associated with visual improvement. The final visual outcome could have been influenced by other factors such as the type, duration and stage of CNV, time of intervention, presence of macular scarring and retinal atrophy.

Our results are comparable to other recent studies.[4 6 7] Spaide *et al.*,[4] in a series of 266 patients, found visual improvement in a third at one month. Nearly 6% had worse visual acuity and 80% of patients had a reduction in optical coherence tomography measurements at one month. Rich *et al.*[6] observed improvements in visual acuity and macular thickness at one week, which continued to month three. At month three, mean visual acuity had improved from 20/160 to 20/125 and mean macular thickness had decreased by 99.6 μm.

We encountered no significant bevacizumab-related systemic side effects. The only ocular adverse events included a case of infectious endophthalmitis in a non-compliant patient and one retinal pigment epithelial rip. These patients had poor visual outcome. Other recent studies also found no serious drug-related ocular or systemic adverse events.[4 6–9]

This study was a non-randomized retrospective study with short-term follow-up. The study included a wide range of patients with various types and stages of CNV, some with previous treatments. The use of Snellen acuity measurements also means that direct comparison with previously published data is difficult. Despite these limitations it clearly demonstrates the efficacy and short-term safety of bevacizumab in the treatment of CNV and confirms the findings of previous studies. These preliminary results suggest that intravitreal bevacizumab is clinically effective in the management of neovascular AMD. Further studies are warranted to establish the long-term safety and efficacy of bevacizumab, and the optimal dosage for different lesions.

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References

1 **Gragoudas ES**, Adamis AP, Cunningham ET Jr, *et al.* VEGF inhibition study in Ocular Neovascularization Clinical Trial Group. Pegaptanib for neovascular age-related macular degeneration. *N Engl J Med* 2004;**351**:2805–16.
2 **Rosenfeld PJ**, Brown DM, Heier JS, *et al.* MARINA Study Group. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006;**355**:1419–31.
3 **Michels S**, Rosenfeld PJ, Puliafito CA, *et al.* Systemic bevacizumab (Avastin) therapy for neovascular age-related macular degeneration twelve-week results of an uncontrolled open-label clinical study. *Ophthalmology* 2005;**112**:1035–47.
4 **Spaide RF**, Laud K, Fine HF, *et al.* Intravitreal bevacizumab treatment of choroidal neovascularization secondary to age-related macular degeneration. *Retina* 2006;**26**:383–90.
5 **Rosenfeld PJ**, Moshfeghi AA, Puliafito CA. Optical coherence tomography findings after an intravitreal injection of bevacizumab (avastin) for neovascular age-related macular degeneration. *Ophthalmic Surg Lasers Imaging* 2005;**36**:331–5.
6 **Rich RM**, Rosenfeld PJ, Puliafito CA, *et al.* Short-term safety and efficacy of intravitreal bevacizumab (Avastin) for neovascular age-related macular degeneration. *Retina* 2006;**26**:495–511.
7 **Avery RL**, Pieramici DJ, Rabena MD, *et al.* Intravitreal bevacizumab (Avastin) for neovascular age-related macular degeneration. *Ophthalmology* 2006;**113**:363–72.
8 **Bashshur ZF**, Bazarbachi A, Schakal A, *et al.* Intravitreal bevacizumab for the management of choroidal neovascularization in age-related macular degeneration. *Am J Ophthalmol* 2006;**142**:1–9.
9 **Fung AE**, Rosenfeld PJ, Reichel E. The international intravitreal bevacizumab safety survey: using the internet to assess drug safety worldwide. *Br J Ophthalmol* Published Online First: 19 July 2006. doi.

British family with early-onset Fuchs' endothelial corneal dystrophy associated with p.L450W mutation in the *COL8A2* gene

Endothelial dystrophies produce characteristic morphological and functional abnormalities of the cornea. The most prevalent is Fuchs' endothelial corneal dystrophy (FECD), which is characterized by bilateral primary cornea guttata and a reduced endothelial cell density that can result in corneal oedema, discomfort, and blurred vision. Histology shows a thickened Descemet's membrane with focal posterior excrescences and endothelial cell loss. The onset of FECD is typically in the fifth decade of life,[1] but an early-onset variant has been described that shows phenotypic differences from the more common late-onset disease.[2 3] A genome-wide search of a three-generation family with early-onset FECD identified a locus on chromosome 1p34.3–p32.[2] Within this locus a pathogenic mutation p.Q455K was found in the *COL8A2* gene in this and two additional pedigrees.[2] Gottsch *et al*[4] recently reported a novel mutation p.L450W in a separate family with early-onset FECD.

Case report

A white British family with early-onset FECD (fig 1) was identified. Patient I:1 (79 years) had been told he exhibited endothelial pathology when he was 23 years old. At the age of 75 years he had a left penetrating keratoplasty with cataract extraction and intraocular lens implantation. Cornea guttata were present in the right eye. Patient II:1 (53 years) experienced visual deterioration in her mid-twenties as a result of bilateral corneal oedema. A right penetrating graft was performed at age 34 years and a left penetrating keratoplasty was performed at age 41 years. Patient II:2 (55 years) was asymptomatic, but non-contact specular microscopy showed endothelial pleomorphism and cornea guttata located both centrally and within the borders of endothelial cells (fig 2A). Patient III:1 (18 years) was documented to have endothelial changes at 9 years of age but still has a corrected acuity of 6/6. Histology of the cornea from patient I:1 showed thickening of Descemet's membrane without cornea guttata (fig 2B).

Using eight primer pairs the coding region of the *COL8A2* gene was sequenced and a previously reported heterozygous point mutation leading to p.L450W substitution[4] was identified in family member I:1. The mutation was subsequently confirmed by direct sequencing in two other affected family members (fig 1). Individual III:1 has not yet been tested for this change.

Comment

Mutations in the *COL8A2* gene account for only a small proportion (less than 5%)[2] of late-onset FECD, but are associated with early onset disease.[2 4] We describe the phenotype of early-onset FECD in a white British family, which is caused by a point mutation (resulting in p.L450W substitution) in *COL8A2*. The age of onset, slit-lamp biomicroscopy findings, and endothelial imaging are similar to the phenotype of a family originally described by Magovern *et al.*[3] in 1979, in which the p.L450W change was subsequently reported.[4 5] The phenotype, the early age of onset with endothelial changes detected as early as the first decade, the presence of apparently intracellular guttae on specular microscopy, and the absence of excrescences on Descemet's membrane on histology are the noteworthy clinical features of the present pedigree. The relationship between the early and late-onset variants of FECD is, at present, uncertain.[6]

In conclusion, the identification of the p.L450W substitution in a second pedigree suggests that codon 450 in the *COL8A2* sequence might be a mutation hotspot. The possibility also exists that the two families share a common ancestor. Unfortunately, no information on other first-degree relatives of patient I:1 is available.

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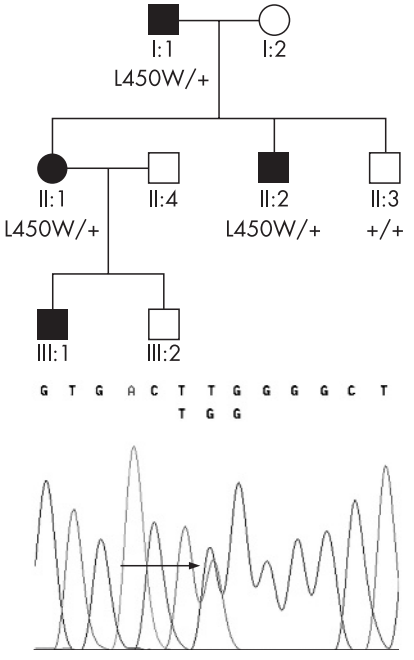

Figure 1 Fuchs' endothelial corneal dystrophy pedigree and mutation segregation. Affected patients are shown as filled symbols. Heterozygous individuals (I:1, II:1 and II:2) carry the c.1349 T>G transversion mutation resulting in a p.L450W change in the *COL8A2* gene, which is indicated by an arrow in the electropherogram. This change was not seen in the unaffected individual (II:3).

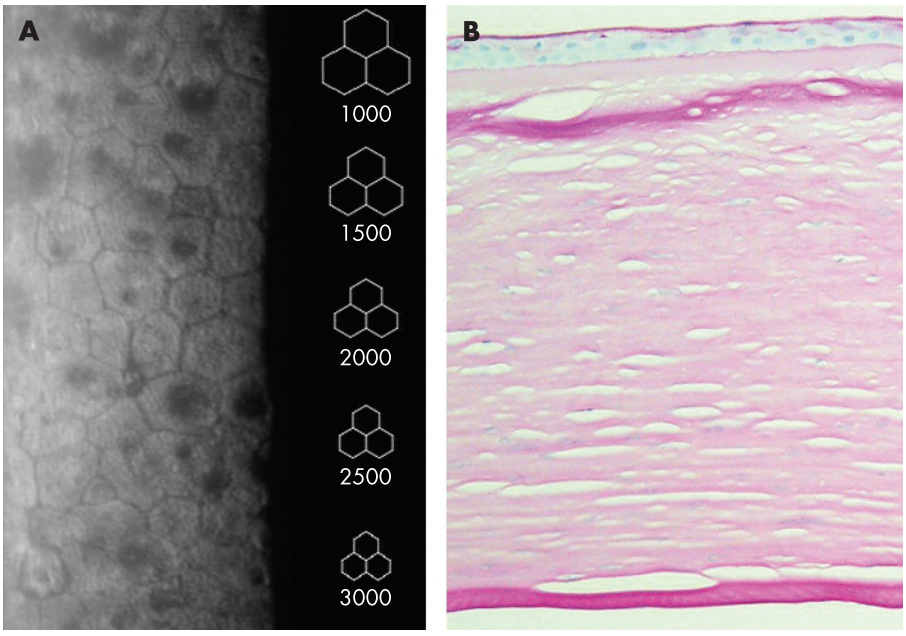

Figure 2 Morphological structure of early-onset Fuchs' endothelial corneal dystrophy corneas (A) specular endothelial microscopy of individual II:2. There is cellular pleomorphism and multiple non-reflecting areas. (B) Histology of cornea of individual I:1. There is a thickened Descemet's membrane but without posterior excrescences.

Local ethics approval was obtained for this study.

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References

1 **Krachmer JH**, Purcell JJ Jr. Young CW, Bucher KD. Corneal endothelial dystrophy. A study of 64 families. *Arch Ophthalmol* 1978;**96**:2036–9.
2 **Biswas S**, Munier FL, Yardley J, *et al.* Missense mutations in COL8A2, the gene encoding the alpha2 chain of type VIII collagen, cause two forms of corneal endothelial dystrophy. *Hum Mol Genet* 2001;**10**:2415–23.
3 **Magovern M**, Beauchamp GR, McTigue JW, *et al.* Inheritance of Fuchs' combined dystrophy. *Ophthalmology* 1979;**86**:1897–923.
4 **Gottsch JD**, Sundin OH, Liu SH, *et al.* Inheritance of a novel COL8A2 mutation defines a distinct early-onset subtype of fuchs corneal dystrophy. *Invest Ophthalmol Vis Sci* 2005;**46**:1934–9.
5 **Gottsch JD**, Zhang C, Sundin OH, *et al.* Fuchs corneal dystrophy: aberrant collagen distribution in an L450W mutant of the COL8A2 gene. *Invest Ophthalmol Vis Sci* 2005;**46**:4504–11.
6 **Sundin OH**, Jun AS, Broman KW, *et al.* Linkage of late-onset Fuchs corneal dystrophy to a novel locus at 13pTel–13q12.13. *Invest Ophthalmol Vis Sci* 2006;**47**:140–5.

Three oncocytomas in a short space of time

Oncocytomas of the caruncle are rare tumours, found in 3–8% of caruncle excision biopsies.[1] They occur most commonly in elderly women. Clinically, these tumours tend to present as a slow-growing, asymptomatic mass that is often tan red in colour.[2] Treatment is by complete surgical excision and recurrence is unusual, although very rare malignant oncocytomas occurring in the ocular adnexae have been reported,[3] and there has been a case of persistent rhinorrhea caused by an oncocytoma occurring in the lacrimal sac with extension into the nasolacrimal duct.[4]

Case reports

A 38-year-old woman presented with a two-year history of a slowly enlarging cystic lesion of the left medial canthus, which was causing increasing irritation. On examination, there was a smooth, pink, fluid-filled lesion measuring 4 mm in maximum diameter (fig 1). The cyst was excised under local anaesthesia.

An 81-year-old man with a history of diabetic retinopathy presented for routine follow-up and was found to have a cystic lesion on the left lower eyelid, lying just proximal to the medial canthus. On examination, there was a smooth, yellow cystic lesion that was thought clinically to be a cyst of Moll. The lesion was excised with no subsequent recurrence.

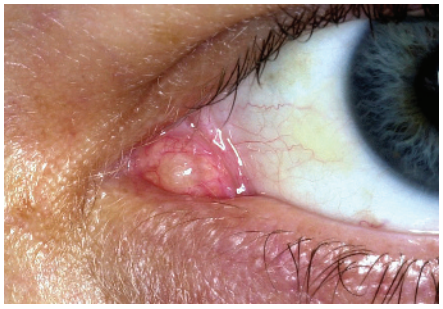

Figure 1 Smooth, fluid-filled lesion of medial canthus. Informed consent was obtained for publication of this figure.

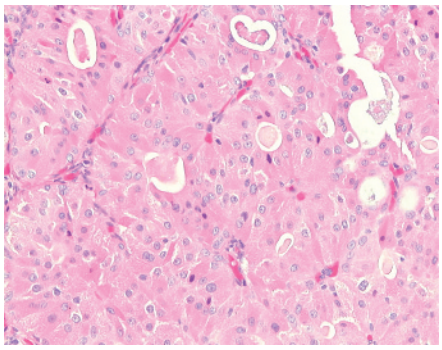

Figure 2 Tumour composed of bland cells with abundant granular, eosinophilic cytoplasm (haematoxylin and eosin, original magnification ×200).

An 80-year-old man presented to the clinic complaining of a lesion affecting the right eye. On examination, a small cyst was noted adjacent to the caruncle. Excision was performed and one 7/0 Vicryl suture was put in to appose the tissue defect, with a provisional clinical diagnosis of a simple conjunctival cyst.

Comment

All three specimens appeared similar upon histological examination (fig 2). Each lesion appeared well circumscribed and was composed of nests and trabeculae of uniform, polygonal cells with abundant, finely granular eosinophilic cytoplasm.

The caruncle is a unique anatomical structure containing elements of both conjunctiva and skin.[5] Oncocytomas (oxyphilic adenomas) of the caruncle are rare tumours accounting for only 3–8% of masses of the caruncle.[6] These cases are unusual in that, to our knowledge, this is the first series in which three cases presented in the space of eight weeks. This begs the question: are we misdiagnosing or indeed underdiagnosing these tumours, because not all are sent for pathology and how important or relevant is this?

Oncocytomas are benign neoplasms of oncocytic cells, which can occur at a variety of sites. Ocular adnexal oncocytomas are usually situated in the lacrimal drainage apparatus of the caruncle.[7] Cases occurring in other sites such as the eyelid[8] have also been documented. The differential diagnosis should include melanocytic melanoma at the top of the list; as this carries the worst prognosis, melanocytic naevus, benign epithelial tumours, pyogenic granulomas and haemangiomas, along with several other rarer lesions.[9]

As already mentioned, oncocytomas are by and large benign in nature and usually only require excision for cosmetic purposes or if they cause irritation to the patient. They do, however, have a real potential to recur in cases of incomplete excision[10] and can be locally aggressive and occasionally turn malignant.

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