A large proportion of SpRs had completed (25%) or were currently undertaking a higher degree (23%). This may reflect the high level of competition for ophthalmology training positions,² however there was a substantial interest in academic ophthalmology among those surveyed, with 26% stating an intention to pursue a career in academia.³ The impact of shrinking education budgets is likely to impact the availability of such posts, however the introduction of defined training programmes in academic medicine^{4,5} may enable this potential to be tapped.

This is the first study to evaluate the popularity and competitiveness of ophthalmology subspecialties, and has identified an imbalance between the skills acquired during training and those in demand. This study indicates that SpRs are able to state their preferred subspecialty interest at an early stage; this information may be used by both trainees and trainers to develop a coherent strategy for workforce planning in both the NHS and academia.

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A case of bilateral endophthalmitis and carriage of β -defensin 1 –44CC genotype

β -defensins are innate antimicrobial peptides found in a variety of ocular tissues and are critical to the immune response.^{1–3} We present a case of bilateral endophthalmitis and show the carriage of the –44CC genotype in β -defensin 1. The polymorphism has previously been linked to increased susceptibility to infection.^{4–7}

Case report

An 80-year-old man underwent cataract surgery in the right eye complicated by a capsular tear. Within 4 days he returned with a hypopyon, painful loss of vision and reddening of the right eye. Endophthalmitis was diagnosed, an urgent vitreous tap was performed and intravitreal cetazidime and vancomycin were started. Microscopical examination revealed Gram-positive cocci, but no final growth of organisms. The right eye responded to treatment, but 1 month later a retinal detachment was diagnosed in the same eye. This was surgically repaired without complications. A year later, after an uncomplicated left cataract surgery in another hospital, the patient presented again with endophthalmitis symptoms, including hypopyon, rapid visual loss (hand movements), pain and reddening of the eye. He responded well to intravitreal amikacin and vancomycin treatment. Microscopy was positive for leucocytes but no organisms were seen. Final visual acuities were 6/9 (right) and 6/6 (left).

This gentleman could have had an underlying genetic predisposition to endophthalmitis, given that he had had the same rare complication after ocular surgery on two separate occasions. DNA sequence variants, or polymorphisms, in the β -defensin gene family may reduce efficacy of defensin activity or production, and predispose an individual to infection. We, therefore, decided to screen two genes of this gene family for polymorphisms.

Methods

We examined the promoter, 5' and 3' untranslated regions (UTRs) and the coding regions of β -defensin 1 and 2 (BD1 and BD2), using PCR primers designed to incorporate all previously reported single-nucleotide polymorphisms (SNPs) in BD2 and 39% of the reported SNPs in BD1. Seven amplicons were produced, sequenced and analysed for new and previously reported sequence variants.

Results

We observed a total of 14 sequence variations: six new and eight previously reported. All new variants were seen in BD2. Seven of the previously reported polymorphisms were in BD1 and one was in BD2 (table 1).

BD1 has been studied extensively and we did not identify any new sequence variants. It is

thought to be constitutively expressed in the vitreous, and one of the SNPs we identified, –44G→C, has been previously linked with a predisposition to infection. Two independent studies have shown an association between –44C allele and HIV infection.^{5,7} Furthermore, Hu *et al*⁶ observed an increase in the –44C allele associated with patients having chronic obstructive pulmonary disease when compared with healthy smokers. Jurevic *et al*⁴ showed that the –44G allele was protective against high Candida carriage in patients with diabetes and healthy controls. All these studies suggest that carriage of the –44C allele is associated with increased predisposition to disease. Although the function of this particular polymorphism is unknown, its position in the 5' UTR suggests that it could influence BD1 expression. Possession of either the G or C allele may lead to a variation in defensin levels among individuals. This poses an interesting question as to whether genotyping this locus can predict those at a greater risk of endophthalmitis. A larger study is now underway to determine whether there is a true association between endophthalmitis and carriage of the –44C allele.

BD2 has been less well studied, but is thought to be upregulated in the eye in response to infection/inflammation.^{3,9} We found six new sequence variants and one previously reported SNP (+319ins9) in BD2. Five of our new sequence changes are in the BD2 promoter region. This region is rich in transcription factor (TF)-binding sites that are known to play a key role in upregulation of BD2.⁹ Polymorphisms in this region could render it unresponsive to TF stimuli thereby inhibiting the production of BD2 peptide. Functional work will be necessary to deal with this in more detail.

One has to be very cautious when interpreting and extrapolating findings from a single individual. However, bilateral endophthalmitis is extremely rare and would be more likely to occur in genetically susceptible individuals. Defensins are natural antimicrobial peptides and it is easy to see how a reduction in their production or function could predispose to endophthalmitis. Given the rarity of the condition, large studies on endophthalmitis are difficult, but we hope that by conducting this screening on more individuals we shall determine the role of defensins in susceptibility to

Table 1 Sequence variations seen in β -defensin 1 and β -defensin 2 genes in a patient with bilateral endophthalmitis

Gene	Sequence change	Region	SNP identifier
BD1	–694 A→G	Promoter	Rs2977829
BD1	–688 C→G	Promoter	Rs2702877
BD1	–44 G→C	5'-UTR	Rs1800972
BD1	–20 G→A	5'-UTR	Rs11362
BD1	+6805 C→T	Intron 1	Rs2741124
BD1	+7181 G→A	3'-UTR	Rs1047031
BD1	+7391 T→C	Beyond 3'-UTR	Rs9314616
BD2	–1257 T→G	Promoter	New
BD2	–823delC	Promoter	New
BD2	–475 A→C	Promoter	New
BD2	–434 A→G	Promoter	New
BD2	–269 C→G	Promoter	New
BD2	+238delT	Intron 1	New
BD2	+319ins9	Intron 1	Vankeerberghen <i>et al</i> ⁹

BD1, β -defensin 1; BD2, β -defensin 2; SNP, single-nucleotide polymorphism; UTR, untranslated region. Changes are numbered from translation start site.

this condition, and whether it may be possible to predict those at a greater risk.

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This study has been approved by The Central and South Bristol Research Ethics Committee, United Bristol Healthcare NHS Trust, and informed consent has been obtained, in accordance with the Declaration of Helsinki. As the patient has since passed away, informed consent for this work was obtained from the patient's next-of-kin.

We believe that this, coupled with the complete anonymity of patient within the case report, is sufficient for publication of this work.

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Symptomatic interferon retinopathy successfully treated by hypertension management

Retinopathy is a common side effect of interferon treatment. We report a case of symptomatic retinopathy caused by interferon α in a

Figure 1 Retinal photography showing multiple cotton wool spots in both retinas before hypertension treatment.

Figure 2 Retinal photography showing reduced cotton wool spots in both retinas after hypertension treatment.

hypertensive patient successfully treated by management of hypertension alone and without stopping interferon α . As far as we know, this is the first reported case of interferon retinopathy successfully treated by hypertension management.

Pathogenesis of interferon retinopathy is most likely related to microcirculation damage and the impairment of angiogenesis. If interferon α therapy offers significant clinical benefit but is complicated by retinopathy, by treating other sources of microcirculation injury such as hypertension or diabetes mellitus, symptomatic retinopathy may be successfully treated without ceasing interferon α treatment.

Case report

The patient is a 55-year-old gentleman with multiple lung metastases from renal cell carcinoma. He had normal vision and no previous history of hypertension. In a clinical trial, he was treated with 9 MIU interferon α -2a administered subcutaneously three times a week and 1000 mg bevacizumab intravenously every two weeks. He had excellent treatment response, with complete radiological remission of metastatic disease.

He developed blurred vision three months after starting interferon. As a side effect of bevacizumab he also became hypertensive, his blood pressure consistently 160/120 mmHg. On examination, visual acuity of his left eye was 6/6 and his right eye 6/5. Fundoscopic examination demonstrated multiple cotton wool spots in both retinas with no other signs of retinopathy (fig 1). Fluorescein angiography was unremarkable.

Considering the excellent cancer response, benefits of continuing interferon treatment outweighed the risk of further visual impairment. The same interferon regimen was continued with close monitoring of retinopathy. Oral anti-hypertensive medication was started with reduction of blood pressure to 140/80. Three months later, blurred vision completely resolved, visual acuity normalized to 6/5 for both eyes and cotton-wool spots were significantly reduced (fig 2). He continued interferon treatment with no further complications.

Comment

Retinopathy, presenting with cotton wool spots, retinal haemorrhage or micro-aneurysms on fundoscopic examination, is the most common ophthalmic side effect of interferon occurring in 24%¹ of patients treated. Retinopathy rarely becomes symptomatic at viral hepatitis dosages, but at higher cancer treatment dosages there are more frequent case reports of symptomatic retinopathy.²

Pathogenesis of interferon retinopathy is still inconclusive. Ischaemia from microcirculation injury seems the most plausible explanation for retinopathy. Immune complexes deposition and inhibition of endothelial cell function, proliferation and migration have been suggested as mechanisms of microcirculation injury.^{3,4} Indeed interferon- α has been shown to cause endothelial cell apoptosis in vitro.⁵

Reported risk factors for interferon retinopathy include hypertension,^{1,6} diabetes mellitus,⁶ high interferon dosages¹ and pegylated interferon.¹ Kawano found 80% of hypertensive patients treated with interferon developed