

The UBM examination was performed according to a standard protocol as described earlier [6]. In short, a Humphrey® high-frequency ultrasound biomicroscope UBM 840, high-resolution system (Humphrey Instruments, Inc. San Leandro, CA) was used. Topical anesthesia was obtained by applying several drops of 1% tetracaine. A 21 mm diameter cylindrical eye cup was inserted between the eyelids and placed on the eyeball. A sterile physiologic salt solution or methyl cellulose solution was used to fill the eye cup. Hourly radial and longitudinal scans were performed on 360 degrees showing the irido-corneal angle, the ciliary body and the pars plana areas. The UBM signs were analyzed and correlated with fundus findings and fluorescein and/or ICG angiographic signs where the media were sufficiently transparent.

Therapy consisted of oral steroids in all Behçet’s patients, associated in seven of eight patients with Azathioprine and/or Cyclosporine A and/or Colchicine.

Results

Nine patients with Behçet’s uveitis or suspected Behçet’s uveitis were included. Our series was composed of 5 female and 4 male patients, with a mean age of 20 years (median: 12.5). In 8 patients the diagnosis of Behçet’s uveitis was established or confirmed. In 7 patients the diagnosis of Behçet’s uveitis was not known before. One patient had a uveitis for the first time 10 months after the occurrence of dermatological features. The delay between the occurrence of the first symptoms and the diagnosis of Behçet’s uveitis in the 7 newly diagnosed patients was 8 ± 6 months.

The uveitis was non granulomatous in all patients. Fundus examination revealed foci of retinitis and hemorrhage in all patients with transparent medias. The HLA B 51 antigen was positive in 5 of 7 investigated cases (71.4%). The fluorescein angiography showed extensive vasculitis of the retinal vessels and disc hyperfluorescence in all Behçet’s patients.