retinal pigment epithelium is unhealthy in a myopic atrophic area, it may still be able to pump away the non-bullous subretinal fluid, especially when the macular hole is small and once the epimacular membrane has separated spontaneously relieving the traction.

As the natural history of retinal detachment secondary to macular hole in severely myopic eyes is not well defined, we have to exercise caution when considering vitreoretinal surgery for this group of patients, as they are prone to risks such as expulsive suprachoroidal haemorrhage and an unfavourable visual outcome.

Supported in part by the Mr I.K. Ho Eye Foundation, Shatin, Hong Kong.

References

1. Akihiro K, Schepens CL, Akiba J, Hikichi T, Trempe CL. Spontaneous resolution of foveal detachment and macular breaks. Am J Ophthalmol 1995;120:767–75.
2. Min WK. Spontaneous reattachment of retinal detachment with macular hole in nonmyopic patients. Korean J Ophthalmol 1995;9:66–8.
3. Bonnet M, Semiglia R. Spontaneous course of retinal detachment with macular hole in patients with severe myopia. J Fr Ophtalmol 1991;14:618–23.
4. Morita H, Ideta H, Yonemoto J, Sasaki K, Tanaka S. Causative factors of retinal detachment in macular holes. Retina 1991;11:281–4.

Barbara S.M. Tam[1]
Alvin K.H. Kwok[1]
Pramod Bhende[1,2]
Dennis S.C. Lam[1]

[1]Department of Ophthalmology and Visual Sciences
The Chinese University of Hong Kong
Hong Kong Eye Hospital
Hong Kong
[2]Medical and Vision Research Foundations
Sankara Nethralaya
Chennai, India

Dr Alvin K.H. Kwok, FRCS ✉
Department of Ophthalmology and Visual Sciences
The Chinese University of Hong Kong
3F, Hong Kong Eye Hospital
Hong Kong

Tel: +852 2855 3788
Fax: +852 2855 4737
e-mail: kwok/ch@ha.org.hk

Sir,

Central retinal vein occlusion complicating treatment with intravenous immunoglobulin

Intravenous immunoglobulin therapy is increasingly used in neurological practice. We describe a case where the use of immunoglobulin therapy may have contributed to the development of visual impairment secondary to central retinal vein occlusion (CRVO).

Case report

A 40-year-old woman with a diagnosis of chronic inflammatory demyelinating polyneuropathy, according to the criteria of Dyck and Prineas,[1] was initially treated with high-dose oral prednisolone therapy. However, due to progression of disease she was admitted to the neurology unit for treatment with pooled intravenous immunoglobulin (IVIg) 400 mg/kg daily for 5 days. A good clinical response was seen and she was discharged home on a combination of prednisolone and azathioprine therapy and followed up in the outpatient clinic. Treatment with monthly day case IVIg 400 mg/kg, in addition to oral maintenance immunosuppression, was commenced 2 months later.

On attendance for the second infusion the patient complained of two episodes of transient partial visual field loss affecting initially the left eye, 1 week after IVIg treatment, and then the right eye, 4 weeks after IVIg treatment. Visual field testing was normal to confrontation, and visual acuity was 6/6 corrected bilaterally. Fundoscopy revealed a small cholesterol embolus in the upper-outer quadrant of the right eye. General examination revealed no stigmata of hypercholesterolaemia, blood pressure was 140/80 mmHg, pulse rate 68 beats/min and regular, heart sounds were normal and no neck bruits were detectable. The patient is a non-smoker and has no family history of vascular disease. Full blood count, urea and electrolytes, thyroid and liver function tests and serum glucose measurements were all within normal limits. Plasma viscosity was slightly elevated at 1.78 with a normal electrophoretic profile, negative skeletal survey and Bence-Jones protein negative. Serum cholesterol was evaluated at 6.5 mmol/l. Carotid Doppler studies demonstrated bilateral low-grade disease with less than 30% stenosis of the internal carotids. The echocardiogram was entirely normal. The patient was given advice regarding a cholesterol-lowering diet and commenced on aspirin 75 mg once daily.

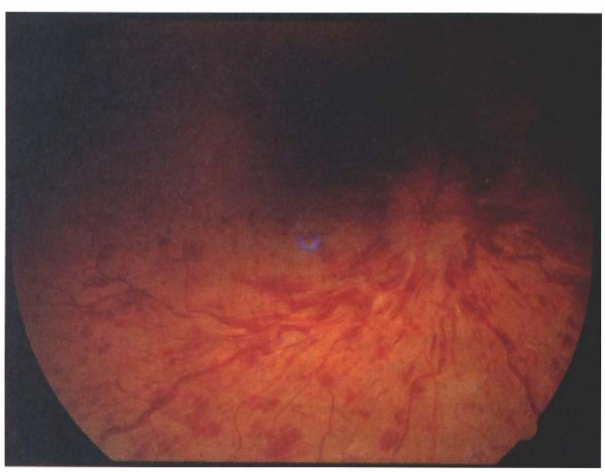

Fig. 1. *Photograph of the right fundus confirming the typical changes of central retinal vein occlusion (CRVO) with disc swelling in conjunction with extensive retinal haemorrhage and cotton wool spots.*

Three weeks following the third day case administration of IVIg the patient developed sudden painless loss of vision affecting her right eye. Right-sided disc swelling was noted in conjunction with extensive retinal haemorrhage and cotton wool spots, indicating a diagnosis of CRVO (Fig. 1). Visual acuity was reduced in the right eye to 6/60. Plasma viscosity was not elevated at 1.64 (normal values < 1.70). Serum immunoglobulin profile was normal. Clotting screen and thrombophilia screen including protein C, protein S, antithrombin 3, factor V Leiden and APC resistance were all normal. Anticardiolipin antibody was not detected. Intraocular pressure was normal and following ophthalmological assessment the patient was managed conservatively. IVIg was discontinued and the patient maintained on treatment with prednisolone 15 mg daily and azathioprine 100 mg daily. The patient has subsequently made a full neuro-ophthalmological recovery with visual acuity recorded as 6/5 bilaterally, with no evidence of optic atrophy or afferent pupillary defect at 2 years after the event.

Discussion

Hyperviscosity syndromes have well-recognised associations with CRVO. *In vitro* studies have confirmed a dose-related increase in viscosity with IVIg products and there are a number of documented cases of thrombotic complications associated with the therapeutic use of IVIg. There has been one case in the literature of bilateral CRVO occurring in a 17-year-old man requiring immune replacement therapy following treatment for acute lymphoblastic leukaemia.[2] To date there have been two other cases of visual loss in association with IVIg therapy reported to the Committee on Safety of Medicines. Raised cholesterol greater than 6.2 g/l has also been reported as an independent risk factor for CRVO.[3]

We propose that in this case the therapeutic use of IVIg, possibly combined with the raised cholesterol, may have precipitated the episode of visual loss, although we do acknowledge that it may have been coincidental as a significant percentage of cases of CRVO have no detectable systemic cause. Hyperviscosity does not appear to be the direct cause as the event occurred 3 weeks after the infusion of IVIg and the viscosity was normal. Nitric oxide plays a critical role in vascular homeostasis through the inhibition of platelet aggregation and promoting vasodilatation, and *in vitro* studies have shown that human immunoglobulins are able to downregulate the production of thrombin-induced nitric oxide production in a dose-dependent fashion.[4] *In vivo* studies have shown a correlation between adverse reactions and elevated levels of the proinflammatory cytokine interleukin 6 and the vasoactive substance thromboxane (TXB_2).[5] It is possible that IVIg-induced alterations in the profile of cytokines and vasoactive substances may have precipitated a localised thrombotic occlusion. This case emphasises the importance of screening for vascular risk factors in patients requiring treatment with IVIg.

References

1. Dyck PJ, Prineas J. Chronic inflammatory demyelinating polyradiculoneuropathy. In: Dyck PJ, Thomas PK, Griffin JW, *et al.* editors. Peripheral neuropathy. 3rd ed. Philadelphia: Saunders, 1993:1498–517.
2. Oh KT, Boldt HC, Dansi RP. Iatrogenic central retinal vein occlusion and hyperviscosity associated with high-dose intravenous immunoglobulin administration. Am J Ophthalmol 1997;124:416–8.
3. McGrath MA, Wechsler F, Hunyor ABL, Penny R. Systemic factors contributing to retinal vein occlusion. Arch Intern Med 1978;138:216–20.
4. Schussler O, Lantoine F, Devynck MA, Glotz D, David-Dufilho M. Human immunoglobulins inhibit thrombin-induced Ca^{2+} movements and nitric oxide production in endothelial cells. J Biol Chem 1996;271:26473–6.
5. Bagdasarian A, Tonetta S, Harel W, Mamidi R, Uemura Y. IVIG adverse reactions: potential role of cytokines and vasoactive substances. Vox Sang 1998;74:74–82.

K.A.C. Harkness ✉
Department of Neurology
Addenbrooke's Hospital
Hills Road
Cambridge CB2 2QQ, UK

P. Goulding
Department of Neurology
St James's University Hospital
Leeds LS9 7TF, UK

Sir,

Pigment dispersion syndrome and butterfly-shaped pattern dystrophy of the retinal pigment epithelium

Pigment dispersion syndrome (PDS) consists of pigment deposition on the corneal endothelium in a vertical spindle pattern (Krukenberg's spindle), in the trabecular meshwork and on the lens periphery.[1] Recent studies have suggested that the retinal pigment epithelium (RPE) may also be involved in PDS.[2–4] We here describe a patient with butterfly-shaped pattern dystrophy of the RPE in addition to PDS.

Case report

A 48-year-old woman presented with metamorphopsia of 3 weeks' duration. Visual acuities were 20/20 right eye and 20/25 left eye. The patient described some parallel wavy lines on the Amsler grid in the left eye. There was no positive family history. Past medical history disclosed hysterectomy for myoma uteri.

Slit-lamp examination revealed pigment deposits on the posterior corneal surface in the form of Krukenberg's spindles bilaterally. Goldmann applanation pressure was 19 mmHg in each eye. Gonioscopy disclosed bilateral open angles with grade 3–4 pigmentation of the trabecular meshwork (Fig. 1). There were no peripheral transillumination defects. After dilatation of the pupils, pigment deposition also on the posterior surface of the lens was noted inferiorly. Funduscopy revealed healthy optic nerve heads with a cup/disc ratio of 0.2. At the macula, butterfly-shaped yellowish flecks were noted in deeper layers of the retina bilaterally (Fig. 2).