Figure 2 (A) Macroscopic specimen showing funnel shaped retinal detachment with prominent tortuous blood vessels on the outer surface and a mass at the optic disc (black arrows). The cataract surgery wound with iris prolapse is identified at the edge of the cornea (white arrow). (B) The mass at the optic disc shows a vascular proliferation in keeping with a capillary haemangioblastoma (arrows) (haematoxylin and eosin, $\times 25$). (C) Histological section of one of the smaller retinal capillary haemangioblastomas showing a vascular proliferation with intervening glial cells and foamy histiocytes (arrows). (periodic acid Schiff, $\times 400$). (D) The prominent abnormal vascular proliferation is highlighted by immunohistochemical staining for factor VIII (factor VIII, $\times 100$).

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Rapid development of severe toxic retinopathy associated with continuous intravenous deferoxamine infusion

Deferoxamine mesylate is a chelating agent used in the treatment of iron overload in patients requiring regular transfusions. Deferoxamine is most commonly administered as a slow subcutaneous infusion but continuous intravenous infusion may be required for treating life threatening cardiac complications due to iron overload.¹ Toxic retinopathy is one of the complications associated with deferoxamine, in which

different manifestations including pigmentary retinopathy, bull's eye maculopathy, and vitelliform maculopathy have been described.^{2–8} We report a patient who had rapid development of irreversible diffuse pigmentary retinopathy with severe visual loss while receiving continuous intravenous deferoxamine infusion.

Case report

A 17 year old β thalassaemic patient was referred for ophthalmic assessment with recent onset of colour vision impairment 4 months after commencement of continuous intravenous deferoxamine infusion. He had been on subcutaneous deferoxamine for 14 years but stopped self administration 6 months before presentation. As a consequence of the poor compliance, he developed iron overload with a serum ferritin level of 6370 $\mu\text{g/L}$, causing dilated cardiomyopathy and arrhythmia. Owing to the severity of the heart condition, he was treated with 44 mg/kg/day (therapeutic index = 0.007) continuous deferoxamine infusion via an indwelling intravenous catheter. On presentation, his visual acuity was 6/18 in both eyes with normal colour vision testing on Ishihara plates. Slit lamp and dilated fundus examinations revealed no abnormality. In view of the severe life threatening cardiac complications, deferoxamine was continued despite the visual symptoms. Three weeks later, his visual acuity deteriorated to counting fingers on reassessment. Fundus examination revealed diffuse pigmentary changes at both macula and peripheral retina (fig 1). Serum ferritin level was found to have decreased to 430 $\mu\text{g/L}$ (therapeutic index = 0.103). Since his heart condition had stabilised, the deferoxamine dosage was reduced to 11 mg/kg/day and later changed to subcutaneous infusion. One year after initial presentation, his visual acuity improved to 6/60 but the diffuse pigmentary retinopathy remained unchanged. Electro-oculogram showed severely reduced response with Arden ratio of 1.1 bilaterally and full field electroretinogram demonstrated reduced scotopic and photopic response amplitudes with normal implicit times in both eyes.

Comment

The use of subcutaneous deferoxamine is generally safe and the development of ocular toxicity is uncommon.^{3,9} However, compliance with subcutaneous therapy may be poor particularly in young patients, and intravenous infusion is sometimes required to treat life threatening complications.^{1,4} It has been suggested that monthly monitoring of serum ferritin to adjust the deferoxamine dosage below a therapeutic index of 0.025 (daily dose per body weight (mg/kg) divided by serum ferritin level ($\mu\text{g/L}$)) may prevent deferoxamine related complications.¹⁰ However, this was derived based on ototoxicity and it was unclear whether it applied to ocular toxicity. Our case illustrated the rapid development of severe pigmentary retinopathy over 3 weeks because of a sudden fall in serum ferritin level, which resulted in a therapeutic index four times above the limit. Despite prompt reduction of deferoxamine dosage, the severe pigmentary retinopathy persisted and resulted in irreversible retinal damage with profound visual loss. A previous study on the long term outcome of continuous 24 hour deferoxamine infusion has described a case of reversible retinal toxicity

Figure 1 Fundus photograph of the right eye showing (A) deferroxamine induced toxic retinopathy with diffuse retinal pigmentary changes and areas of hyperpigmentation and hypopigmentation in the macula, with (B) extension of the pigmentary changes to the equatorial region and the peripheral retina areas.

when the therapeutic index was briefly elevated to 0.030.¹ Davies *et al* also reported the development of pigmentary retinopathy in a patient who had intravenous deferroxamine infusion with a therapeutic index of 0.039 but the visual symptoms resolved after cessation of therapy and the patient's final vision was not affected.⁴ Our case highlighted the importance of frequent serum ferritin level monitoring and maintaining the deferroxamine dosage with therapeutic index <0.025 as severe irreversible retinopathy can develop rapidly. Frequent regular ophthalmic assessments should also be carried out in patients who are on continuous intravenous deferroxamine infusion, as prompt drug discontinuation might potentially arrest the retinal damage.

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Epstein-Barr virus infected cells in the aqueous humour originated from nasal NK/T cell lymphoma

Nasal natural killer (NK)/T cell lymphoma is a definitive diagnostic entity in the World Health Organization lymphoma classification.¹ In many cases, NK/T cell lymphoma is invariably associated with Epstein-Barr virus (EBV). Although ocular involvement is found in less than 10% of patients with systemic lymphoma,² because of its anatomical proximity, nasal NK/T lymphoma can sometimes complicate uveitis and orbital infiltration.³ We experienced a case of nasal NK/T lymphoma, and the cells collected from the aqueous humour originated from the lymphoma which was infected by EBV.

Case report

A 53 year old man noticed nasal obstruction and imaging demonstrated a mass lesion in the nasal cavity. The biopsy specimen from the cavity demonstrated a variety of diffuse

atypical lymphoid cell infiltration. Immunohistochemically, the atypical cells showed cytoplasmic reactivity for CD56, CD3, granzyme B and perforin, but not for CD20. Many EBV encoded small RNA (EBER) positive cells were detected in the lymphoma tissues. The patient was diagnosed with nasal NK/T cell lymphoma in May 2004. Magnetic resonance imaging (MRI) showed multiple metastatic lesions in the brain in June 2004. He underwent combined chemotherapy and radiotherapy. Since he had blurred vision in both eyes during the treatment, he visited our clinic on 1 September 2004. Visual acuities were 20/13 in both eyes. Intraocular pressures were 10 mm Hg in the right eye, and 11 mm Hg in the left. Biomicroscopy showed anterior segment inflammation with 1+ flare and 2+ cells in the anterior chamber, and small iris nodules were also sporadically seen in both eyes. A fundus examination showed no particular findings. Since then, although he was treated with eye drops of a mydriasis agent and betamethasone for 3 weeks, his symptoms had not improved. Moreover, the number of cells in the anterior chamber increased and pigmentation on the lens was noted. After informed consent was obtained, we performed anterior chamber paracentesis to obtain aqueous humour for cytological diagnostic analysis. May-Giemsa staining disclosed a variety of severe atypical lymphoid cells with a high nuclear/cytoplasmic ratio (fig 1A, arrowheads) mimicking lymphoma cells in the nasal cavity. Only a few macrophages in intracytoplasmic phagocytosed nuclei were intermingled (fig 1A, arrow). The EBV genome was detected by polymerase chain reaction (PCR) using primers targeting the infranuclear region in the aqueous humour. Furthermore, EBV DNA was clearly detected by PCR Southern blot analysis (fig 1B). Despite continuous chemotherapy, he died as a result of multiple organ dysfunction associated with lymphoma invasion on 13 December 2004.

Comment

Nasal NK/T cell lymphoma can sometimes lead to ocular complications such as orbital infiltration owing to its anatomical proximity.³ Although it is reported that NK/T cell lymphomas complicate anterior uveitis,³ invasion of lymphoma cells into the ocular

Figure 1 Cytological examination (A) and detection of EBV DNA by Southern blot analysis (B) in the aqueous humour. (A) A variety of atypical lymphoid cells proliferated with a high nuclear/cytoplasmic ratio (May-Giemsa staining (A) arrowheads). Macrophages with intracytoplasmic phagocytosed nuclei are intermingled (A, arrow). (B) EBV DNA was markedly detected in the aqueous humour. Lane S: aqueous humour sample aspirated from the patient; lane N: distilled water as an EBV DNA negative control; lane P: EBV DNA integrated plasmid as a positive control.