CASE REPORT

Presumed latent ocular tuberculosis diagnosed with the positive quantiFERON–TB Gold In-Tube Test in a HLA-A29-positive patient

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SUMMARY

A 59-year-old Hispanic woman presented with a 3-year history of floaters associated with bilateral reduced visual acuity. Her best-corrected visual acuity (BCVA) was 20/40. Both anterior segments were without inflammation, but funduscopy showed mild vitreous inflammation and multiple inflammatory choroidal lesions. Tests for inflammatory and infectious diseases were negative except for human leucocyte antigen A29. The patient was diagnosed with birdshot choroidoretinopathy, and treatment was initiated with cyclosporine A 2.5 mg/kg/day. One year after treatment, the patient reported systemic symptoms with no improvement in visual acuity. Fundus findings remained with vitreal inflammation. QuantiFERON-TB Gold In-Tube Test was positive, and a diagnosis of presumed latent ocular tuberculosis (TB) was made. We initiated anti-TB treatment for 9 months. At 6 months of anti-TB therapy, there was no active inflammation. The patient was followed for 2 years with no medications and no active inflammation. Her final BCVA was 20/25.

BACKGROUND

Inflammatory diseases, such as birdshot choroidoretinopathy, are associated with the presence of human leucocyte antigen (HLA) A29; however, the presence of HLA-A29 does not exclude the possibility of infectious diseases such as tuberculosis (TB), among others. Thus, it is important to test for this possibility. Interferon-gamma release assay (IGRA) tests are now inexpensive and can assist the physician in the differential diagnosis of presumed latent TB in a patient with intraocular inflammation, especially in the case of multifocal choroiditis. Treatment of the aetiological factor and control of inflammation could help the patient recover visual acuity and avoid risk of long-term systemic therapy.

CASE PRESENTATION

A 59-year-old Hispanic woman, with a history of dyslipidaemia treated with atorvastatin, presented with a 3-year history of floaters. The floaters increased in the past year and were associated with decreased visual acuity in both eyes. On examination, the best-corrected visual acuity (BCVA) was 20/40. The anterior segment was unremarkable, but the fundus examination showed mild vitreous cellularity. There were also multiple inflammatory lesions at the level of the retinal pigment epithelium and choroid, emanating from the optic nerve

(figure 1). After an initial diagnosis of bilateral white dot syndrome, tests for inflammatory and infectious diseases were negative except for HLA-A29. Birdshot choroidoretinopathy was diagnosed, and treatment was initiated with cyclosporine A (CsA, 2.5 mg/kg/day). One year after treatment, the patient reported no improvement in her visual acuity. Further, there was associated fatigue, weakness and hyporexia. Fundoscopy showed continuing active vitreal inflammation. The QuantiFERON-TB Gold In-Tube Test (Cellestis, Ltd, Carnegie, Australia) was positive, leading to the diagnosis of presumed latent ocular TB. Anti-TB therapy was initiated with rifampicin, isoniazid and pirazinamide for 2 months, followed by isoniazid and rifampicin for 7 months. There was no active inflammation after 6 months of anti-TB therapy, and CsA was stopped at that time. At 3 months after completion of the anti-TB treatment, the patient had better visual acuity, fewer floaters, no vitreal inflammation and no structural complications. The patient was followed for 2 years with no medication and no active inflammation (figure 2). Her final BCVA was 20/25.

INVESTIGATIONS

The following tests were run to detect the presence of inflammatory or infectious diseases: blood cell count and differential cell analysis, erythrocyte

Figure 1 Fundus photography and optical coherence tomography at presentation. Fundus photographs of the right (top left) and left (bottom left) eyes displayed some media opacity due to minimal vitreal inflammation and yellowish-white subretinal lesions around the optic disc and temporal vascular arcades. Optical coherence tomography of the right eye (top right) showed intraretinal fluid in the foveal area. The left eye (bottom right) showed no alterations.

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Figure 2 Fundus photography and optical coherence tomography 2 years after the completion of anti-inflammatory and antituberculosis treatment. Fundus photography of the right (top left) and left (bottom left) eyes showed no vitreal inflammation; however, yellowish-white subretinal lesions around the optic discs and temporal vascular arcades persisted. Optical coherence tomography of the right (top right) and left (bottom right) showed no morphological alterations.

sedimentation rate, renal and liver functions, circulating immune complexes, Angiotensin converting enzyme (ACE), antinuclear antibody, anti-DNA, anti-Ro, anti-La, antineutrophil cytoplasmic antibody, HLA-A29, HLA-B27, HLA-B51, skin test for TB, treponemic test for lues (fluorescent treponemal antibody absorption), chest radiographs and antibodies against borrelia, toxocara, toxoplasmosis, rickettsia and bordetella. All were negative or within control limits except for HLA-A29.

DIFFERENTIAL DIAGNOSIS

For patients with white dot lesions, there are two types of pathologies: inflammation and infectious disease. Within the inflammatory group, sarcoidosis and white dot syndrome are the first diagnostic choice. Within the infectious group, TB and syphilis are the first entities to suspect.

TREATMENT

Once the initial diagnosis of birdshot choroidoretinopathy was made, treatment with low doses of CsA was indicated. The diagnosis of presumed latent TB was made after 1 year of CsA treatment. While anti-TB therapy was instituted at that time, CsA therapy was continued for another 6 months without any adverse effects. When the diagnosis of presumed latent ocular TB was made, we initiated treatment with rifampicin, isoniazid and pirazinamide for 2 months. This treatment was followed by isoniazid and rifampicin for the next 7 months. No adverse effects were detected during anti-TB treatment.

OUTCOME AND FOLLOW-UP

The patient was followed for 2 years with no medications and no active inflammation. The final BCVA was 20/25.

DISCUSSION

Birdshot choroidoretinopathy is an uncommon form of posterior uveitis.^{1 2} The natural course of the diseases is chronic, with multiple exacerbations and remissions,³ and poor response to systemic corticosteroids alone.^{4 5} The early diagnosis and introduction of immunomodulatory therapy offers the best strategy for long-term control.^{6 7} The presence of HLA-A29 has a strong association with birdshot choroidoretinopathy,¹ but even among normal subjects, 7.7% are HLA-A29 positive.³ Additionally, a high level of HLA-A29 does not exclude the presence of other ocular inflammatory or infectious diseases.

That is why it is important to rule out the presence of other diseases so that patients can receive the best care possible. In our case, after 1 year of a low-dose CsA regimen, the patient remained unchanged and with constitutional symptoms including anorexia, weight loss and fatigue. Although the initial laboratory tests, TB skin test and chest radiographs were negative, to be thorough, we performed QuantiFERON-TB Gold In-Tube Test, which was introduced at our institution in December 2011. This test identifies presumed latent ocular TB infection better than the tuberculin skin test in a population vaccinated by BCG.⁸ In Spain, people born before 1970 received mandatory TB vaccinations. The IGRA QuantiFERON-TB Gold In-Tube Test can differentiate the presence of latent TB from patients with positive skin tests due to vaccinations and those with negative skin tests due to anergy, such as occurs with sarcoidosis. The QuantiFERON-TB test is performed on all patients scheduled to undergo immunosuppressive or biological therapy. Treatment for at least 9 months is mandatory to prevent systemic and ocular damage secondary to recurrences.⁹

Learning points

- ▶ Birdshot choroidoretinopathy is an uncommon form of posterior uveitis, with multiple recurrences, structural ocular complications and an impact on visual acuity.
- ▶ The presence of positive biomarkers and specific morphological patterns does not rule out the presence of other diseases.
- ▶ In a patient with uveitis, it is always necessary to rule out infectious diseases.
- ▶ QuantiFERON-TB Gold In-Tube Test identifies presumed latent ocular tuberculosis (TB) infection better than the tuberculin skin test.
- ▶ Presumed latent ocular TB should be treated for at least 9 months to prevent inflammatory recurrences.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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