Presumed interferon-associated bilateral macular arterial branch obstruction

Interferon alpha (INF α) has been shown to have antiviral, antifibroblastic and antineoplastic effects, may induce inhibition of vascular endothelial cells and can modulate the immune system.^{1,2} Because of

these numerous effects, INF α is commonly included in the treatment protocols of selected systemic and ocular disorders.^{1,2} However, ocular side-effects of INF α use are also increasingly reported. We describe a patient who simultaneously developed bilateral macular arterial branch occlusions while under INF α therapy.

(a)

(b)

Fig. 1. (a) Right fundus view showing a well-delineated superficial retinal whitening sparing the foveola, due to occlusion of the inferior macular arteriolar branches. (b) Corresponding superonasal visual field defect on the Humphrey Field Analyser.

(a)

(b)

Fig. 2. (a) In the left fundus, in addition to numerous cotton-wool spots, superior macular arteriolar occlusions caused retinal opacification superior and temporal to the fovea producing typical inferonasal visual field defects (b).

Case report

A 45-year-old man presented with a sudden decrease of his visual acuity in both eyes. He described scotomas in his right upper and left lower visual fields. Six months earlier, he was coincidentally diagnosed as having chronic myelocytic leukaemia while being investigated for 90% occlusion of his cardiac left anterior descending artery because of which he experienced chest pain. At

that time, his white blood cell (WBC) count was 30 000/ml and platelet count was 800 000/cm³. His blood lipid profile was normal. He was immediately put on hydroxyurea for 2 months but as the WBC count increased to 5400/ml and platelets persisted at the same level, he started to receive subcutaneous citarabine (Alexan, Rhone Poulenc) 10 mg 10 days each month and INFα2 (Roferon, Roche) 9 × 10⁶ U/day. Except for the

recently developed chest pain, he was in good health previously without a history of diabetes or hypertension. He did not have any ocular complaints during the first 6 months of his disease.

On our examination, his best-corrected visual acuity was 20/25 in the right eye and 20/30 in the left. There was no afferent pupillary defect. Fundoscopy showed retinal opacification of the inferior half of the right macula (Fig. 1a) and cotton-wool spots scattered around the optic disc. The fovea appeared intact. Fluorescein angiography demonstrated occlusion of the macular branches of inferior temporal retinal artery after the first bifurcation. On the left side, there was a milder retinal opacification on the superior half of the macula (Fig. 2a) with more cotton-wool spots and intraretinal haemorrhages. On fluorescein angiography, two small branches of the superior temporal retinal artery supplying the upper papillomacular bundle and upper nasal macula appeared occluded. There was minimal perifoveal retinal oedema. The peripheral retina was normal. Visual field testing performed for medicolegal documentation of the functional loss showed the corresponding quadrantic defects (Figs. 1b, 2b). A day before his presentation to us, his WBC count was 3000/ml and the platelet count was 80 000/cm³. His systemic status dictated the continuation of INF α 2. No immediate ocular treatment but observation was recommended to the patient. Two months later, retinal opacifications resolved completely while the number of cotton-wool spots increased considerably. His visual acuity did not change. Four months later, while still under INF α 2 treatment, his visual acuity improved to 20/20 in both eyes, and almost all cotton-wool spots disappeared. A year after the sudden onset of his ocular symptoms, he is alive and well without any signs of systemic recurrence. He is currently in a medication-free period and has no visual complaints.

Comment

INF α 2 therapy may result in deposition of immune complexes in the retinal vasculature and leucocyte infiltration that cause retinal ischaemia leading to capillary non-perfusion and nerve fibre layer infarctions.³ In animal studies, INF α has been shown to induce leucocyte adherence to vascular endothelium and leucocyte trapping in the retinal capillaries.⁴ The incidence of retinopathy is thought to depend on the initial dose of INF α and patients receiving 9×10^6 U/day, 6 days per week, are usually at increased risk for the evolution of retinopathy.² Diabetes and systemic hypertension are also risk factors in the development and progression of INF α -associated retinopathy.² In fact, INF α retinopathy may initially be mistaken for diabetic retinopathy.⁵ The most common presumed interferon-associated ocular complications include retinal ischaemia in the form of cotton-wool

spots and haemorrhages, which usually appear within 3 months after the onset of therapy.^{3,6} Involvement of larger-calibre arterioles is rather rare and a single case similar to ours was reported by Guyer *et al.*³ Atypical retinal findings include vitreous haemorrhage and central and branch retinal vein occlusions.² Two patients with INF α -induced anterior ischaemic optic neuropathy have also been reported.⁷ In the majority of patients, retinal capillary non-perfusion, retinal oedema and haemorrhages, vascular occlusions and leakage usually regress without significant sequelae whether the drug is discontinued or not.^{3,6,8} This observation led some investigators to suggest that INF α 2 could not be linked to the formation of retinal complications.⁸ Despite this controversy, it is currently accepted that the drug should be discontinued if severe toxicity occurs or visual acuity drops significantly.²

Our patient with unusual manifestations of presumed INF α 2-associated retinopathy provides further evidence that this type of ischaemic retinopathy, however severe it might appear initially, could run a self-limited and relatively benign clinical course despite continuation of the drug. Patients should still be closely monitored until larger studies clarify the issue.

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