absolutely discriminatory. For example in case reports of RPE adenocarcinomas basement membrane elaboration has been detected.^{2,3} Likewise, no mitoses were observed by light microscopy in a lesion eventually determined to be neoplastic⁴ and there were no unique histological patterns that differentiated hyperplasia from neoplasia. To complicate the issue there is evidence that neoplasia can arise from sites of hyperplasia/inflammation⁵ and RPE hyperplastic lesions can assume tumorous proportions.⁶ Therefore, some tumours still have to be placed equivocally in spectrum between definite benign hyperplasia and definite neoplasia.¹

Case report

A 10 year old girl presented with idiopathic left anterior iritis, visual acuity was Snellen 20/20 bilaterally. Over the next year the condition progressed to bilateral panuveitis necessitating the use of oral corticosteroids. Bilateral submacular haemorrhages secondary to choroidal neovascular membrane developed (fig 1A) and visual acuity decreased to 20/200 bilaterally. Fundal examination at this time also showed bilateral "punched out" chorioretinal lesions in the peripheral retina but more prominent inferiorly. Right visual acuity improved to 20/80 after surgical removal of choroidal neovascular membrane in this eye.

The excised choroidal neovascular membrane had a fibrovascular core as has been reported with CNV of various aetiologies in other series.⁷ The cortex was unorthodox in structure, consisting of a thick mass of RPE cells in a tubulo-acinar pattern separated from each other by periodic acid Schiff positive extracellular material as opposed to a thin layer of RPE cells and fibrin normally expected⁷ (fig 1 B, C). By immunohistochemistry these RPE cells were cytokeratin (CK) 7 positive but CK8/18 negative (fig 1D, E). The intervening extracellular material stained for collagen IV and laminin indicating that it is essentially basement membrane (data not shown).

Comment

An unusual feature in this patient is the RPE pattern, which is akin to that usually found in RPE neoplasia⁴ or rare tumour-like hyperplasia associated with inflammatory scars⁶ rather than CNV.

Previously, we have examined cytokeratin expression in hyperplastic RPE cells in a series of subretinal lesions (where the cells may also adopt a variety of shapes ranging from spindle to oval or cuboidal). In these cells, CK7 is prominent and the simple epithelial cytokeratins 8 and 18 tend to be downregulated⁸ (fig 1F, G). True RPE neoplasia is rare. However, we were able to compare the cytokeratins in one such neoplasm with those of normal and reactive RPE cells. Consistent with neoplasia in other simple epithelia,⁹ neoplastic RPE cells retained CK8/18. Moreover, these cells did not express CK7 (fig 1H, I). Thus the pattern of CK in the present specimen, with loss of CK8/18 and gain of CK7, is consistent with that of hyperplastic rather than neoplastic RPE. Therefore, the final histological diagnosis was CNV of inflammatory aetiology with associated RPE gross hyperplasia. It can be difficult to discriminate between neoplastic and hyperplastic RPE when the latter adopt a tubulo-acinar arrangement: our findings suggest that cytokeratin subtyping may help distinguish between these two forms of growth.

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Use of pulmonary interferon γ responses to mycobacterial antigen to distinguish sarcoid associated optic neuropathy from tuberculosis

The clinical distinction between sarcoidosis and tuberculosis (TB) can be difficult.¹ Abnormal CD4 T cell function, demonstrated as cell mediated hyporesponsiveness

(anergy), is considered to be a feature of sarcoidosis.² Here we report the use of a sensitive assessment of mycobacterial specific CD4 T cell response to assist in the diagnosis of sarcoid associated optic neuropathy in a subject at high risk of TB.

Case report

A 53 year old Asian-Indian woman was referred with a 2 month history of intermittent blurred vision in her right eye and right optic disc swelling. She developed right eye ache and her vision deteriorated over 3 days to counting fingers in this eye. She also complained of malaise and night sweats though her weight was stable. She had recently returned to the United Kingdom after living in Uganda. Examination revealed a right afferent pupillary defect, chronically swollen right optic disc, and a partial macular star with peripheral retinal vascular sheathing (fig 1).

Investigations showed a normal chest radiograph, full blood count, renal and hepatic function, erythrocyte sedimentation rate and C reactive protein; with a moderately raised serum angiotensin converting enzyme of 90 IU/l (normal range 27-82). Treponemal antibodies were not detected. *Toxocara*, *Bartonella henselae*, and *B quintana* IgM and IgG were negative; as were HIV-1 and HIV-2 antibody tests. Toxoplasma IgG was not detected. A tuberculin skin test (TST) was negative. A magnetic resonance imaging (MRI) scan of her brain and orbits showed gadolinium enhancement of her right optic nerve head. Gallium scanning demonstrated tracer uptake in the lacrimal and parotid glands, pulmonary hila and liver, as well as diffusely in the lungs. Bronchoscopy and bronchoalveolar lavage (BAL) revealed no mucosal abnormalities. TB smear, nucleic acid amplification test, and culture were negative. Absolute leucocyte and lymphocyte numbers, as well as the percentages of CD3+, CD4+, and CD8+ T cells were determined using CD45, CD4, and CD8 antibodies.³ The lymphocyte percentage was elevated at 36.3% (normal <15%) as was the CD4/CD8 lymphocyte ratio among CD3+ lymphocytes at 27.7 (normal range 1-3). The BAL was then examined for interferon γ (IFN- γ) production by lymphocytes in response to overnight stimulation with purified protein derivative of *M tuberculosis* (PPD) as previously described.⁴ Within the CD4+ T cell population the frequency of PPD specific IFN- γ lymphocytes was 0.47%. This is one tenth of the frequency observed in pulmonary and extra-pulmonary TB.⁴ Taking all data together, a

Figure 1 Colour fundus photograph of patient's right eye showing optic disc swelling with a partial macular star.

diagnosis of sarcoid associated optic neuropathy was made.

Treatment with oral prednisolone 80 mg daily resulted in resolution of her disc swelling and retinal vascular changes with modest improvement in her visual field. Her systemic symptoms abated.

Comment

Our patient had several risk factors for TB. She is Asian-Indian and had developed night sweats and an unusual inflammatory optic neuropathy with severe visual loss shortly after her return from living in a part of the world where TB is endemic. Thus, it was important in terms of her clinical management to distinguish between sarcoidosis³ and TB⁶⁻⁷ as reliably as possible. Although she had a marked BAL lymphocytosis and elevated CD4/CD8 ratio, both of which are associated with sarcoidosis, these measures may also be increased in TB.⁸ We believe that flow cytometric analysis can help here by providing on one sample not only BAL T cell data but also an indication of pulmonary IFN- γ production in response to mycobacterial antigen (PPD). While strongly positive in almost all cases of active pulmonary or extrapulmonary TB,⁴ the PPD test appears to be negative in sarcoidosis.

Other reported antigen specific T cell based TB assays have used blood.⁹ We think that these might be less sensitive than tests using either BAL or body fluids from sites of active TB.¹⁰ Given we are proposing that a negative result assists in distinguishing sarcoidosis from TB it is likely to be quicker and more effective to use BAL as a single, sensitive test than an algorithm where one moves from TST through blood tests to BAL analysis if the preceding step is negative.

Although our data require validation, we think our findings may have application in cases where the clinical diagnosis is equivocal, laboratory tests are unhelpful, and the need for appropriate, specific treatment is urgent.

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MAILBOX

Polymicrobial keratitis

We read with great interest the clinical report by Pate *et al* in which bacterial co-infection in keratomycosis was reported by smear, culture, or both.¹ We have seen in our own practice in a series of 110 cases of infectious keratitis (unpublished data) between 2001 and 2005, six cases of bacterial co-infection in keratomycosis. Five of them were smear positive and one case was only culture positive for bacteria. In all these cases, the mycotic element was septate fungus—*Fusarium* spp, and not yeast as reported by these authors. We had suspected polymicrobial keratitis clinically in all these cases because of certain distinctive features at presentation. The typical raised dry infiltrate with hyphate margins, which is so characteristic of keratomycosis, was modified into wet looking necrotic infiltrate in some areas; epithelial defect overlying the infiltrate showed extension beyond the infiltrate in some areas. Treatment in all these cases is incomplete if a thorough microbiological investigation is not done. Clinical judgment does not suffice to treat microbial keratitis in many cases; rather we advocate laboratory support.

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NOTICES

Managing human resources

The latest issue of *Community Eye Health* (No 56) assess the use of human resources in the delivery of eye care. For further information please contact: Journal of Community Eye Health, International Resource Centre, International Centre for Eye Health, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, UK (tel: +44 (0)20 7612 7964; email Anita.Shah@lshtm.ac.uk; url: ; online edition: www.jceh.co.uk). Annual subscription (4 issues) UK £28/US\$45. Free to developing country applicants.

8th EUNOS Meeting – 2007

The 2007 European Neuro-ophthalmology Society meeting (EUNOS; www.eunos.web.org) will be taking place in Istanbul, Turkey on 26-29th May 2007. For further information please visit www.eunos2007.org or contact Pinar Aydin aydinp@eunos2007.org

Teaching courses on Retinal and Vitreous Surgery

Several teaching courses on Retinal and Vitreous Surgery have been organised throughout 2006 and 2007 around the world in association with the International Faculty. For further information on each of these courses please contact Ingrid Kressig, Univ.-Augenlinik Theodor-Kutzer-Ufer 1-3, 68164 Mannheim, Germany; email: Ingrid.kressig@augen.ma.uni-heidelberg.de; website: <http://kressig.uni-hd.de/>.

EVER 2006

The EVER 2006 meeting will take place in Vilamoura, Portugal on 4-7th October 2006. For further information please contact the EVER Office, Kapucijnenvoer 33, 3000 Leuven, Belgium; website www.ever.be

Prevention of Blindness Fellowship Programme

Applications are invited for BCPB Fellowships to start in 2007. The aim of the Fellowships is to fund research and training in prevention of blindness for high caliber clinicians and scientists from the UK and overseas. Projects must further the goals of VISION 2020: THE RIGHT TO SIGHT, the elimination of avoidable blindness. In 2007, the BCPB seeks to fund one Fellow from the UK and one Fellow from a low-income country to undertake projects that focus on Africa.

Priority will be given to applicants who:

- Demonstrate that their project is innovative and increases knowledge of the causes of blindness and/or its prevention in line with the priorities of VISION 2020
- Demonstrate the ability and ambition to pass on their skills in blindness prevention

The fellowships will be worth up to £60,000pa for 2 or 3 years. Applications must be submitted jointly by the Fellowship candidate and the supervisor at the host institution in the UK.

For full information and an application form, see www.bcpb.org or contact Jackie Webber at BCPB, 59-60 Russell Square, London WC1B 4HP or by email: info@bcpb.org. Closing date for applications is 30 September 2006.