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Clinicopathological Report

Clinicopathological features of severe corneal blood staining associated with proliferative diabetic retinopathy

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Abstract

A 54-year-old man with a history of severe proliferative diabetic retinopathy in both eyes and profound visual impairment presented with severe corneal blood staining in the left eye secondary to a 'spontaneous' total hyphaema and raised intraocular pressure in an eye with iris neovascularization. Despite anterior chamber washout, the cornea remained virtually opaque and thickened. The subject subsequently underwent pars plana vitrectomy with endolaser using a temporary keratoprosthesis, insertion of a Morcher iris-surround intraocular lens and penetrating keratoplasty. Histopathology of the excised corneal button revealed fine eosinophilic granules composed of aggregations of haemoglobin and its breakdown products dispersed throughout the stroma, with occasional foci of weakly positive Perl staining for intracellular haemosiderin. Fluorescence confocal microscopy revealed a marked increase in fluorescence throughout the corneal stroma and the basal epithelial layer. This case highlights the microstructural features and aspects of the surgical management of severe corneal blood staining.

Key words: confocal microscopy, corneal blood staining, hyphaema, pathology.

Introduction

Corneal blood staining is a serious complication of persistent hyphaema associated with elevated intraocular pressure (IOP). The reported incidence of corneal blood staining following traumatic hyphaema is 2–11%,[1–4] whereas it is significantly greater following total hyphaema (33–100%).[4] We report a case of severe corneal blood staining secondary to a rubeosis iridis-related total hyphaema associated with elevated IOP.

Case report

A 54-year-old Maori man presented with a 2- to 3-week history of a painful and 'blind' left eye. He had a 15-year past history of very poorly controlled non-insulin-dependent diabetes mellitus with severe bilateral proliferative diabetic retinopathy and maculopathy, complicated by recurrent vitreous haemorrhages and tractional retinal detachments. Two years prior to presentation he underwent a pars plana vitrectomy in the left eye (OS), followed 6 months later by phacoemulsification with intraocular lens. Three months prior to presentation he required a YAG capsulotomy OS and 1 month later fine iris neovascularization was noted in this eye. At this time best-corrected visual acuities (BCVA) were 6/60 in both eyes although the diabetic retinopathy OS was thought to be stable.

At presentation BCVA was 6/60 in the right eye (OD) and vague perception of light OS. Slit-lamp biomicroscopy revealed a total hyphaema OS (Fig. 1a), an IOP of 48 mmHg, and severe corneal blood staining extending from the endothelium to Bowman's layer (Fig. 1b). B-scan ultrasonography OS highlighted a vitreous haemorrhage and a flat retina. Examination OD revealed a cataract, IOP of 14 mmHg and peripheral tractional retinal detachment.

Medical treatment (topical timolol maleate 0.5% twice a day, dorzolamide 2% three times a day, apraclonidine 1% three times a day and oral acetazolamide 250 mg three times a day) was used to lower IOP. The following day IOP was 28 mmHg and an anterior chamber washout was performed.

Subsequently, the cornea remained markedly opaque although the IOP was controlled at less than 25 mmHg. Two weeks after presentation, using a temporary intraoperative keratoprosthesis (Fig. 1c), the subject underwent further pars plana vitrectomy with endolaser and (because of a fixed dilated pupil) insertion of a sulcus-based Morcher iris-surround intraocular lens, with an 8-mm-diameter penetrating keratoplasty. The initial postoperative course was

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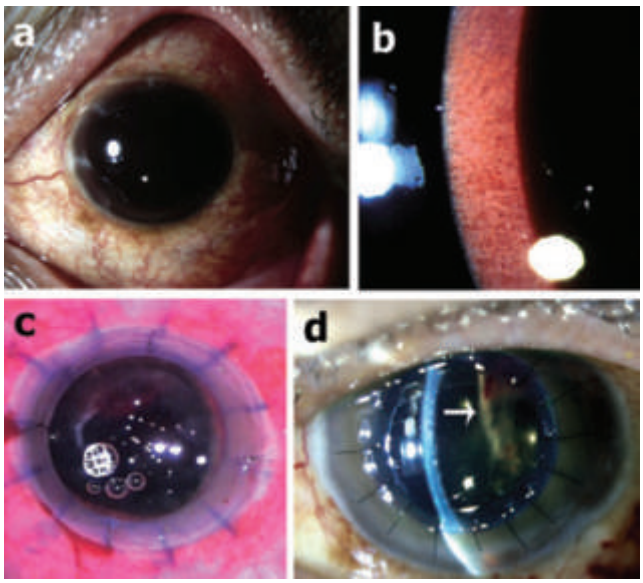

Figure 1. (a) Preoperative photograph of the anterior segment of the left eye highlighting a total hyphaema and corneal blood staining. (b) Slit-lamp photograph of the left cornea showing corneal blood staining extending from the endothelium to Bowman's layer. (c) Temporary keratoprosthesis used intraoperatively. (d) The anterior segment of the left eye 2 weeks postoperatively, showing residual fibrinous exudate in the anterior chamber (arrow).

complicated by fibrinous exudate in the anterior chamber (Fig. 1d), which responded to intensive topical prednisone acetate 1% (initially hourly with reducing dosage over 3 weeks) and dexamethasone alcohol 0.1% ointment at night. Three weeks postoperatively, the cornea was entirely clear and the anterior chamber quiet, although BCVA remained hand movements OS because of diabetic maculopathy.

Histopathology of the corneal button revealed fine eosinophilic granules, composed of aggregates of haemoglobin and its breakdown products, dispersed throughout the stroma, with greatest density anteriorly (Fig. 2a,b,d). This material was mainly extracellular, with only occasional foci of weakly positive Perl staining for intracellular haemosiderin. There was marked hypocellularity of the posterior stroma and more obvious Perl staining associated with the relatively sparse endothelial cells. The epithelium, Bowman's layer and Descemet's membrane were intact. Fluorescence confocal microscopy, using a Leica TCS 4D confocal laser-scanning microscope (Leica, Heidelberg, Germany), revealed a marked increase in autofluorescence throughout the entire corneal stroma and the basal epithelial layer (Fig. 2c,e). The pattern of fluorescence in the stroma correlated with that of the eosinophilic granules observed by light microscopy.

Discussion

Predisposing factors for corneal blood staining include prolonged duration of hyphaema, large or total hyphaema, sustained increased IOP and dysfunction of the corneal endothelium.[1–4] The reported case exhibited a total hyphaema with markedly elevated IOP for 2–3 weeks prior to review.

The natural history of corneal blood staining has been documented by slit-lamp microscopy.[1–5] Initially, corneal oedema occurs as a result of endothelial dysfunction indicating that blood staining is imminent. The earliest sign is the presence of fine yellow granules in the posterior stroma. A straw yellow discoloration of the stroma subsequently develops, progressing to a reddish-brown discoloration over several days. Over time, the discoloration changes through various shades of greenish-black to grey. Corneal blood staining extending to Bowman's layer and the epithelium has been reported in severe cases.[6] Clearance of the blood staining begins peripherally and progresses centrally, and can take up to 3 years. Occasionally clearance is incomplete leading to permanent opacification.[1]

Therapeutic efforts are best directed at preventing corneal blood staining in early cases.[6] Corneal blood staining is most likely with a total hyphaema and an IOP greater than 25 mmHg for longer than 6 days.[3] Surgical evacuation of the hyphaema is indicated at this stage or at the first microscopic sign of blood staining.[3] Thereafter, management options include awaiting spontaneous clearance or penetrating keratoplasty.[5,6] In this case, despite evacuation of the hyphaema, penetrating keratoplasty was required because of the severity of grey-black corneal blood staining and need for additional retinal photocoagulation.

The following pathogenesis of corneal blood staining has been postulated.[6–9] Initially, endothelial degeneration occurs because of mechanical disruption, toxicity from erythrocytic debris and possibly porphyrin-induced phototoxicity. Subsequently, haemoglobin and breakdown products diffuse into the posterior stroma. Haemoglobin is phagocytosed by posterior keratocytes and degraded to haemosiderin, with released haemosiderin subsequently phagocytosed by anterior stromal keratocytes. A gradient of haemoglobin degradation from posterior to anterior stroma is therefore observed. Excess intracellular haemoglobin and haemosiderin causes keratocyte death, resulting in hypocellularity of the posterior stroma. The cornea is repopulated with keratocytes as a result of ingrowth of fibrocytes from the limbus; corneal clearance therefore begins peripherally. Fluorescence confocal microscopy indicated that the basal epithelial layer was involved in the current case. Interestingly, McDonnell *et al.* have also reported positive epithelial staining and suggested epithelial cell shedding might have a role in clearing the anterior stroma of haemoglobin pigment.[6]

The reported case is of interest for a number of reasons, including: the severity of corneal staining, the associated vitreous haemorrhage with the consequent management and surgical challenges, and the histopathological and fluorescence confocal microscopy observations of corneal blood staining from endothelium to epithelium.

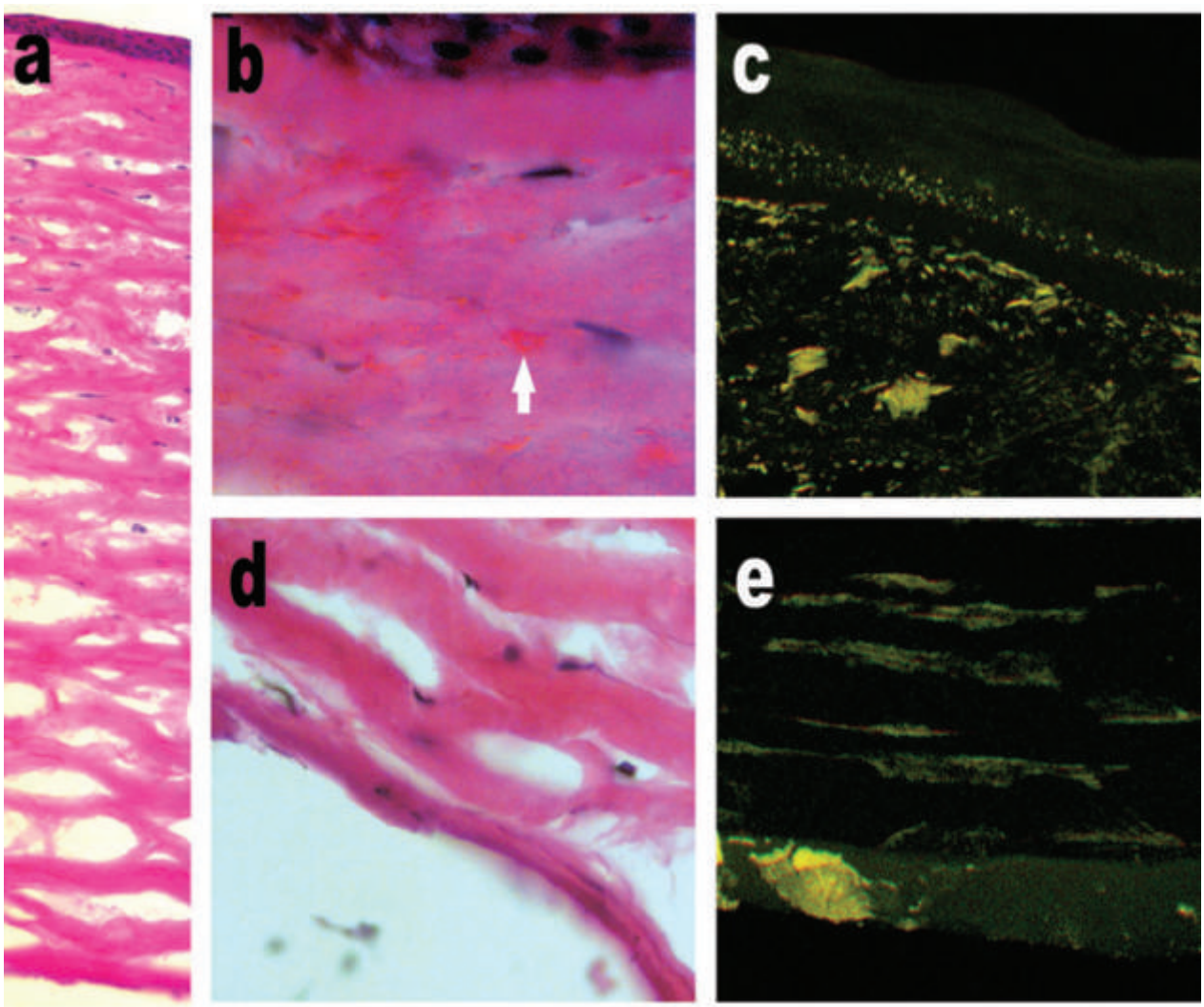

Figure 2. (a) Montage of entire antero-posterior section through a section labelled with haematoxylin and eosin ($x = 1148$ μm). (b) The basal epithelium and anterior stroma labelled with haematoxylin and eosin ($x = 95$ μm). Note the orange eosinophilic labelling of the haemoglobin particles. (c) Red-green stereo image of the endogenous autofluorescence in the basal epithelium and anterior stroma ($x = 158.7$ μm; $z = 9$ slices through 8.22 μm). Note the deposition in the basal epithelial cells and the anterior stroma. (d) Posterior stroma and endothelium labelled with haematoxylin and eosin ($x = 223$ μm). (e) Red-green stereo image of the endogenous autofluorescence in the posterior stroma and endothelium ($x = 158.7$ μm; $z = 13$ slices through 12.75 μm).

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