

Spontaneous hyphaema and corneal haemorrhage as complications of microbial keratitis

L DAVID ORMEROD¹ AND KATHLEEN M EGAN²

From the Departments of ¹Ophthalmology and ²Epidemiology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, and the ¹Eye Research Institute of Retina Foundation, Boston, Massachusetts, USA

SUMMARY Hyphaema developed spontaneously in 16 of 458 patients with microbial keratitis treated at two centres on the East and West Coasts of the United States. Chronic corneal conditions were often present, and three cases had rubeosis iridis. Inflamed iris vessels were assumed to be the source of the haemorrhage. The hyphaemas tended to persist longer than is usual, particularly when coincident with a hypopyon. Recurrent hyphaemas are reported in two patients from outside this series. Spontaneous corneal haemorrhage was seen in three cases. Subepithelial bleeding settled rapidly, but a combined midstromal and pre-Descemet's haematoma cleared more slowly. Anterior segment bleeding was significantly associated with advanced age, female sex, infection with Gram-positive organisms, and hypopyon.

Anterior segment haemorrhage is uncommon in the absence of trauma. Bleeding diatheses¹⁻⁴ or the rupture of pathological blood vessels are sometimes implicated. Bleeding may be caused by iris neovascularisation, as in diabetic rubeosis,⁵ or by abnormal tumour vessels in melanoma,⁶ retinoblastoma,⁷ or juvenile xanthogranuloma.⁷ Vascularised surgical wounds^{8,9} and iris neovascular tufts, occurring in proximity to the pupillary frill,^{10,11} have recently been described as causes of spontaneous hyphaema. Occlusive vasculitic processes¹² in, for example, herpetic uveitis or Stevens-Johnson syndrome, may also disrupt iris vessels. The spontaneous hyphaemas of Fuchs's uveitis syndrome¹³ probably arise from the iris rubeosis characteristic of this condition. Bleeding originating from presumably normal, if secondarily inflamed, iris vessels has not been reported.

Intracorneal haemorrhage¹⁴ has generally been described after surgery or incidental trauma; other associated conditions have included severe glaucoma and chemical burns.^{14,15}

We report the clinical findings and course of 16 patients with spontaneous hyphaema and three with corneal haemorrhage occurring in a large series of patients with suppurative inflammation of the cornea. Two illustrative case reports are included.

Subjects and methods

Bacterial keratitis was defined as an inflammatory infiltration and ulceration of the corneal stroma, associated with an epithelial defect, from which one or more bacterial or fungal species were cultured. The records of the patients were studied retrospectively at the University of Southern California (USC), Los Angeles, and at the Massachusetts Eye and Ear Infirmary, Boston. Standard microbiological techniques¹⁶ were used at both centres.

The inpatient and outpatient charts of 458 consecutive cases of microbial keratitis were examined by

Table 1 Prevalence data comparing microbial keratitis groups with and without haemorrhagic complications

Group	Age at presentation*				Total
	≤54 years		>54 years		
	Male No. (%)	Female No. (%)	Male No. (%)	Female No. (%)	
Patients with haemorrhagic complications	2 (1.3)	1 (1.3)	4 (3.5)	11 (9.6)	18
Patients without haemorrhage	152 (98.7)	74 (98.7)	111 (96.5)	103 (90.4)	440
Total	154	75	115	114	458

*Data stratified round the median age of 54 years.

Correspondence to Dr L David Ormerod, Eye Research Institute, 20 Staniford Street Library, Boston, MA 02114, USA.

Table 2 Clinical characteristics of microbial keratitis patients with spontaneous hyphaema

Case	Age	Sex	Microbial aetiology	Ulcer size*	Predisposing causes	Other ocular conditions
1	28	M	<i>Staph. aureus</i>	M	Staple injury	—
2	78	F	<i>Staph. aureus</i>	M	Aphakia, extended-wear CL	—
3	87	F	<i>Staph. aureus</i>	M	Trauma, pseudophakia	—
4	78	F	<i>Staph. aureus</i>	M	Bullous keratopathy	Rubeotic glaucoma
5	68	F	Coagulase-negative staphylococcus	M	Bullous keratopathy	Granulomatous uveitis
6	69	M	Coagulase-negative staphylococcus	M	Zoster keratitis	—
7†	76	F	<i>Str. pneumoniae</i>	M	Bullous keratopathy	Rubeotic glaucoma
8	79	F	<i>Str. pneumoniae</i>	M	2 months post-PK	Postoperative glaucoma
9	81	M	<i>Str. pneumoniae</i>	M	—	—
10	63	M	β -streptococcus + β -streptococcus (2 types)	M	Assault	—
11	60	F	β -streptococcus	L	Table injury	—
12	73	F	<i>Pseudomonas aeruginosa</i>	L	Aphakia, daily-wear CL	—
13	58	M	<i>Pseudomonas aeruginosa</i>	S	Bullous keratopathy	Late-stage glaucoma
14	68	F	<i>Pseudomonas mesophilica</i>	M	Neurotrophic keratitis	—
15	62	F	NA	M	Bullous keratopathy	Rubeotic glaucoma
16	52	M	Culture negative	M	Tree branch injury	—

*S=small (<2 mm); M=moderate (2–6 mm); L=large (>6 mm). †Hyphaema and corneal haemorrhage developed concurrently. CL=Contact lens. PK=Penetrating keratoplasty. NA=Not available.

means of detailed protocols. The study population was distributed as follows: Los Angeles County-USC Medical Center (LAC-USC)—227 patients, 1972–1983; the Estelle Doheny Eye Foundation (EDEF), Los Angeles—55 patients, 1978–1984; and the Massachusetts Eye and Ear Infirmary (MEEI), Boston—176 patients, 1977–1981. Information was collected on several demographic and clinical variables including age, sex, duration of the condition, systemic and local predisposing factors, prior medications, features of the corneal ulcer, microbiological culture results, complications, and treatment. Patients with a spontaneous onset of hyphaema or intracorneal haemorrhage, occurring at presentation or during the treatment period, were selected for additional study. Two patients from outside the series are included for discussion.

Results

Of the 458 cases 16 developed a spontaneous hyphaema and three (including one combined with hyphaema) had intracorneal bleeding. Therefore during the acute stage of the inflammation approximately 4% of the patients had anterior segment haemorrhage.

The median age of the 458 patients was 54 years. The median age of the group with haemorrhagic

complications was 68.5 years (range 28 to 87 years). Twelve (67%) of the haemorrhagic group were female. Prevalence data for patients with and without haemorrhage are contrasted in Table 1. The patients with haemorrhagic complications were significantly older ($t=2.96$, with df 456; $p<0.005$) and more likely to be female ($\chi^2=5.05$, df 1; $p<0.05$) than the group without haemorrhage. Male patients developing haemorrhagic complications were on average 10 years older, and female patients were 14.5 years older, than their counterparts without such complications.

To explore whether women were at greater risk because they were older we stratified the patients by age, using the median (54 years) as an arbitrary cut-off point (Table 1). In the younger group there were twice as many men as women, and both sexes were equally likely to have haemorrhage into the anterior segment. The numbers of males and females over 54 years of age were equal, and the age distribution by decade was almost identical. The proportion of older patients with haemorrhage was significantly greater than that of younger patients ($\chi^2=8.32$, df 1; $p<0.01$). Older patients of both sexes were at higher risk than younger patients, but hyphaema or intracorneal bleeding developed in women nearly three times as often as in men in patients over 54 years old.

The clinical characteristics of the 16 patients with

(Table 2 continued)

Systemic conditions	Hypopyon	Prior topical steroids	Hyphaema coincident with S/C injections	Onset of hyphaema (days from admission)	Outcome
—	+	—	+	1	Small. Settled in 4 days
—	+	+	—	5	20% hyphaema. Layered. Slow to resolve
Diabetes	+	—	—	0	Small. Endophthalmitis developed
—	—	+	—	0	50% hyphaema. Organised. Enucleation day 27.
Warfarin (pulmonary embolism)	—	—	+	3	15% hyphaema. Settled in 1 week
—	+	+	—	12	10% hyphaema. Layered. Cleared in >2 weeks
—	+	—	+	4	30% hyphaema. Cleared in 2 weeks
—	+	+	+	5	Small. Settled in 5 days
Dementia	+	+	—	7	75% hyphaema. Layered. Slow to resolve. Late enucleation
Chronic alcoholism	—	—	—	0	25% hyphaema. Slow to resolve
Diabetes	+	—	—	12	Microhyphaema. Settled in 3 days
—	+	—	—	12	Small. Cleared rapidly
—	—	—	—	8	Small. Settled in 1 week
—	+	+	—	2	20% hyphaema. Intermixed with hypopyon. Slow to resolve
—	+	—	—	0	10% hyphaema. Intermixed with hypopyon. Enucleated
—	+	—	—	3	Small. Intermixed with hypopyon. Settled in 6 days

spontaneous hyphaema are shown in Table 2 and of the three patients with corneal haemorrhage in Table 3. Late hyphaemas developed in five traumatised eyes (patients 1, 3, 10, 11, 16), all following the onset of corneal infection. Both hyphaema and corneal haemorrhage developed spontaneously in one patient (case 7).

The microbial keratitis involved Gram-positive organisms in 13 of the 16 culture-positive cases. Hypopyon was twice as prevalent in patients with spontaneous haemorrhage into the anterior segment (13 of 18) as in patients in the overall series (149 of 440) without bleeding ($\chi^2=11.1$, df 1; $p<0.001$).

The two subepithelial corneal haemorrhages cleared rapidly, but the midstromal and pre-Descemet's haematoma (case 7), associated with hyphaema, cleared much more slowly. Blood staining or other sequelae were not noted, and corneal bleeding did not pose a significant problem in this series.

The bleeding site was not seen in any patient; the conditions of microbial keratitis inhibit fine observation of the iris and anterior chamber. Iris neovascular tufts were not reported. Secondary bleeding, glaucoma (apart from the four cases with premorbid glaucoma), and corneal blood staining were not observed. However, we have recently seen two patients with major complications of hyphaema not observed in this series; their case reports follow.

CASE A

A 65-year-old South African black male developed a moderate-size paracentral *Streptococcus viridans* microbial keratitis. Several days later, at admission, he had a 10% hyphaema, without hypopyon, and was treated with subconjunctival injections of cephalothin and gentamicin and with topical chloramphenicol. The corneal infection improved rapidly, but on day 4 after admission secondary bleeding into the anterior chamber and a 50% hyphaema developed. Resolution occurred over a period of three weeks. There were no permanent sequelae.

CASE B

A 72-year-old male was treated at Massachusetts Eye and Ear Infirmary for a moderate-size suppurative corneal ulcer caused by a *Klebsiella oxytoca* infection of a herpes simplex trophic ulcer. When admitted, he had a 50% hyphaema, without hypopyon, and an intraocular pressure of 42 mmHg. He was treated with frequent high-dose topical cephazolin and gentamicin eye drops. Despite a rapid improvement of the keratitis the hyphaema increased to fill most of the anterior segment, and early corneal blood staining was noted on day 5. Three anterior chamber irrigations were performed over the next two weeks, each followed by severe bleeding. The intraocular pressure remained at 40 mmHg for nearly one month despite maximal glaucoma therapy. Ultimately the

Table 3 Clinical characteristics of microbial keratitis patients with intracorneal haemorrhage

Case	Age	Sex	Microbial Aetiology	Ulcer size*	Predisposing causes	Other ocular conditions	Systemic conditions
7†	76	F	<i>Str. pneumoniae</i>	M	Bullous keratopathy	Rubeotic glaucoma	—
17	78	F	Coagulase-negative staphylococcus	M	Zoster keratouveitis	—	Chronic lymphatic leukaemia
18	49	F	α -streptococcus + coagulase-negative staphylococcus + <i>Enterococcus</i> spp.	L	Dry eye	—	Chronic alcoholism

*S=small (<2 mm); M=moderate (2–6 mm); L=large (>6 mm). †Hyphaema and corneal haemorrhage developed concurrently. SC=subconjunctival.

ocular hypertension cleared and the hyphaema resolved slowly. The patient died before long-term sequelae could be assessed.

Discussion

Haemorrhagic complications of microbial keratitis are uncommon. They occurred in 4% of 458 patients in this series and also in 4% (6 of 140) of patients with microbial keratitis admitted to St Johns Hospital, Soweto, South Africa, in March 1981–February 1982 (unpublished data). The aetiology of the bleeding appeared to be multifactorial. Advancing age was a significant prognostic factor in both men and women. The risk of anterior segment bleeding was also two to three times greater for women than for men in the older age groups. These findings, however, are based on a relatively small number of patients. The preponderance of Gram-positive bacteria and the remarkably high prevalence of hypopyon (72%) suggest that the microbial infection involved strains of moderate virulence but high phlogogenicity. Bacterial proteases, cytolytic toxins, and streptokinases might play an important part in causing haemorrhage.

Two-thirds of the patients had local ocular predisposing factors (besides trauma), some of which may have been associated with chronic anterior segment inflammation. Prior treatment with topical steroids in six patients may also have contributed to the intraocular bleeding by increasing local vascular fragility. Trauma associated with subconjunctival injections appeared unrelated. Three patients presumably bled from pre-existing iris rubeosis (thrombotic glaucoma), and hyphaema developed spontaneously in one patient when long-term warfarin therapy was complicated by the advent of microbial keratitis. Two patients were chronic alcoholics and one patient had chronic lymphatic leukaemia, but all three had normal haemostatic profiles.

Spontaneous hyphaema has been reported as a complication of severe vasculitic uveitis,^{12,17,18} but not following microbial keratitis. An important observation is that the course of hyphaema complicating microbial keratitis often differs from that of traumatic hyphaema.¹⁹ Early bleeding mixed with the hypopyon to variable degrees; later haemorrhage layered over the hypopyon. In three eyes the bleeding filled >25% of the anterior chamber. Further bleeding did not occur in this series, but was seen in two other patients (cases A and B). In case B corneal blood staining and a prolonged pressure rise were major problems. In several cases the resorption of the blood and hypopyon was unduly prolonged.

The available follow-up was insufficient to provide an adequate analysis of the long-term sequelae of haemorrhage in these severely inflamed eyes, as distinct from those caused by the inflammatory process itself. Retention of blood in the anterior chamber can lead to fibrovascular organisation, posterior and peripheral anterior synechiae formation, corneal blood staining, glaucoma, and optic atrophy.¹⁹ The frequently prolonged natural history of hyphaema in these inflamed eyes suggests that intraocular bleeding is a potentially serious complication of microbial keratitis, as illustrated in case B.

When spontaneous hyphaema has occurred, mydriasis may tamponade irideal vessels and control bleeding.¹¹ It may sometimes be possible to photo-coagulate the bleeding site with argon laser, as suggested for iris neovascular tufts.²⁰ Aspirin therapy should be stopped³ and the haemostatic status investigated.¹ The intraocular pressure must be closely monitored. After the corneal infection is controlled, topical steroids may be beneficial in reducing the inflammation.¹⁹

Duke-Elder and Leigh²¹ noted that corneal haemorrhage almost invariably occurs from areas of neovascularisation, particularly following interstitial and mustard gas keratitis. There are several isolated

Hypopyon	Prior topical steroids	Corneal haemorrhage coincident with SC injections	Onset of corneal haemorrhage (days from admission)	Corneal site	Outcome
+	—	—	4	Midstromal and pre-Desemet's membrane	Still present at 1 month
+	—	+	2	Subepithelial	Cleared rapidly
—	—	—	22	Subepithelial	Cleared over 1 week

reports of corneal haemorrhage complicating microbial keratitis.²²⁻²⁴ Muenzler believes that haemorrhages may not be uncommon in the vascularised cornea and may go unnoticed because of their usually small size and limited duration.¹⁴ Large, superficial corneal haemorrhages may be drained by removing the overlying epithelium with a moist cotton-tipped applicator.²⁵ Deep corneal haemorrhages may, however, require formal surgical drainage^{26,27} because of their tendency to occlude the drainage angle, their chronicity,²⁸ and organisation with scarring.

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