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Visual loss secondary to fludarabine toxicity: optical coherence tomography findings in two patients

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Fludarabine is a purine analogue used to treat haematological malignancy and for conditioning prior to allogenic bone marrow transplant. In early clinical trials [1] high-dose fludarabine caused high rates of severe neurotoxicity (56%) and death (44%). Fludarabine is now used at lower doses in combination with other chemotherapy drugs (e.g. FLAG-Ida regimen). However, the risk of severe sight loss and blindness in one study [2] was 1% and 0.3%, respectively.

We present two patients with painless loss of vision secondary to fludarabine toxicity. Both had normal ophthalmic examination and optical coherance tomography (OCT) at presentation. Patient 1 developed blurred vision 14 days after FLAG-Ida cycle 2. At presentation visual acuities (VA) bilaterally were 6/18. Six weeks later VA worsened to 6/36 and high-dose oral prednisolone was prescribed. Initially VA improved to 6/9 bilaterally, but declined to 6/60 over 3 years.

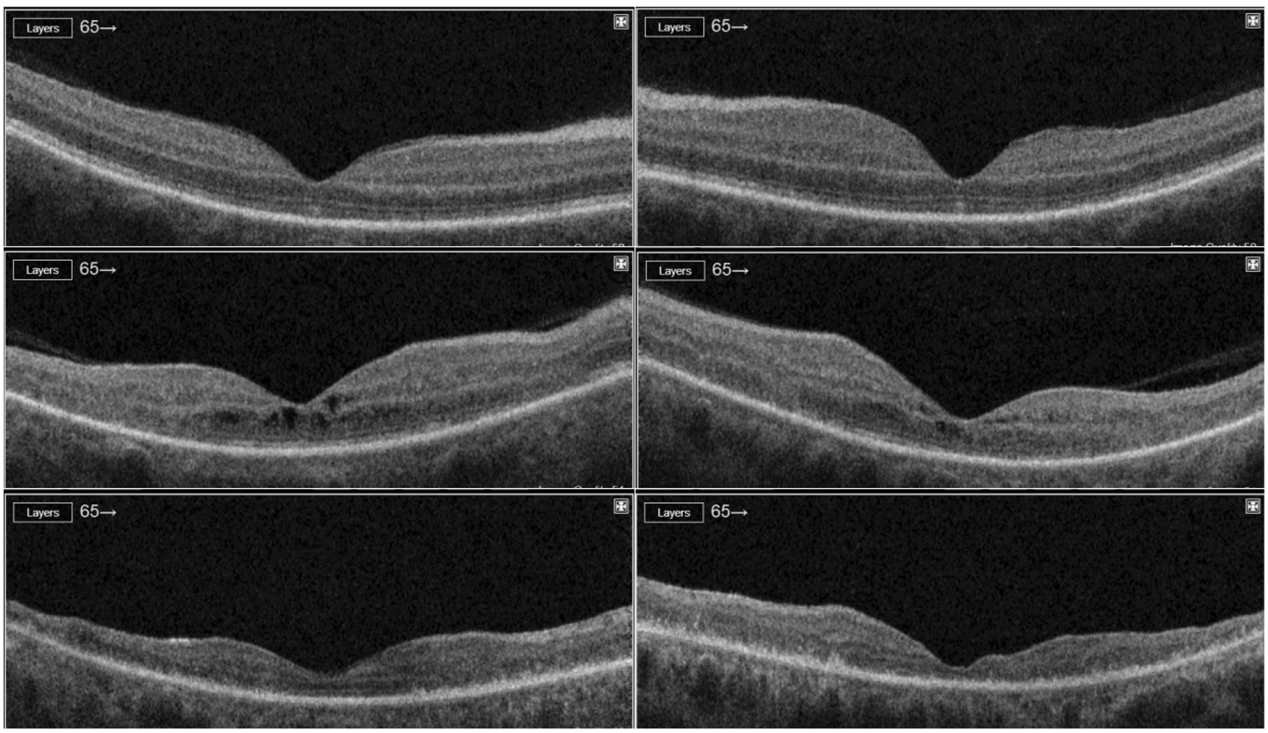

Fig. 1 Macular optical coherence tomography from patient 1 at 30 days post chemotherapy (top), 10 months post chemotherapy (middle) and 3 years post chemotherapy (bottom)

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Patient 2 experienced dimming of vision during FLAG-Ida cycle 1, with VA 6/9 bilaterally. Despite a healthy ocular surface, keratoconjunctivitis secondary to cytarabine was diagnosed and the dose halved. During cycle 2 VA dropped to perception of light in both eyes, but recovered in <1 week to 6/9 with high-dose oral prednisolone and remained stable throughout 8 months' follow-up.

Punctate yellow intraretinal macular flecks, previously reported with fludarabine toxicity [3], were not observed in our patients. OCT features have not previously been reported. Electronegative electroretinogram (ERG) and bipolar cell dysfunction are previously reported findings [3, 4]. Histopathology shows loss of retinal ganglion cells, loss of bipolar cells and inner nuclear layer oedema; inner retina and optic nerve head gliosis and inflammatory cell infiltrate are also reported [3, 4]. Fludarabine can also cause brain white matter toxicity [5], affecting the occipital lobes with central visual loss.

Initially, bright flash rod ERGs from patient 1 were electronegative with reduced oscillatory potentials (OPs), indicating inner retina dysfunction. Over time the B wave improved, but OPs did not. Multifocal ERGs were globally reduced and delayed, and worsened over 2 years. OCTs, normal at presentation, over time showed microcystic macular oedema (inner nuclear layer oedema), outer nuclear layer oedema and photoreceptor layer disruption involving the external limiting membrane and ellipsoid zone, along with generalised retinal thinning (Fig. 1).

Bright flash rod ERGs from patient 2 were also electronegative. Pattern ERGs showed a low N95/P50 ratio suggesting retinal ganglion cell dysfunction. OCTs, normal at presentation, developed microcystic macular oedema, outer

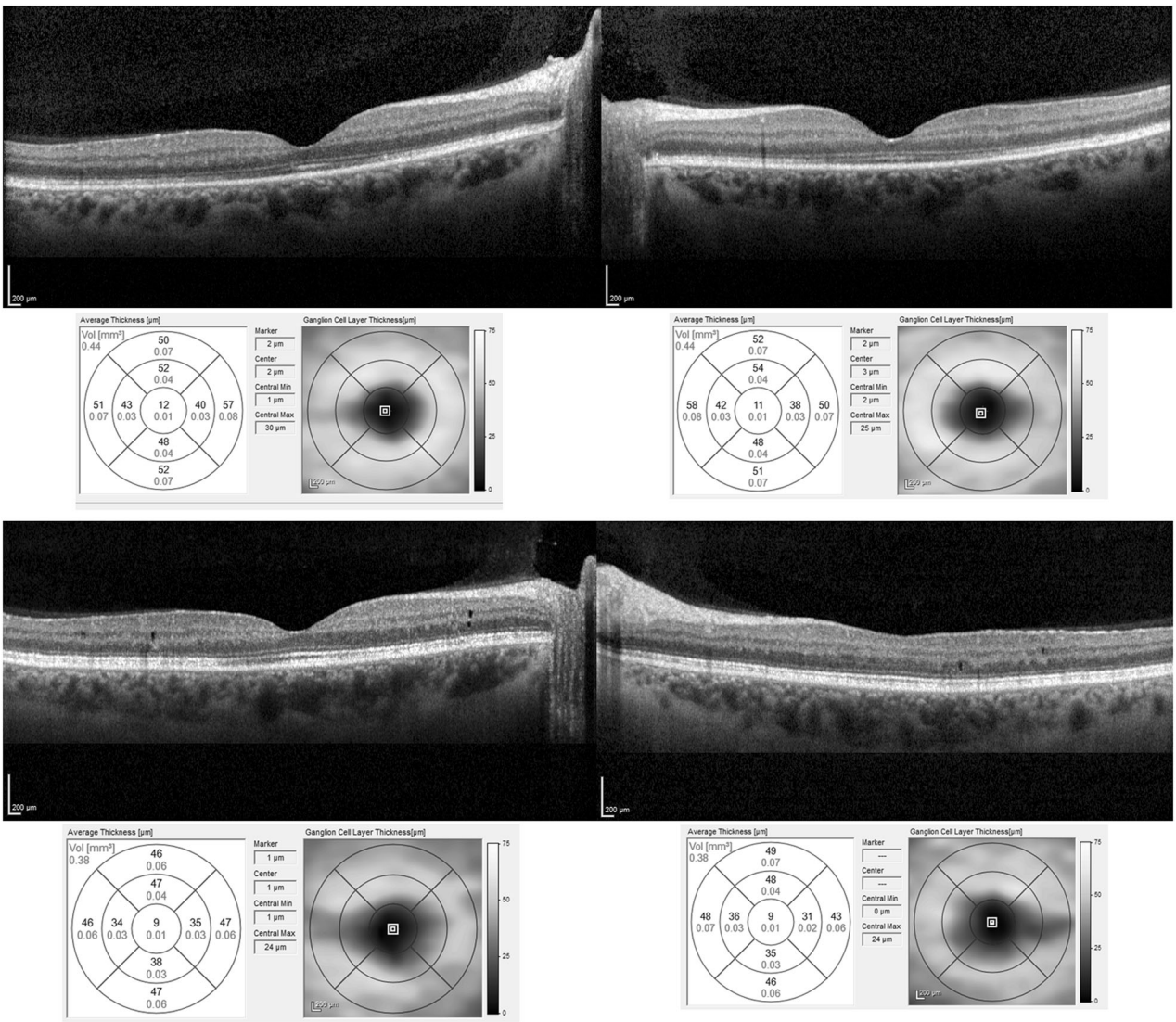

Fig. 2 Macular optical coherence tomography from patient 2 at 4 days post chemotherapy (top two rows) and 8 months post chemotherapy (bottom two rows)

nuclear layer oedema and thinning of the ganglion cell layer during follow-up (Fig. 2). At presentation magnetic resonance imaging (MRI) showed subtle white matter changes in the occipital lobes.

Fludarabine-related visual loss is well documented and our patients had several classic features. Diagnosis must be made based on history, as initial examination and OCT are normal. Fludarabine must be stopped when toxicity is suspected and investigated with ERG and brain MRI. This report is the first to include OCT. Serial OCTs during follow-up show the evolution of various retinal changes (see above), most of which have previously been shown via histopathology in case reports. There is currently no good quality evidence to guide treatment.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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Needles as a source of silicone oil during intravitreal injection

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Introduction

The presence of silicone oil (SO) droplets in the vitreous, even though frequently considered harmless, has been reported in 0.03–1.7% of eyes receiving intravitreal injections [1].

The source of these droplets is supposedly the syringes, since they are coated with SO in order to facilitate the

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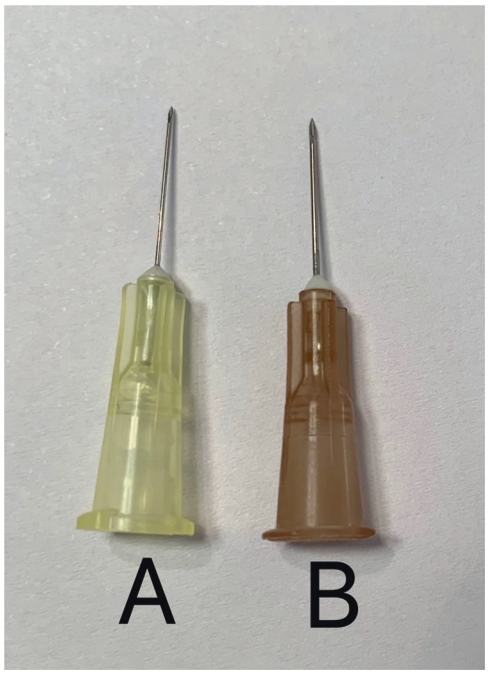

Fig. 1 BD PrecisionGlide needles. **a** 30-gauge needle; **b** 26-gauge needle