Three weeks later she was readmitted with increasing dyspnoea and blurred vision. Chest *x* ray and computed tomography findings were compatible with diffuse interstitial fibrosis in both lungs. Funduscopy revealed peripapillary choroidal lesions with disc swelling bilaterally (fig 2). This time the choroidal lesions were peripapillary only rather than throughout the posterior pole, with exudative detachments inferiorly. Recurrent *P jiroveci* pneumonia and choroiditis was diagnosed and oral atovaqoune and high dose prednisolone were commenced. Within 3 weeks her fundal appearance resolved leaving only some pigmentary changes. Her discharge medication included daily oral prednisolone 40 mg, cotrimoxazole 960 mg, and inhaled pentamidine. There have been no further intraocular recurrences.

Comment

Pneumocystis jiroveci is a commensal, found in the respiratory tract of healthy individuals. It can cause infections of almost any organ in immunocompromised hosts.[1–3] *P jiroveci* choroiditis has been reported in immunocompromised patients despite prophylactic use of inhaled pentamidine.[4 5] The diagnosis is based on the clinical findings of multifocal yellowish circular choroidal lesions at the posterior pole. *P jiroveci* has been found in these lesions on histological sections[3 5] and the lesions resolve on systemic anti-pneumocystis treatment.[4] However, most cases of *P jiroveci* choroiditis are diagnosed histologically post mortem.[3 6]

Thus, the acute clinical findings may be more varied than previously described. In our patient, massive exudative retinal detachments were associated with the previously described choroidal lesions. The clinical picture varied on the second presentation, but there was complete and rapid resolution of the signs with anti-pneumocystis therapy. To the best of our knowledge, this is the first report of *P jiroveci* choroiditis causing exudative retinal detachments. *P jiroveci* should be considered in the differential diagnosis of susceptible patients, even if the ophthalmological findings are ''atypical.''

K Sabri, K Bibby
Department of Ophthalmology, Leicester Royal Infirmary, Leicester LE1 5WW, UK

Correspondence to: K Sabri, Department of Ophthalmology, Leicester Royal Infirmary, Leicester LE1 5WW, UK; ksabri@yahoo.com

doi: 10.1136/bjo.2005.077479

Accepted for publication 21 August 2005

References

1 **Dugel PU**, Rao NA, Forster DJ, *et al*. Pneumocystis carinii choroiditis after long term aerosolized pentamidine therapy. *Am J Ophthalmol* 1990;**110**:113–17.
2 **Whitcup SM**, Fenton RM, Pluda JM, *et al*. Pneumocystis carinii and Mycobacterium avium-intracellulare infection of the choroid. *Retina* 1992;**12**:331–5.
3 **Northfelt DW**, Clement MJ, Safrin S. Extrapulmonary pneumocystosis: clinical features in human immunodeficiency virus infection. *Medicine* 1990;**69**:392–8.
4 **Sneed SR**, Blodi CF, Berger BB, *et al*. Pneumocystis carinii choroiditis in patients receiving inhaled pentamidine. *N Engl J Med* 1990;**322**:936–7.
5 **Rao NA**, Zimmerman PL, Boyer D, *et al*. A clinical, histopathologic, and electron microscopic study of pneumocystis carinii choroiditis. *Am J Ophthalmol* 1989;**107**:218–28.
6 **Macher A**, Bardenstein D, Zimmerman L, *et al*. Pneumocystis carinii choroiditis in a male homosexual with AIDS and disseminated pulmonary and extrapulmonary P carinii infection. *N Engl J Med* 1987;**316**:1092.

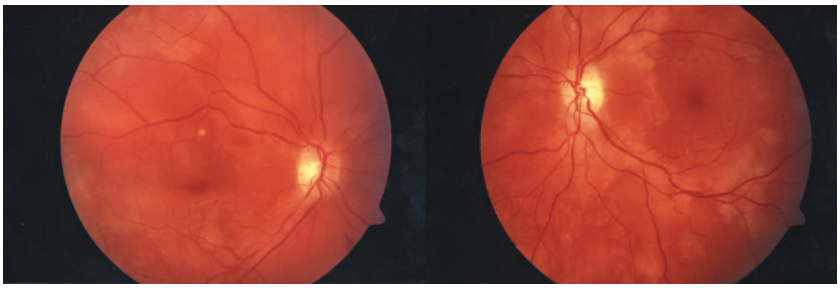

Figure 1 Multifocal, creamy-yellow choroidal lesions at both posterior poles with massive exudative retinal detachments at the maculae.

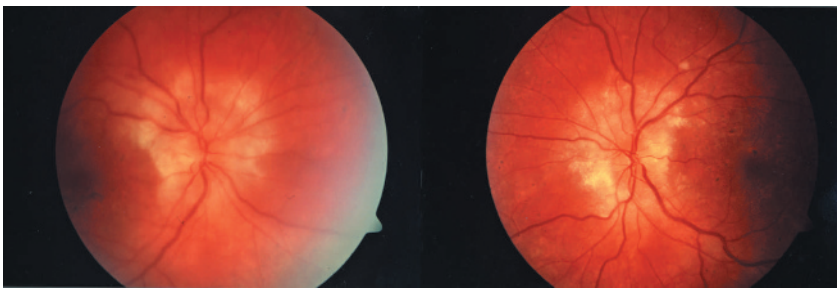

Figure 2 peripapillary choroidal lesions with disc swelling.

Prothrombotic and atherosclerotic risk factors lack significance in NAION patients harbouring mitochondrial DNA mutations

We recently reported that a group of patients with non-arteritic anterior ischaemic optic neuropathy (NAION) had an increased prevalence of potentially pathological mitochondrial DNA (mtDNA) mutations, implying a link between mitochondrial disease and this optic neuropathy.[1] We decided to investigate the association of other risk factors for NAION in these same patients.

Case reports

NAION patients were genotyped for the presence of prothrombotic polymorphisms that have been reported in association with NAION,[2 3] including factor II G20210A prothrombin variant, factor V Leiden G1691A variant, MTHFR C677T and A1298C variants, platelet glycoprotein receptor IIIa (PI^{A2}) allele, and apolipoprotein E (4) allele, as described previously.[4–8] These reports included large control groups that were ethnically matched to our NAION patients and that had been queried regarding the presence of atherosclerotic risk factors. Controls older than 50 years were selected for comparison with NAION patients.

Table 1 shows that the prevalence rates for prothrombotic variants among NAION patients did not differ from controls. Reported prevalence of diabetes, hypertension, and hyperlipidaemia was relatively high in NAION patients but was also not significantly different from controls.

Comment

The lack of a significant association between NAION patients and controls in relation to thrombophilic genetics markers has been reported before,[9] and the role of these factors remains uncertain. More surprising is the lack of a statistical association with atherosclerotic risk factors. For example, in our group of NAION patients, 68% were diabetic, but this figure did not differ significantly from the prevalence of more than 50% in well matched controls. This observation reflects the high, and rising, frequency of diabetes and other atherosclerotic risk factors in the developing world.

A few qualifications are appropriate. NAION patients were a relatively small group of Middle Eastern Arabs, and it is possible that a larger group would have yielded statistically significant results or that the observations reported here are specific to this genetically homogeneous population. Atherosclerotic risk factors were assessed by individual report from patients and controls, and the actual prevalence of these disorders may be different from that recognised. Finally, other risk factors, such as homocysteine levels, nocturnal hypotension, or environmental factors[10] were not consistently investigated.

Nevertheless, the fact that the occurrence of NAION cannot be easily explained by the presence of prothrombotic or atherosclerotic risk factors shifts focus to the possibility that mitochondrial abnormalities may be important in the development of NAION. Based on these observations, testing for mitochondrial abnormalities may be warranted in NAION patients, especially the ones without a

Table 1 Comparison of risk factors in NAION patients and controls

Risk factor		NAION patients	Controls	Odds ratio	95% CI	p Value
Apo E4	Homo	0/19	0/593	31.2	0.60 to 1615.3	1
Factor II G20210A	Homo	0/19	0/593	31.2	0.60 to 1615.3	1
	Hetero	0/19	10/593	0	0.00 to 17.52	1
Factor V G1691A	Homo	0/19	0/200	10.5	0.20 to 545.6	1
	Hetero	0/19	5/200	0	0.00 to 13.10	1
MTHFR C677T	Homo	0/19	12/625	0	0.00 to 15.06	1
	Hetero	4/19	161/625	0.77	0.21 to 2.52	0.79
MTHFR A1298C	Homo	0/19	57/625	0	0.00 to 2.71	0.39
	Hetero	7/19	322/625	0.55	0.19 to 1.52	0.30
PI^{A2} allele	Homo	0/19	12/509	0	0.00 to 12.22	1
	Hetero	3/19	137/509	0.51	0.12–1.89	0.41
Age, mean (SD)	–	58.8 (8.5)	57.1 (4.2)	–	–	0.40
Sex (M:F)	–	14:5	351:160	1.28	0.42 to 4.13	0.64
Diabetes	–	13/19	256/511	2.16	0.75 to 6.47	0.18
Hypertension	–	10/19	209/511	1.61	0.59 to 4.38	0.43
Hyperlipidaemia	–	2/19	59/511	0.68	0.11 to 3.17	1
CAD	–	1/19	27/511	0.55	0.03 to 4.03	1
NS mtDNA changes	–	14/19	11/100	22.6	6.03 to 91.07	< 0.001

NAION, non-arteritic ischaemic optic neuropathy; CAD, coronary artery disease; NS mtDNA changes, non-synonymous (changing an amino acid in the resultant protein) mitochondrial DNA nucleotide change; Homo, homozygous; Hetero, heterozygous. Diabetes, hypertension, hyperlipidaemia, and CAD were assessed by patient report both from NAION patients and from controls. Controls previously reported for mtDNA changes and for atherosclerotic and prothrombotic risk factors (see text). Odds ratio and p values compare prevalence of different risk factors in NAION patients to controls.

medical or family history of a thrombotic or vascular event.

K K Abu-Amero
Mitochondrial Research Laboratory, Department of Genetics, King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia

T M Bosley
Neuro-ophthalmology Service, King Khaled Eye Specialist Hospital, Riyadh, Kingdom of Saudi Arabia

Correspondence to: Dr Khaled K Abu-Amero, Mitochondrial Research Laboratory, Department of Genetics, King Faisal Specialist Hospital and Research Center (MBC # 03), PO Box 3354, Riyadh 11211, Kingdom of Saudi Arabia; kamero@kfshrc.edu.sa

doi: 10.1136/bjo.2005.078071
Accepted for publication 9 July 2005

References

1 **Bosley TM**, Abu-Amero KK, Ozand PT. Mitochondrial DNA nucleotide changes in non-arteritic ischemic optic neuropathy. *Neurology* 2004;**63**:1305–8.
2 **Nagy V**, Facsko A, Takacs L, *et al*. Activated protein C resistance in anterior ischaemic optic neuropathy. *Acta Ophthalmol Scand* 2004;**82**:140–3.
3 **Glueck CJ**, Wang P, Bell H, *et al*. Nonarteritic anterior ischemic optic neuropathy: associations with homozygosity for the C677T methylenetetrahydrofolate reductase mutation. *J Lab Clin Med* 2004;**143**:184–92.
4 **Abu-Amero KK**, Wyngaard CA, Kambouris M, *et al*. Prevalence of the 20210 G→A prothrombin variant and its association with coronary artery disease in a Middle Eastern Arab population. *Arch Pathol Lab Med* 2002;**126**:1087–90.
5 **Abu-Amero KK**, Wyngaard CA, Dzimiri N. Prevalence and role of methylenetetrahydrofolate reductase 677 C→T and 1298 A→C polymorphisms in coronary artery disease in Arabs. *Arch Pathol Lab Med* 2003;**127**:1349–52.
6 **Abu-Amero KK**, Wyngaard CA, Dzimiri N. Association of the platelet glycoprotein receptor IIIa (PlA1/PlA1) genotype with coronary artery disease in Arabs. *Blood Coagul Fibrinolysis* 2004;**15**:77–9.
7 **Dzimiri N**, Meyer BF, Hussain SS, *et al*. Relevance of apolipoprotein E polymorphism for coronary artery disease in the Saudi population. *Arch Pathol Lab Med* 1999;**123**:1241–5.
8 **Dzimiri N**, Meyer B. World distribution of factor V Leiden. *Lancet* 1996;**347**:481–2.
9 **Salomon O**, Huna-Baron R, Kurtz S, *et al*. Analysis of prothrombotic and vascular risk factors in patients with nonarteritic anterior ischemic optic neuropathy. *Ophthalmology* 1999;**106**:739–42.
10 **Hayreh SS**. Risk factors in AION. *Ophthalmology* 2001;**108**:1717–18.

Inflammatory cytokine of basal and reflex tears analysed by multicytokine assay

Tear cytokine has a major role in various pathophysiological conditions of the ocular surface. So far, studies on tear cytokines have shown significant progress in providing an understanding of ocular surface diseases.[1–3] The information that could be acquired from each subject, however, until recently has been severely hampered by limited sample volume and assay sensitivity. More importantly, it has become apparent that the relative balance between various cytokines and combinations of cytokines could be more important than absolute concentrations. Previous studies showed that the composition of basic and reflex tears was different, which made it more difficult to understand the ocular surface disorder correctly or to treat the patients suitably.[4 5] Cytometric bead array (CBA) is a microparticle based flow cytometric assay that allows us to quantify multiple molecules from a very small sample.[3 6 7] Using this method, we evaluated the inflammatory cytokines of basal and reflex tears from a single sample of individual eyes.

Methods

Twenty three normal volunteers (11 males and 12 females, 22–44 years of age, average 28 years) were recruited for this study. None of the subjects had signs of ocular diseases. The study was performed with the approval of the institutional review board. The basal tear samples of 10–15 µl were obtained from each eye by capillary flow, with no nasal stimulation or previous instillation of drugs or vital dyes. Each sample was collected at 5 pm. No anaesthetic drops were instilled. The samples were collected non-traumatically from the inferior meniscus. Successively, reflex tear samples were collected by inserting application sticks into a participant's nose. The amounts of six inflammatory molecules interleukin (IL)-1β, IL-6, IL-8, IL-10, IL-12p70, and tumour necrosis factor α (TNF-α), were measured by CBA (BD Biosciences, San Diego, CA, USA), according to the manufacturer's instructions. Briefly, for the tear sample and cytokine standard mixture, 10 µl of sample or standard were added to 40 µl sterile purified water, a mixture of 50 µl each of capture Ab-bead reagent and detector Ab-phycoerythrin (PE) reagent. The mixture was subsequently incubated for 3 hours at room temperature, and washed to remove any unbound detector Ab-PE reagent before data acquisition using flow cytometry. A two colour flow cytometric analysis was performed using a FACScan flow cytometer (Beckton Dickinson Immunocytometry Systems). Data were acquired and analysed using BD cytometric bead array software.

Results

The concentrations of IL-1β, IL-6, IL-10, IL-12p70, and TNF-α were not significantly different between basal and reflex tears. In contrast, the concentration of IL-8 was significantly decreased in reflex tears compared with basal tears in each eye (paired *t* test, $p<0.01$, fig 1). In order to illuminate the inter-relation of each cytokine, the ratio of two different cytokines is shown in table 1.

Comment

Previously published studies have demonstrated that CBA correlates well with enzyme linked immunosorbent assay (ELISA), but the absolute concentrations obtained from each assay were differed for kits of different manufacturers.[7] Indeed, the concentrations of tear cytokines in the present results were almost equal to the previous report using the same kit.[3] Nakamura *et al* performed ELISA for multiple cytokines measuring pooled tears.[1] The pooled tears enable measurement of multiple cytokines; however the results