Sir,

Reply to Alexander *et al* (Subconjunctival anaesthesia for intravitreal injections)

We would like to thank Alexander *et al*[1] for their interest in our study. We reported the incidence, features and outcomes of post-intravitreal anti-VEGF endophthalmitis (PIAE) in a prospective, population-based study to provide ophthalmologists with important clinical information. We also performed a case–control study to identify risk factors, as this is recognised as a valid methodology to identify possible risk factors for rare conditions.[2]

Our conclusions regarding the use of subconjunctival anaesthesia are based on the analysis of 3 out of 47 PIAE cases compared with 1 out of 200 control cases receiving this anaesthesia.[3] Although this study reports one of the largest known series of PIAE, due to the relatively small number of patients with individual risk factors, it was not possible to fit our results to a multivariate model (as acknowledged in our paper). However, of these four patients, other than all four not receiving pre-procedural antibiotics, none were reported to have any of the other potential risk factors. After excluding these four patients, the other risk factors (failure to administer topical antibiotics immediately post-injection, blepharitis, patient squeezing, and failure to administer pre-procedural topical antibiotics) had no significant change in respective odds ratios (ORs). Therefore, it would be difficult to attribute the large OR of 13.669 for subconjunctival anaesthesia to confounding risk factors alone.

We hypothesised that a possible explanation for subconjunctival anaesthesia as a risk factor was that it compromised the conjunctival surface before intravitreal injection, allowing the introduction of pathogens into the subconjunctival space.

We read with interest your experience in Southampton. The incidence rate of 0.07% that you report is comparable to our reported rate of 0.025%. However, by only reporting the incidence rate at a single centre, it is unclear whether any of the other risk factors that we analysed in our paper have been controlled for. Therefore, it is not possible to make any further conclusions on whether the use of subconjunctival anaesthesia is a risk factor for PIAE based on the data you supply. One cannot ascertain the effect that individual risk factors will have on the incidence rate of PIAE based on the odds ratio calculated as part of the case control study that we performed.

Owing to the anonymous way the information is collected through the British Ophthalmological Surveillance Unit, we were unable to ascertain whether subconjunctival anaesthesia was the standard of care at the reporting institutions. Further evidence of risk factors for PIAE is always welcome. Comparing the figures from your centre to others, where subconjunctival anaesthesia is not used, in a matched, case–control study may provide firmer evidence as to whether subconjunctival anaesthesia is a significant risk factor.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Kyrieleis plaques in herpes zoster virus-associated acute retinal necrosis: a case report

Kyrieleis plaques were described in 1933 in ocular tuberculosis.[1] They have been primarily described in association with infections of the retina, Toxoplasma gondii chorioretinitis being the most common.[2] Other described associated causes include cytomegalovirus (CMV) retinitis, syphilitic retinitis, acute retinal necrosis (ARN) due to Herpes Simplex Virus-2, Varicella-Zoster Virus, and Rickettsia conorii infections.[3–5] Orzalesi and Ricciardi[6] suggested they are an immune response, resulting from deposition of immune cells and inflammatory debris in arterial walls. Others have debated this hypothesis as these plaques can persist despite resolution of the infection and treatment with steroids.[7]

Case report

A 56-year-old immunocompetent male presented with a 2-day history of decreased vision and floaters in the left eye. His past ophthalmic history included a single episode of Herpes Zoster Ophthalmicus in his right eye 3 months previously, which was successfully treated with 1 week of oral acyclovir.

Examination of the affected left eye revealed 3+ of anterior chamber cellular activity, with associated mutton fat keratic precipitates (KPs) on the inferior aspect of the corneal endothelium (Figure 1). There was no evidence of synechiae. Dilated examination of the posterior segment was hazy due to 2+ of vitritis and haze 1+ but despite this, 360 degrees of confluent retinal necrosis encircling the arcades was apparent. Kyrieleis plaques were present, without any evidence of sheathing of the retinal veins (Figure 2). Examination of the right eye was unremarkable, with no evidence of any inflammation. Best-corrected visual acuity was 0.1 Log Mar in the right and 0.5 in the left eye.

Polymerase chain reaction of the aqueous tap was positive for HZV and negative for HSV, CMV, and Toxoplasma gondii DNA.

The patient was treated with 1 g intravenous Acyclovir three times/day for 5 days, followed by 2 g of oral Valacyclovir three times/day. After 7 days of antiviral treatment, concern over the safety of the optic nerve in the presence of an occlusive vasculitis meant that a course of 60 mg of oral Prednisone was introduced. This dose was maintained for 7 days.

Vitritis and haze significantly resolved after 10 days of treatment. Fluorescein angiography (FFA) demonstrated normal arterial filling and no evidence of active vasculitis. Therefore, prednisone was reduced to 40 mg/day. Kyrieleis plaques did not leak or have late staining on the FFA (Figure 3). The anterior uveitis and mutton fat KPs resolved over 2 weeks following initiation of treatment. Conversely, the Kyrieleis plaques increased in number and became confluent along the retinal arteries (Figure 4). Despite the visual acuity improved to Log Mar 0.2, the patient remained on a dose of 40 mg Prednisone daily. The plaques started to resolve over the following 4 weeks. Prednisone was tapered and discontinued gradually over a period of 8 weeks. At 3 months, Valaciclovir was reduced to 1 g three times/day and was eventually discontinued 14 weeks after initiation.

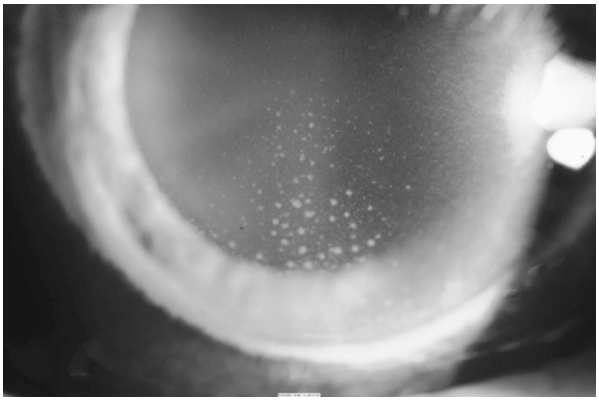

Figure 1 Slit-lamp photo of the left anterior chamber on the day of presentation. It demonstrates 3+ of anterior chamber cellular activity and multiple mutton fat keratic precipitates on the inferior corneal endothelium.

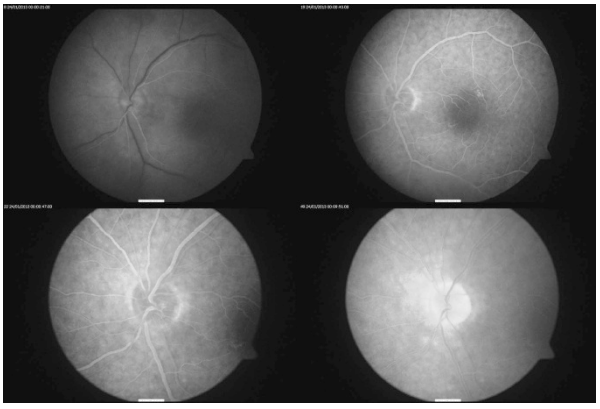

Figure 3 Fundus fluorescein angiography (FFA) of the left eye, demonstrating normal retinal arterial filling. There is no fluorescein dye leakage in the macular area. The Kyrieleis plaques did not leak or have significant late staining of fluorescein dye.

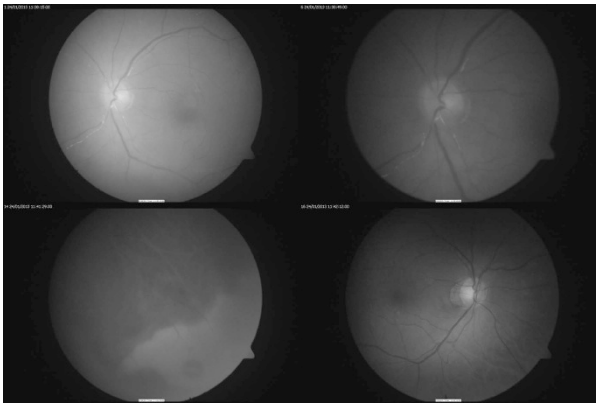

Figure 2 Left eye fundus photograph demonstrating kyrieleis plaques within the arteries that do not extend outside the vessel. There is no significant sheathing or involvement of the retinal veins.

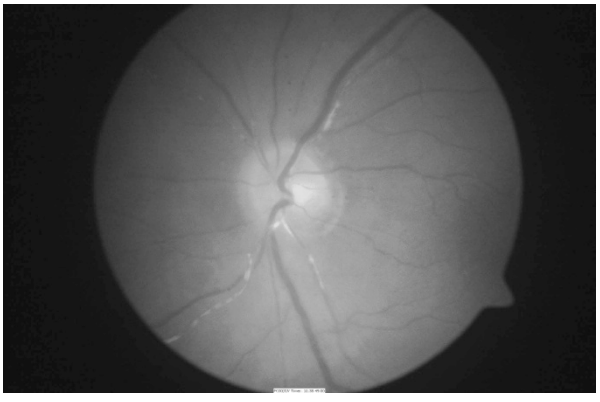

Figure 4 Red-free fundus photograph (30°) of the left eye 2 weeks after initiation of treatment. Vitreous inflammation settled down, while the retinal lesion's margins became more prominent, demarcated and some pigmentation started to appear in the margins.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Comment

Contralateral ARN is well described is cases with Herpes Zoster Ophthalmicus. Second eye involvement occurs in approximately a third of patients, typically within 6 weeks,[8] although fellow eye involvement decades following an initial infection has been described.[9]

Frances-Munoz *et al*[3] report an association between Kyrieleis' plaques and inflammation. In our case, the plaques increased as the vitritis and retinitis resolved. Interestingly, despite the high doses of steroids initiated in this case, the Kyrieleis' plaques appeared to increase in number and spread around the optic disc while the overall inflammation was settling down. Eventually the plaques started to dissolve 4 weeks after presentation.

This case highlights the already known importance of examining the retina of the fellow eye when patients present with Herpes Zoster Ophthalmicus. In addition, the case provides further evidence that Kyrieleis plaques can potentially increase in size and number as inflammation settles down. The high-dose steroid treatment did not appear to have a role in limiting or reversing the development of these plaques.

Conflict of interest

The authors declare no conflict of interest.

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Sir,

Does the timing of treatment affect the ocular phenotype in patients with Mucopolysaccharidosis I homozygous for the L490P mutation?

Mucopolysaccharidosis I (MPS I) has autosomal recessive inheritance and has been associated in some cases with a single base mutation L490P.[1] Defective breakdown of glycosaminoglycans (GAGs) in MPS I causes accumulation in musculoskeletal, cardiorespiratory, and ophthalmic systems. In eyes, GAG deposition results in: (i) glaucoma, (ii) retinal degeneration, (iii) corneal haze, and (iv) optic disc swelling or atrophy.[2] We report 13 children (Table 1) homozygous for L490P, treated with either haematopoietic stem cell transplantation (HSCT) or enzyme replacement therapy (ERT). This is the first report to correlate ocular phenotype and timing of treatment in a subset of MPS I patients with a defined mutation.

Comment

The effects of early treatment on the ocular phenotype in MPS are at present unclear. An animal study has demonstrated improved corneal clarity with ERT, particularly when started shortly after birth.[3] Previous retrospective case series of MPS I patients without defined genotype treated with ERT have not shown significant improvement in vision, corneal, or optic nerve changes.[4,5]

Little is known about genotype-ocular phenotype correlation in MPS I, but it may be expected that a series of patients with a single L490P mutation would have less ocular phenotypic variability than a group of patients with a variety of mutations. This case series demonstrates that the severity of corneal haze at final follow-up correlated with the timing of treatment with either ERT or HSCT (Figure 1a), although children treated earlier were younger at follow-up (Table 1). Timing of treatment did not correlate with retinal or optic nerve findings.

Children treated earlier had better final visual outcomes, although again they were younger at follow-up (Figure 1b). Three patients who were treated at younger than 60 months (cases 2, 5, and 8) showed improvement in vision, whereas none treated over 60 months of age had any improvement in vision and three had a deterioration (cases 9, 12, and 13). These results suggest that earlier treatment with ERT/HSCT for patients with MPSI may result in improved visual outcomes, but methods for objective assessment of ocular phenotype and longer follow-up of treated patients is needed to clarify this.

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