Fuchs' heterochromic uveitis and sarcoidosis

Richard R Goble, Philip I Murray

Abstract

Aims/Background—The aetiology of Fuchs' heterochromic uveitis (FHU) is unknown although it can occur in combination with a number of different ocular conditions. Five patients with FHU who show an association with sarcoidosis were studied.

Methods—Four patients with clinical signs compatible with FHU who had elevated serum angiotensin converting enzyme levels (sACE), and a fifth case with a normal sACE and a positive Kveim test were described.

Results—All five cases had iris nodules, two later developed mutton fat keratic precipitates, and one had peripheral retinal periphlebitis. Of the four cases with elevated sACE, one had respiratory function test abnormalities and an abnormal chest x ray compatible with pulmonary sarcoidosis. Another had a chorioretinal scar and developed intermediate uveitis 2 years after presentation.

Conclusions—In all of these cases a diagnosis of FHU may represent a specific secondary ocular response to sarcoidosis rather than a primary idiopathic uveitis syndrome. Although FHU remains a clinical diagnosis, routine uveitis investigations should still be performed in this group of patients.

(*Br J Ophthalmol* 1995; 79: 1021–1023)

Fuchs' heterochromic uveitis (FHU) is described as an inflammatory condition of unknown aetiology which is usually unilateral. Some of the features which typify FHU include uniformly distributed stellate keratic precipitates (KPs), anterior chamber cells, iris stromal atrophy with heterochromia, iris nodules, abnormal angle vessels which bleed on gonioscopy or hypotony, and vitreous opacities. Cataract is common and secondary glaucoma occurs in 15% to 30% of patients.¹ An acutely red eye, posterior synechiae, retinal vasculitis, and cystoid macular oedema (CMO) are not associated. The uveitis is poorly responsive to steroid treatment.

More recent reviews have suggested that far from being a specific clinical entity, FHU may have multiple causes as well as a spectrum of clinical features and merely represents a particular ocular response.^{1,2} FHU has been reported in combination with numerous conditions including toxoplasmosis,³ Horner's syndrome,⁴ retinitis pigmentosa,⁵ Coats' disease,⁶ and progressive hemifacial atrophy.⁷

We report a possible association between FHU and sarcoidosis.

Materials and methods

We present the clinical details of five patients attending the uveitis clinics of the Birmingham and Midland Eye Hospital. In four cases the clinical picture was of FHU in a case of possible sarcoidosis as each patient had elevated serum angiotensin converting enzyme (sACE) concentrations. The fifth case showed the characteristic findings of FHU with a normal sACE and a positive Kveim test, consistent with a diagnosis of sarcoidosis.

Results

CASE 1

A 14-year-old Afro-Caribbean girl was referred from her optometrist complaining of floaters in her right eye. Her visual acuities were 6/18 right and 6/6 left. Her right eye was white and painless with stellate, uniformly distributed KPs, diffuse iris stromal atrophy with mild heterochromia, Koeppe nodules, 1+ cells in both the anterior chamber and anterior vitreous, an early posterior subcapsular lens opacity (PSCLO), and peripheral retinal periphlebitis. There were no posterior synechiae, CMO, intermediate uveitis, or choroidal lesions. The left eye was entirely normal. Investigations revealed an elevated sACE of 90 U/l (normal range 15–71). Chest x ray demonstrated a ground glass appearance in the mid zone with poor visualisation of pulmonary vessels in both mid and upper zones. Spirometry was consistent with a restrictive lung disease. Bronchoscopy with lavage was inconclusive. Other investigations – full blood count, plasma viscosity, urea and electrolytes, and blood sugar – were all within normal limits, and the Venereal Disease Research Laboratory/Treponema pallidum haemagglutination test (VDRL/TPHA) was negative.

The findings have remained unchanged during 3 years of follow up.

CASE 2

A 28-year-old Asian woman presented to casualty with an inflamed meibomian cyst in her left upper eyelid. There were no other ocular symptoms. Her mother had sarcoidosis. On examination her visual acuities were 6/6 in either eye. Her right eye had characteristic stellate KPs, cells in the anterior chamber, and there was iris heterochromia with crystals on the surface of the right iris. There were aggregations of cells in the right inferior vitreous gel. There were no posterior synechiae, retinal vasculitis, CMO, intermediate uveitis, retinal or choroidal lesions. The left eye was normal. Chest x ray was unremarkable, and sACE was elevated at 98 U/l (normal 15–71). Other investigations – full blood count, plasma viscosity, urea and

Academic Unit of Ophthalmology, Birmingham and Midland Eye Hospital
R R Goble
P I Murray

Correspondence to:
Mr P I Murray, Academic Unit of Ophthalmology, Birmingham and Midland Eye Hospital, Church Street, Birmingham B3 2NS.

Accepted for publication
18 July 1995

electrolytes, and blood sugar – were all within normal limits, and the VDRL/TPHA was negative.

The meibomian cyst was incised and curetted under local anaesthesia, with histological examination of the curettings not demonstrating any granulomata. The patient has been followed up for 3½ years without any significant clinical change.

CASE 3

A 14-year-old white girl presented with a 1 month history of floaters in her left eye. She had no other ocular symptoms. Her visual acuities were 6/5 in either eye. Examination of her left eye revealed stellate KPs mainly inferiorly, with iris stromal atrophy, particularly noticeable at the collarette, with associated heterochromia. Koeppe nodules were present. There were 2+ anterior chamber and anterior vitreous cells. There were no posterior synechiae, retinal vasculitis, CMO, intermediate uveitis, retinal or choroidal lesions. Chest x ray was normal and sACE was elevated at 98 U/l (normal 15–71). Other investigations – full blood count, plasma viscosity, urea and electrolytes, and blood sugar – were all within normal limits, and the VDRL/TPHA was negative.

Four months' follow up has not revealed any clinical change.

CASE 4

A 43-year-old Afro-Caribbean woman noticed that her left iris was a different colour from her (normal) right iris and that the vision in her left eye was blurred. The visual acuities were 6/5 right and 6/12 left. The left cornea had uniformly distributed stellate KPs with a few inferior mutton fat KPs. The left iris had marked stromal atrophy with both Busacca and Koeppe nodules. The intraocular pressure was elevated at 26 mm Hg and there was an early PSCLO. There were no posterior synechiae, retinal vasculitis, CMO, or intermediate uveitis. A peripheral pigmented chorioretinal scar without overlying vitritis was noted. There was an elevated sACE of 75 U/l (normal 15–71). Chest x ray was normal and toxoplasma IgG was positive at a titre of 1 in 128. A Mantoux test was negative, but the patient had never received a BCG vaccination. Other investigations – full blood count, plasma viscosity, urea and electrolytes, and blood sugar – were all within normal limits, and the VDRL/TPHA was negative.

The glaucoma responded to topical β blockers. Two years after presentation, the patient developed intermediate uveitis with mild CMO in the left eye. Six years after presentation, the patient developed bilateral gelatinous conjunctival follicles without associated conjunctival injection or keratitis. A conjunctival biopsy was performed which showed non-specific inflammatory changes.

CASE 5

A 34-year-old white woman presented with blurred vision and floaters in her right eye.

Her eye was white and painless. She had had a BCG vaccination 8 years previously as a family contact had contracted tuberculosis. The visual acuities were 6/12 right and 6/6 left. In the right eye, there were uniformly distributed stellate KPs, 1+ cells in the anterior chamber, and the intraocular pressure was 33 mm Hg. The iris showed characteristic stromal atrophy and heterochromia, and there were numerous Koeppe nodules. Gonioscopy was unremarkable. There was an early PSCLO and 1+ cells in the anterior vitreous. There were no posterior synechiae, retinal vasculitis, CMO, intermediate uveitis, retinal or choroidal lesions. The left eye was entirely normal. Chest x ray was normal and the sACE was 30 U/l (normal 15–71). Two Mantoux tests were negative at doses of 1/10 000 and 1/1000. A Kveim test demonstrated granulomata, consistent with a diagnosis of sarcoidosis. Other investigations – full blood count, plasma viscosity, urea and electrolytes, and blood sugar – were all within normal limits, and the VDRL/TPHA was negative.

The glaucoma was initially treated with a topical β blocker. Three years after presentation, some of the KPs had become mutton fat in appearance, although they remained uniformly distributed. The right cataract progressed and the visual acuity reduced to counting fingers. The right intraocular pressure was increased at 34 mm Hg. The patient underwent a combined right trabeculectomy and extracapsular cataract extraction with implantation of a heparin surface modified intraocular lens. Despite the latter, giant cells accumulated on the anterior implant surface. These were successfully dispersed using a Nd:YAG laser. Postoperative visual acuity was reduced to 6/18 by dense anterior vitreous opacities. There is no biomicroscopic evidence of CMO and she has now been followed up for 8 years.

Discussion

Diagnosing ocular sarcoidosis may be difficult as the Kveim test is now little used and there may be no granulomatous tissue that can be readily biopsied. Blind endobronchial or conjunctival biopsy in patients without evidence of systemic disease may be unnecessarily invasive. An elevated sACE in patients with uveitis implies a granulomatous aetiology.⁸ It is not a specific test for sarcoidosis, but a recent study has shown that 73% of biopsy proved sarcoidosis compared with 17% of non-sarcoid controls had elevated sACE.⁹ Interestingly one of the 12 in the latter group was a patient with FHU. In young children, sACE levels may be slightly higher than in adults,¹⁰ but we would still consider cases 1 and 3, who were both 14 years old, to have abnormally raised levels. A study at our unit has compared a group of biopsy proved ocular sarcoid patients with a group of patients with signs considered typical of ocular sarcoid and an elevated sACE (half of whom also had an abnormal chest x ray). There was no statistically significant difference between the two groups in age, race or the incidence of anterior uveitis, posterior uveitis with retinal vasculitis,

iris nodules, or hypopigmented spots in the peripheral fundus (Stavrou *et al*, submitted for publication). It could be argued that an elevated sACE and a typical uveitis are enough to make a diagnosis of ocular sarcoidosis, once other granulomatous causes have been excluded. Workers in Cleveland, USA have recently presented similar findings (E M Dodds, personal communication).

All our five cases had classic features of FHU with no clinical features of other diseases associated with elevated sACE such as leprosy, primary biliary cirrhosis, or Gaucher's disease.⁸ Case 5 had histological evidence of sarcoidosis from the Kveim test. Of the other four possible sarcoidosis cases, case 1 had an abnormal chest x ray and respiratory function tests consistent with pulmonary sarcoidosis and was also noted to have retinal periphlebitis, which would be atypical of FHU. Case 3, although typical in almost every other way, had stellate KPs which were distributed only inferiorly. Cases 4 and 5 developed mutton fat KPs which are more compatible with a diagnosis of granulomatous uveitis. There is an association between the chorioretinal scar seen in case 4 and FHU, although the aetiological significance remains unclear.¹⁻³ Case 4 also developed classic intermediate uveitis 2 years after presentation. Intermediate uveitis is said to be one of the main differential diagnoses of FHU, although other authors consider posterior cyclitis with secondary FHU to be an alternative diagnosis.¹¹ The incidence of iris nodules in FHU is about 20–30%.¹² All five of our cases had iris nodules which, although consistent with the diagnosis of FHU, would equally fit with ocular sarcoidosis or another granulomatous uveitis.

The aetiology of FHU is still widely debated, and it may be that it is merely a secondary phenomenon or a clinical end state

of one of a number of possible infective and/or immunological triggers.^{1 2 13 14} Our five cases of possible/probable ocular sarcoidosis presenting as secondary FHU would support this view. The association between FHU with elevated sACE has not been widely reported. Although FHU remains a clinical diagnosis, concurrent systemic and ocular abnormalities should be looked for and routine uveitis investigations should still be performed.

- 1 Jones NP. Fuchs' heterochromic uveitis: an update. *Surv Ophthalmol* 1993; 37: 253–72.
- 2 La Hey E, de Jong PTVM, Kijlstra A. Fuchs' heterochromic cyclitis: review of the literature on the pathogenetic mechanisms. *Br J Ophthalmol* 1994; 78: 307–12.
- 3 De Abreu MT, Belfort R, Hirata PS. Fuchs' heterochromic cyclitis and ocular toxoplasmosis. *Am J Ophthalmol* 1982; 93: 739–44.
- 4 Regenbogen LS, Naveh-Floman N. Glaucoma in Fuchs' heterochromic cyclitis associated with congenital Horner's syndrome. *Br J Ophthalmol* 1987; 71: 844–9.
- 5 Vourre I, Sarre M, Tilikainen I, Rasanen O. Fuchs' heterochromic cyclitis associated with retinitis pigmentosa: a family study. *Can J Ophthalmol* 1979; 14: 10–6.
- 6 Tsalamas MD, Kritzing EE, Murray PI. Coats' disease and Fuchs' heterochromic cyclitis. *Ocular Immunol Inflamm* 1994; 1: 49–50.
- 7 La Hey E, Baarsma GS. Fuchs' heterochromic cyclitis and retinal vascular abnormalities in progressive hemifacial atrophy. *Eye* 1993; 7: 426–8.
- 8 Weinreb RN, Kimura SJ. Uveitis associated with sarcoidosis and angiotensin converting enzyme. *Am J Ophthalmol* 1980; 89: 180–5.
- 9 Neves RA, Rodriguez A, Power WJ, Pedroza-Seres M, Foster CS. The value of combined serum angiotensin converting enzyme and gallium scan in the diagnosis of ocular sarcoidosis. In: Nussenblatt RB, Whitcup SM, Caspi RR, Gery I, eds. *Advances in ocular immunology*. Amsterdam: Elsevier, 1994: 353–6.
- 10 Baarsma GS, La Hey E, Glasius E, de Vries J, Kijlstra A. The predictive value of serum angiotensin converting enzyme and lysozyme in the diagnosis of ocular sarcoidosis. *Am J Ophthalmol* 1987; 104: 211–7.
- 11 Saraux H, Laroche L, Le Hoang P. Secondary Fuchs' heterochromic cyclitis: a new approach to an old disease. *Ophthalmologica* 1985; 190: 193–8.
- 12 Rothova A, La Hey E, Baarsma GS, Breebaart AC. Iris nodules in Fuchs' heterochromic uveitis. *Am J Ophthalmol* 1994; 118: 338–42.
- 13 Murray PI, Hoekzema R, van Haren MAC, de Hon FD, Kijlstra A. Aqueous humor interleukin-6 levels in uveitis. *Invest Ophthalmol Vis Sci* 1990; 31: 917–20.
- 14 Murray PI. Fuchs' heterochromic cyclitis: an immunological disease or an immunological response? *Int Ophthalmol* 1995; 18: 313–4.