CMV to replicate and eventually cause retinitis. Takakura et al. (2014) reports on a relatively large series of viral retinitis following local steroid administration, but in this paper the injected steroid was triamcinolone or fluocinolone and the contribution of systemic immunosuppression remained unclear. Meanwhile, exclusion criteria of the GENEVA Study did not include systemic immunosuppressive treatment but only the use of systemic steroids (Haller et al. 2010). Moreover, it is possible that in retinal vein occlusion, the retinal blood flow stasis and the breakdown in the blood–retina barrier may increase the susceptibility of ocular tissues to virus penetration. In conclusion, ophthalmologists using intravitreal steroids in iatrogenic compromised patients should be aware of the potential risk of CMV retinitis.

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Early panretinal abnormalities on fundus autofluorescence and spectral domain optical coherence tomography after intravitreal ocriplasmin

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Editor,

Intravitreal ocriplasmin, a recombinant truncated form of plasmin with proteolytic activity against laminin and fibronectin (Hermel et al. 2010), has recently been approved as treatment strategy for vitreomacular traction (VMT). However, concerns have been raised regarding its ocular safety (Kim 2014). Clinical trials reported adverse events that included transient visual loss, dyschromatopsia and photopsias, usually associated with decreased amplitudes on electroretinography (ERG) (Stalmans et al. 2012). Spectral domain optical coherence tomography (SD-OCT) abnormalities have been detected within the macula, and ERG studies have demonstrated diffuse retinal dysfunction related to presumed ocriplasmin toxicity (Fahim et al. 2014; Tibbetts et al. 2014). Herein, we demonstrate that early structural abnormalities to the photoreceptors as detected by fundus autofluorescence (FAF) and SD-OCT may affect not only the macula but also the peripheral retina as well.

A 69-year-old woman presented with visual acuity of 20/32 and metamorphopsia in her right eye. Fundus examination and SD-OCT revealed VMT with small detachment of the foveal cones; FAF was normal (Fig. 1A,E). The day after uneventful intravitreal ocriplasmin (0.125 mg/0.1 ml), her vision decreased to 20/50 and she complained of dyschromatopsia. SD-OCT demonstrated the appearance of subfoveal fluid and multifocal shallow subretinal detachments (Fig. 1J–L), as well as focal areas of attenuation/thinning of the ellipsoid zone line and disappearance of the interdigitation zone line of the photoreceptors. Photoreceptor abnormalities corresponded to patchy areas of abnormally increased FAF signal within the macula (Fig. 1B,F) as well as to radial lines of abnormally increased FAF signal towards the retinal periphery (Fig. 1I). At day 7, her vision improved to 20/40 and dyschromatopsia was resolved. SD-OCT demonstrated the released VMT, decreased subfoveal fluid and shaggy photoreceptors in the fovea (Fig. 1C,G). Persisting attenuation/thinning of the ellipsoid zone line and further disappearance of the interdigitation zone line were noted. After 4 months, FAF and SD-OCT abnormalities disappeared completely (Fig. 1D,H).

Clinical trials that compared intravitreal ocriplasmin to placebo in treatment of VMT indicated that visual symptoms were greater in patients receiving ocriplasmin (Stalmans et al. 2012). In addition, decreased amplitudes in all ERG variables were noted, indicating the presence of panretinal dysfunction that persisted for several months (Fahim et al. 2014; Tibbetts et al. 2014). Our imaging study supports these functional findings; indeed, structural damage to the photoreceptors was not confined within the macula, but was actually widespread throughout the periphery. These abnormalities may be due to a protease effect on laminin, which is present not only in the vitreous but also throughout the retina, including the interphotoreceptor matrix (IPM) (Fahim et al. 2014). Interestingly, in our case, there was greater and broader damage to the interdigitation zone line compared to the ellipsoid zone line. Normal reflectivity of the interdigitation zone line arises from well-oriented and aligned interdigitations of apical processes of the retinal pigment epithelium (RPE) with outer segments of the photoreceptors. We hypothesize that lysis of the IPM caused by ocriplasmin may create

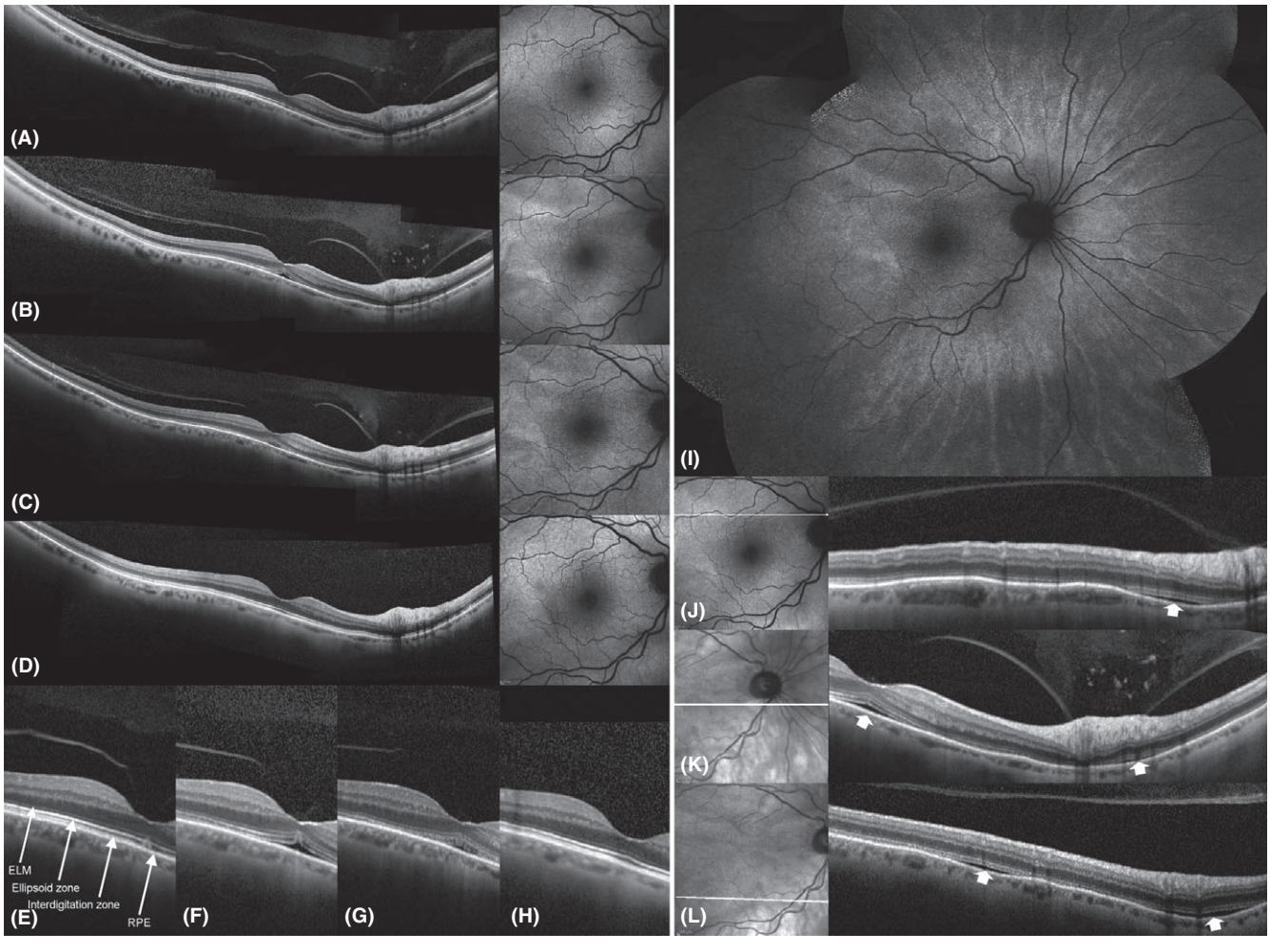

Fig. 1. Baseline horizontal wide-angle SD-OCT scan centred on the fovea (A, E) shows vitreomacular traction (VMT), as well as vitreous attachment peripapillary and temporally to the macula. A small detachment of the cones is well visible subfoveally, and well-delineated lines corresponding to the ELM, ellipsoid zone, interdigitation zone and retinal pigment epithelium (RPE) are present throughout the entire scan. Fundus autofluorescence (FAF) is normal. At day 1 after intravitreal ocriplasmin injection (B, F), SD-OCT scan reveals persistent VMT, appearance of subretinal fluid in the fovea, as well as perifoveal areas of attenuation/thinning of the ellipsoid zone line and disappearance of the interdigitation zone line of the photoreceptors. Wide-angle FAF (I) reveals patchy areas of increased signal within the macula, as well as lines of increased signal with a radial distribution from the optic disc head towards the periphery. Beside thinning or disappearance of photoreceptors lines, multifocal shallow detachments (*arrows*) of the retina from the RPE (J–L) are appreciated superonasally to the fovea, subfoveally and peripapillary, and inferiorly to the macula and optic disc. At day 7 (C, G), VMT has been released, subfoveal fluid has decreased, and shaggy photoreceptors are present in the fovea. The ellipsoid zone line is persistently attenuated, but the interdigitation zone line has experienced further and more diffuse disappearance. FAF is substantially unchanged from day 1. At month 4 (D, H), SD-OCT shows complete vitreous detachment, resolved subfoveal fluid and complete restoration of the outer retinal layers. FAF abnormalities resolved.

a loss of the normal alignment between photoreceptors and RPE microvilli, therefore causing reduced reflectivity of the interdigitation zone line. In addition, given the pivotal role of a healthy IPM for maintaining adhesion between retina and RPE, lysis of the IPM may reduce strength of the adhesion and thus cause multifocal detachments of the retina in areas where vitreoretinal traction was not significant.

In summary, although ocriplasmin is effective in releasing VMT, presumed toxic effects of the drug may lead to visual disturbances as well as to early but transient panretinal structural abnormalities, especially involving the interdigitation zone. We suggest evaluating carefully the retinal periphery after ocriplasmin injection to detect any possible toxicity for the photoreceptors. Given the limited follow-up of patients who experienced presumed ocriplasmin toxicity, further research is needed to investigate risk factors, duration of recovery and ways to prevent or minimize toxic effects of the drug.

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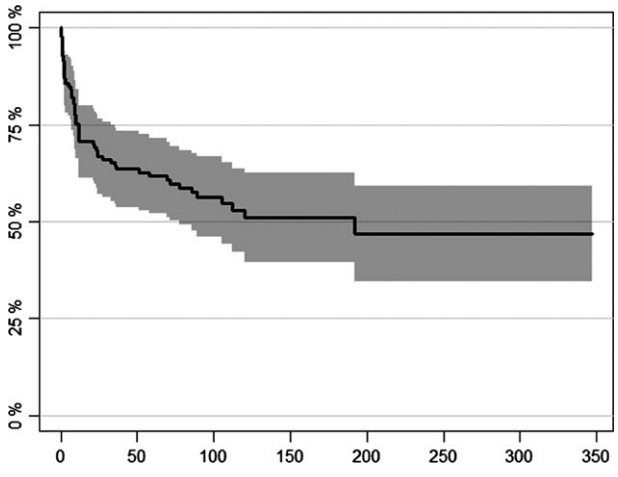

Fig. 1. Survival probability after first intervention using Kaplan–Meier method for clustered data. *X*-axis represents time (months), and *Y*-axis represents survival probability. Qualified success rate was 70.6% at the first year and 61.8% at 5 years, when defined as a final intra-ocular pressure (IOP) <21 mmHg with or without antiglaucoma medications. The probability that primary congenital glaucoma (PCG) patients will receive second operation was 29.4% at 1 year, 33.3% at 5 years and 38.2% at 10 years, after which the slope stabilized.

Long-term outcome of primary congenital glaucoma in South Korea

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Editor,

In primary congenital glaucoma (PCG), even after initial successful intra-ocular pressure (IOP) control with prompt surgical intervention, PCG children still face vision-threatening difficulties, such as corneal scarring and anisometropia, and resultant amblyopia (M S 2005). De Silva et al. (2011) reported a lack of progression rate in 90.3% of patients after 1 year, 70.8% at 10 years and 48.6% at 40 years and also reported that stable PCG patients could have glaucomatous progression with sight threatening complications when followed for a prolonged time. We evaluated the long-term outcome according to surgical interventions, prognosis related to visual acuity, IOP and ocular morbidities in South Korean patients.

Medical records of PCG patients from seven hospitals in South Korea were examined. Mean follow-up period was 137.8 months. Statistical analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA) and package 'PRODLIM' in R 2.13.2 (Vienna, Austria; http://www.R-project.org). In a total of 154 eyes of 92 PCG patients, 50.64% received one operation and 45.2% received more than two operations. Qualified success rate defined as a final IOP <21 mmHg with or without antiglaucoma medications was 70.6% and 61.8% at postoperative 1 and 5 years, respectively. In success rate analysing with Kaplan–Meier method for clustered data, the probability that requires a second operation was 29.4% at 1 year, 33.3% at 5 years and 38.2% at 10 years (Fig. 1). Thereafter, the slope of the probability of a second operation became stable. Final prognosis were categorized according to World Health Organization classification of visual impairment and IOP control (Group 1: IOP well controlled, no visual impairment; Group 2: IOP well controlled, low vision; Group 3: IOP well controlled, lower vision; Group 4: legally blind; Group 5: uncontrolled IOP). Groups 1, 2 and 3 comprised 33.7%, 21.3% and 21.3% of PCG patients, respectively. About 19.1% had blindness in one or both eyes. Although IOP is often well controlled after surgical intervention, over half (61%) of the PCG patients had visual impairment. Mean visual acuity at the final visit was 0.48, when excluding lower than finger count, and mean IOP was 15.2 mmHg. In multivariate analysis of the association of prognosis and other ocular factors, the number of surgical interventions was weakly positively correlated with poor prognosis (Spearman's correlation coefficient = 0.31154, $p = 0.004$). Other factors including the involvement of both eyes, age at initial presentation, sex and IOP at initial presentation were not statistically associated with final prognosis (all $p > 0.05$). About 20.9% still had amblyopia, excluding the number of patients who displayed improved vision after amblyopia therapy, and 13.9% had strabismus at the most recent visit or had previously received strabismus surgery. In univariate and multivariate analyses, the presence of these ocular morbidities was not associated with age at initial presentation, sex, IOP at initial presentation or the number of surgical interventions (all $p > 0.05$). Three patients had retinal detachment, and one had suprachoroidal haemorrhage. These complications were associated with IOP at initial presentation in both univariate and multivariate analysis ($p = 0.009$ and 0.026, respectively).

In conclusion, the probability of a second operation after the first intervention was continuously increased during follow-up. In final prognosis,