Sir,
Late onset of Leber's hereditary optic neuropathy precipitated by anaemia

Leber's hereditary optic neuropathy (LHON) is an uncommon maternally inherited disease producing bilateral visual loss, usually in men. In 69% of affected individuals, visual loss begins in the second or third decade of life, although onset may occur as late as 65 years of age.^{1,2} Various precipitating factors have been reported.

Case report

A 67-year-old man was referred in November 2001 by his optician with deteriorating vision in the left eye of 1-month duration and raised intraocular pressures (IOPs). He was on treatment for systemic hypertension and hyperlipidaemia. In March 2001 he was found to be anaemic (Hb 9.9 g/dl) due to haemorrhage from multiple small bowel arteriovenous malformations that were treated in June and October 2001 with argon plasma coagulation (APC). He drank two glasses of whisky per

Figure 1 Goldman visual fields showing dense central scotoma bilaterally: (a) left eye and (b) right eye.

night and had stopped smoking in 1996. Two maternal uncles were blind from unknown cause.

Visual acuities were 6/6 in the right eye and 6/12 in the left eye and IOPs were 33 and 36 mm Hg, respectively. Treatment was started with timolol 0.25%. Latanoprost and dorzolamide drops were subsequently added with IOPs falling to 15 and 18 mm Hg. By March 2002, vision in the left eye had fallen to counting fingers. In May 2002, haemoglobin had fallen to 7.4 g/dl due to further gastrointestinal haemorrhage. In July 2002, further APC was performed and vision in the right eye began to deteriorate, falling to counting fingers by August 2002. There were dense bilateral central scotomas on Goldman perimetry (Figure 1). There was mild diffuse pallor of left optic disc. The right optic disc was normal. The optic discs cups were moderately large but not glaucomatous. Further APC was performed in November 2002.

mtDNA studies were positive for the point mutation at base position 11778 establishing a diagnosis of LHON. Normal investigations included CT scan of brain and orbits and serum autoantibodies, angiotensin-converting enzyme, B12 and folate.

Comment

It remains unclear why most affected individuals with LHON lose vision in the second or third decade of life but onset may be at almost any age. Smoking and high alcohol consumption have been implicated but disputed.^{3,4} Head or ocular trauma,¹ childbirth alone or complicated by postpartum haemorrhage,¹ onset of diabetes mellitus,⁵ vitamin B₁₂ deficiency,⁶ antiretroviral therapy,^{7,8} cyanide toxicity,⁹ carbon monoxide poisoning,¹⁰ and ephedra alkaloids¹¹ have all been implicated.

The trigger to visual loss is generally hypothesised to be additional impairment of oxidative respiration within the optic nerve, already compromised by the biochemical effects of the mitochondrial gene defect. It is likely that the site of neuronal dysfunction is the intraocular nonmyelinated portion of the retinal ganglion cell axons.¹²

This case is unusual in the late age at presentation. The oldest patient previously reported was 65 years old when visual loss began.² Acute blood loss precipitating visual loss has been reported.¹ The probable precipitant of visual loss in this case was chronic anaemia secondary to small bowel arteriovenous malformations, although high IOPs were also identified.

hereditary optic neuropathy defined by the presence of a pathogenic mitochondrial DNA mutation. *Brain* 1995; **118**: 319–337.

- 2 Mackey DA, Buttery RG. Leber hereditary optic neuropathy in Australia. *Aust NZ J Ophthalmol* 1992; **20**(3): 177–184.
- 3 Kailenn T, Aitken, Johns DR. Smoking as an aetiological factor in a pedigree with Leber's hereditary optic neuropathy. *Br J Ophthalmol* 1999; **83**: 577–581.
- 4 Kerrison JB, Miller NR, Hsu F, Beaty TH, Maumenee IH, Smith KH *et al.* A case-control study of tobacco and alcohol consumption in Leber hereditary optic neuropathy. *Am J Ophthalmol* 2000; **130**: 803–812.
- 5 DuBois LG, Feldon SE. Evidence for a metabolic trigger for Leber's hereditary optic neuropathy. A case report. *J Clin Neuroophthalmol* 1992; **12**: 15–16.
- 6 Rizzo III JF. Adenosine triphosphate deficiency: a genre of optic neuropathy. *Neurology* 1995; **45**: 11–16.
- 7 Shaikh S, Ta C, Basham AA, Mansour S. Leber hereditary optic neuropathy associated with antiretroviral therapy for human immunodeficiency virus infection. *Am J Ophthalmol* 2001; **131**: 143–145.
- 8 Mackey DA, Fingert JH, Luzhansky JZ, McCluskey PJ, Howell N, Hall AJ *et al.* Leber's hereditary optic neuropathy triggered by antiretroviral therapy for human immunodeficiency virus. *Eye* 2003; **17**: 312–317.
- 9 Berninger TA, von Meyer L, Siess E, Schon O, Goebel FD. Leber's hereditary optic atrophy: further evidence for a defect of cyanide metabolism? *Br J Ophthalmol* 1989; **73**: 314–316.
- 10 Hwang JM, Park HW. Carbon monoxide poisoning as an epigenetic factor for Leber's hereditary optic neuropathy. *Korean J Ophthalmol* 1996; **10**: 122–123.
- 11 Warner RB, Lee AG. Leber hereditary optic neuropathy associated with use of ephedra alkaloids. *Am J Ophthalmol* 2002; **134**: 918–920.
- 12 Bristow EA, Griffiths PG, Andrews RM, Johnson MA, Turnbull DM. The distribution of mitochondrial activity in relation to optic nerve structure. *Arch Ophthalmol* 2002; **102**: 791–796.

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References

- 1 Riordan-Eva P, Sanders MD, Govan GG, Sweeney MG, Da Costa J, Harding AE. The clinical features of Leber's

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