The ocular surface toxicity of paraquat

We describe the clinical appearance and progress of bilateral ocular chemical injury caused by paraquat, a herbicide. Paraquat is used more commonly in developing countries and it has been associated with severe and prolonged ocular surface abnormalities due to the nature of the chemical. The current concepts in managing such an injury are reviewed.

Case report

A 69-year-old fruit farmer splashed a 20% solution of paraquat into both his eyes. The exposure of the right eye to the solution was more marked. The eyes were irradiated for less than 5 minutes at the time of the injury, and a formal irrigation, using Ringer’s solution for each eye, was not performed until presentation 5 hours later.

General medical history revealed that apart from controlled hypertension he was otherwise well and he had no previous history of ocular problems.

On arrival uncorrected visual acuity was 6/9 on the right and 6/12 on the left. The intraocular pressure was 14 mm Hg on the right and 19 mm Hg on the left. There was a circular 90% epithelial defect centred over the right cornea. The remaining corneal epithelium was opaque, leathery and oedematous (Fig 1). The left cornea was epithelialised although the conjunctival defect only extended to the nasal limbus in the right eye. The bulbar and tarsal conjunctiva remained inflamed.

The conjunctiva in the left eye was diffusely chemotic. There was extensive thrombosis of superficial and deep conjunctival vessels over the entire bulbar conjunctiva; however, the epithelial vessels remained intact and patent. The right cornea had punctate epithelial erosions over most of its surface and an epithelial defect involving the inferonasal quadrant of the cornea although the conjunctival defect only enlarged slightly.

A severe pseudomembranous conjunctivitis developed in the right eye by the third day with fibrinous adhesions developing in the inferior fornix. Periodic glass rod ling was commenced to break early symblepharon formation and the steroid was changed to non-preserved dexamethasone 1% hourly by day.

At 6 days post-injury there was evidence of epithelial healing from the margin of the epithelial defect in the inferior fornix of the right eye. Topical citrate and ascorbate were stopped and treatment was altered to non-preserved topical medication only: topical dexamethasone 1% every 2 hours, chloramphenicol four times daily, and hypromellose every 2 hours. Autologous serum tears (diluted to 20% in sterile saline solution) were also commenced 2 hours later.

Two weeks after the injury there were persistent epithelial defects in both eyes but the healing edge of conjunctival epithelium had reached the nasal limbus in the right eye. Best corrected visual acuity was 6/24 right and 6/6 left. At this stage there was no pseudomembrane present although the conjunctiva remained inflamed.

By 4 weeks after injury the ocular surface in both eyes had re-epithelialised. The cornea of the right eye at this stage was clear with no vascularisation. Visual acuity remained 6/24 on the right.

Impression cytology of both central corneas was undertaken at this point. The right cornea showed conjunctival-type epithelium with scattered goblet cells, polymorphonuclear leucocytes, and numerous apoptotic bodies. The left cornea demonstrated a corneal phenotype epithelium.

The last review was at 6 months post-injury. Uncorrected visual acuity was 6/9 in both eyes. The conjunctiva of both eyes remained minimally inflamed with mild erythema, chemosis, and subepithelial fibrosis now evident. These changes were more marked in the right eye (Fig 3). There was superficial pannus encroaching onto the right cornea predominantly superonasally. The affected area in the left eye shows subconjunctival fibrosis with vascular disorganisation and localised scleral translucency (Fig 4). Current treatment was dexamethasone 1% twice daily in both eyes.

Comment

Paraquat is a dipyridylidium quaternary ammonium salt that acts as an indiscriminate killer of all plant life. Preparations made commercially commonly contain the related compound diquat as well as surfactants to increase distribution over the leaf and aid penetration. Toxicity in humans is thought to relate to paraquat recycling in the redox reaction of the bipyridylidium cation with ascorbic acid (Fig 5). This depletes NADPH and interrupts cell metabolism. The reduced...
paraoquat then reoxidises using oxygen to generate a superoxide radical.

The oxygen free radicals generated binding macromolecules and damage membrane lipids. Intracellular processes involving calcium are also affected. Paraquat may not be effectively cleared from the cell, resulting in persistent cell damage. Prolonged clinical effects lasting up to a year have been reported. Documented cases of paraquat toxicity, although few, have noted a relatively mild initial appearance with a poor visual outcome in the long term. This has been the result of the development of a conjunctivalised corneal surface and chronic inflammation.

Paraquat ingestion can result in early fatality due to multorgan failure. In less severe cases, acute renal and hepatic toxicity is common. Pulmonary fibrosis may result in death. Pulsed methylprednisolone and cyclophosphamide during the inflammatory stages may have a profound effect on reducing the mortality. It is unclear whether a similar regimen would circumvent the long term sequelae of ocular paraquat injury.

The patient in this case had significant exposure to a commercial preparation with minimal first aid measures being implemented at the time of injury. He developed a severe surface injury over the first 48 hours with marked epithelial loss over one eye. This implied there were few, if any, viable limbal stem cells remaining. A severe pseudomembranous conjunctivitis then developed.

Previous reports of this extensive type of surface injury show that eventually conjunctivalisation of the cornea with vascular pannus is to be expected. Severe injury may result in a disordered ocular surface with dryness, symblepharon, ankyloblepharon, fornical shortening, entropion, and trichiasis.

Patients with total limbal stem cell loss invariably develop superficial pannus and conjunctivalisation of the cornea. Evidence that previously conjunctival phenotypic epithelium can transdifferentiate into corneal epithelium is derived from animal experiments with a debrided cornea and limbus where corneal epithelium healed the resultant defect. Viable limbal stem cells may thus have remained in the perilimbal crypts of Vogt. The right eye of this patient healed from conjunctival epithelium, confirmed by impression cytology, although most of the cornea remains clear without pannus. It has been reported that transdifferentiation is inhibited once neovascularisation occurs. In the left eye, which only had a small zone of limbal stem cell loss if any, the epithelium over the cornea was confirmed as corneal phenotype on impression cytology and there was no neovascularisation.

A suitable microenvironment for healing should be encouraged through the use of medical therapy. Topical corticosteroids in the first week after injury promote successful healing of epithelial defects by controlling inflammation. Adequate lubrication is also important. Autologous serum tears have been reported to relieve the symptoms of dry eye and improve the ocular surface disease more successfully than conventional tear substitutes in dry eye states. These drops have also been instrumental in the healing of persistent epithelial defects. Essential components of the tear film present in serum tears include epidermal growth factor, vitamin A, and transforming growth factor β, which are important for the proliferation, differentiation, and maturation of the surface epithelium.

We present a case of severe paraquat chemical injury to both eyes that had a good outcome from treatment. This case demonstrates a very good result from a usually devastating injury.

Preventing conjunctivalisation of the corneal surface after total loss of the limbal stem cell population remains a challenge. Therapeutic intervention may help restore a more functional surface visually. The use of intensive early antioxidant therapy followed by autologous serum tears and non- preserved ocular lubricants may have improved the outcome.

Figure 5 Redox cycling reaction with paraquat.

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Accepted for publication 23 July 2001

References

Henoch-Schönlein purpura with bilateral central retinal artery occlusion

Henoch-Schönlein (H-S) purpura is an acute leukocytoclastic vasculitis that primarily affects children and mainly involves skin, joints, gastrointestinal tract, and kidney. Reported ophthalmic manifestations of Henoch-Schönlein purpura include episcleritis, scleritis, keratitis, anterior uveitis, and central retinal vein occlusion. However, central retinal artery occlusion, to the best of our knowledge, have not been reported. We report on a girl with H-S purpura complicated with bilateral central retinal artery occlusion.

Case report
A 6 year old girl visited our paediatric department with the chief complaint of multiple erythematous rashes over the lower extremities and buttock for 2 weeks. Under a presumptive diagnosis of H-S purpura, oral prednisolone was prescribed. Nevertheless, arthralgia, haematuria, and moderate hypertension developed 3 weeks later. The histopathological findings of renal biopsy were compatible with H-S purpura nephritis. Unfortunately, acute renal failure occurred despite aggressive systemic treatment and haemodialysis was started.

Two days before haemodialysis, the patient noticed sudden visual loss. Visual acuity was hand movement in both eyes. Anterior segment and intraocular pressure were normal. Fundus examination revealed a cherry red spot with severe retinal oedema at the macular and peripapillary area in both eyes. Disc oedema and venous engorgement were also noted in both eyes (Figs 1 and 2). The retinal manifestations were compatible with bilateral central retinal artery occlusion. Fundus fluorescein angiography was not performed because of her poor general condition.

Three days after haemodialysis, her systemic condition deteriorated due to drowsiness that was proved to be cerebral vasculitis by brain computed tomography.

Figure 1 Fundus photograph of the right eye demonstrating cherry red spot with severe retinal oedema at macular and peripapillary area, disc oedema, and venous engorgement.

Figure 2 Fundus photograph of the left eye demonstrating cherry red spot with severe retinal oedema at macular and peripapillary area, disc oedema, and venous engorgement.

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One month later, her visual acuity was counting finger in both eyes. Fundus examination revealed a pale disc, arterial sheathing, and drusen-like RPE change at foveal area in both eyes. Six months later, her best correction visual acuity was 6/30 in the right eye, and 6/60 in the left.

Comment
The dominant clinical manifestations of H-S purpura are cutaneous purpura (100%), abdominal pain (63%), gastrointestinal bleeding (33%), and nephritis (40%). In general, H-S purpura is an acute, self-limiting illness though one third of patients will have one or more recurrences of symptoms. H-S purpura was the cause of renal failure in 2% and 5% of groups of children undergoing haemodialysis in California and France, respectively.

Although the aetiology of H-S purpura remains unknown, it is clear that IgA has a critical role in the immunopathogenesis. The clinical features of H-S purpura are a consequence of widespread leucocytoclastic vasculitis due to IgA deposition in vessel walls. Treatment is limited to symptomatic and supportive care. Corticosteroids are often used depending on the severity of the disease.

According to the previous reports, the ocular manifestations of H-S purpura are rare, including episcleritis, scleritis, keratitis, anterior uveitis, and central retinal vein occlusion. In this case, H-S purpura vasculitis may have an important role in the pathogenesis of bilateral central retinal artery occlusion. To our knowledge this might be the first case of H-S purpura complicated with bilateral central retinal artery occlusion in the literature.

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Accepted for publication 23 July 2001

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Primary iris pigment epithelial hyperplasia and glaucoma
Primary iris pigment epithelial hyperplasia (PIPH) is a rare condition characterised by the presence of iris pigment epithelium on the anterior surface of the iris stroma. There are few reports that are available in the literature and they generally refer to it as congenital ectropion uveae (CEU). CEU, however, is a misnomer, since the iris pigment layer is known to be separate from the uvea. Yet, the term CEU persists in clinical use.

Primary iris pigment epithelial hyperplasia is a congenital non-progressing condition that is easily differentiated from acquired progressive ectropion uveae, the latter resulting from tractional erosion of posterior pigment layer and sphenicter muscle, secondary to glaucoma and/or uveitis.

The most common association is neurofibromatis (1; 2) though other ocular (3; 4) and systemic associations (5; 6) have been described, including a chromosomal abnormality.

This report describes two cases of primary iris pigment epithelial hyperplasia with glaucoma and reviews the available literature on this rare abnormality. In one case the presentation of glaucoma was in adolescence and in infancy in the other. Associated ocular features are described. In these two patients there were no systemic features of diagnostic significance.

Case 1
A 15 year boy presented with occasional watering in the left eye for 4 years. There was no history of any visual disturbance.

On examination his left eye was apparently normal and Hertel exophthalmometry readings were 19 mm in the left eye and 13 mm in the right with bar reading of 105. He had a ptosis of 2 mm (Fig 1, top right) with good levator function. The appearance of the left upper lid was suggestive of plexiform neurofibroma but no mass was palpable. The patient’s vision was 20/20 right eye (emmetropic) and 20/25 left eye (cylinder of –1.50 D at 110°, keratometry left eye –42.00 × 15°, 45.5 × 105°).

Case 2
A 5½ year old girl presented with gradual enlargement of the right eye since the age of 6 months. There was a history of mild photophobia but none of lacrimation or deterioration of vision.

On examination the patient’s Snellen acuity was 20/240 in the right eye (−1.50 sph, –4.00

Figure 1 Case 1 with PIPH and associated abnormalities. Top left: Extensive hyperplasia of the iris pigment epithelium overlying the stroma of the iris in an irregular manner but did not reach the angle (Fig 1, top left). The normal iris architecture was lost, but no nodules were seen. There was pigment on the anterior surface of the lens but the iris did not transilluminate. There was anisocoria of 1.5 mm, the left pupil being larger but round, regular and reacting to light. Indirect gonioscopy (Fig 1, bottom left) demonstrated an open angle with iridodetrabeculodysgenesis in the form of an anterior insertion of the iris into the trabecular meshwork with excessive pigment deposition and a prominent Schwalbe’s line, this being very marked in some areas. The right eye had a fully open angle with all structures clearly seen. Intracocular pressure (IOP) on the first examination was 52 mm Hg in the left eye and 12 mm Hg in the right. On fundus examination there was an oblique insertion of the disc, with inferonasal crescent and an oval oblique cup involving 0.81 × 0.61 part of the disc (Fig 1, bottom right). A B-scan ultrasound of orbit confirmed the apparent proptosis of the left eye was due to a longer axial length (24.36 mm compared with 22.60 mm in the right eye). There were two cafe au lait spots on the trunk but there was no other systemic abnormality. None of the family members had similar ocular findings or any evidence of neurofibromatosis.

The IOP responded poorly to topical medication and a trabeculectomy was performed which controlled the IOP.
but may be oval and associated with PIPH.
Neuropigment epithelial layer eversion is the result of hyperplasia of the derm, usually a hyperplasia of the former. Growth between the ectoderm and the mesoderm is unknown but is probably due to imbalance of unknown factors.

The extent to which the pupillary abnormalities discussed above, PIPH is frequently associated with significant ocular abnormalities. Spinal cord palsy with good levator function was presented in six of nine cases reported by Dowling et al. in one case each by Ritch et al. and Herzberg. The eye may be slightly proptotic in some cases. The appearance of the upper lid may suggest plexiform neurofibroma even though no mass may be palpable. All these features were present in the first case in this report.

Glaucoma was present in most of the cases reported. Ritch et al. found glaucoma in seven out of eight cases of PIP. Dowling et al. in eight of nine cases, and it was also noted and in other reported cases of PIP. It is usually of onset in childhood or early adolescence. The diagnosis is confirmed with late onset also has been reported. The intraocular pressure shows an initial decrease when the patient is instead but rises again quickly and filtering surgery was required in most cases. Surgical intervention was necessary in both the cases in this report.

The features of PIPH detailed in this report are in concordance with those previously published. There may be other associated ocular abnormalities, palsy being the commonest. Neurorubromatosis is the most frequently associated systemic disorder. Glaucoma may develop at any stage, therefore these cases should be recognised early by healthcare professionals and followed for development of glaucoma.
In our patient during the caudal epidural injection the fluid wave of injection did not spread uniformly in the epidural space and break the adhesions but, instead, got trapped in tiny compartments formed by the adhesions and caused lateral pressure on the spinal cord, thus increasing subarachnoid space pressure, resulting in vitreous haemorrhage in the left eye (Fig 1).

Therefore, we feel the cases with pathogenesis of intraocular haemorrhage, secondary to a sudden rise of intracranial pressure, should be considered as the variant of Terson's syndrome.

The clinical course of Terson's syndrome is typically one of gradual resolution of the vitreous haemorrhage and return of normal vision. Haemorrhages that do not resolve may require vitrectomy, but several studies have proposed that early vitrectomy also may improve visual outcome. Indications for early pars plana vitrectomy in children include vitreous haemorrhage in infants (precluding a favourable visual outcome).

References


Severe macular pucker after retinal detachment surgery in an infant

The appearance and clinical course of rhegmatogenous retinal detachments in children are more complicated than those of adults, because the retinal detachments are generally associated with trauma or congenital anomalies. 1, 2 In an infant, especially, an unexpected course may develop; however, the incidence of these detachments is so low that treatment and complications have scarcely been described in the literature. We report an infant who developed severe macular pucker after retinal detachment surgery.

Case report

A 2 week old male infant was referred with a diagnosis of bilateral congenital cataracts. The patient had no associated ocular problems on slit lamp biomicroscopy or gonioscopy and no abnormalities on physical examination. He underwent bilateral lensectomy and anterior vitrectomy by limbal approach at 3 weeks of age; both fundi were unremarkable. Although his right eye underwent sufficient anterior vitrectomy, retropillary membrane developed on the residual vitreous surface and the pupil closed 3 months postoperatively. During the second surgery, pupilloplasty was performed and we found a tear in the ciliary epithelium of the pars plana resulting from traction of the retropillary membrane tissue, and also discovered a localised detachment of the retina and ciliary epithelium (Fig 1A). We performed cryopexy with encircling scleral buckle, vitrectomy, and fluid-air exchange, and the retina was reattached. One month later, macular pucker rapidly developed and enfolded the entire posterior retina (Fig 1B). The original tear was completely sealed, and signs of the recurrent rhegmatogenous retinal detachment with proliferative vitreoretinopathy, including vitreous haze and wrinkling of retina in the other location, were not identified. After additional vitrectomy to remove residual cortex and to perform membrane peeling, the retina was finally reattached with a residue of degeneration near the fovea (Fig 1C).

Comment

Macular pucker in this infant is significantly different from that in adults. The severe posterior retinal folds may be formed by strong contraction of the epiretinal membrane, a firm vitreoretinal juncture, and an extensible retina. A previous histopathological report on recurrent proliferation after vitrectomy in two children with tractional retinal detachments showed that retinal glial cells were the main reactive cells. 3 However, in our case, the major component of the pucker was retinal pigment epithelium (RPE) cells, the same as in adults with rhegmatogenous retinal detachment. 4, 5 Cytoplasmic actin within the membrane, rather residual vitreous cortex on the retinal surface, may be involved in forming strong contractile elements, which also may underlie idiopathic cases in children. 6 Vessels in the pucker may have originated from the adherent retina, because no residual hyaloid vessels were identified during surgery.

Because excessive cryopexy tends to disperse and activate RPE cells, minimal cryopexy is recommended; laser may be preferable.
to treat rhegmatogenous retinal detachment in infants. Enzyme assisted vitrectomy to separate the firm vitreoretinal juncture may prevent the development of subsequent macular pucker. Frequent examinations and careful management are required even after successful reattachment surgery.

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Accepted for publication 16 August 2001

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Microbial keratitis associated with extended wear of silicone hydrogel contact lenses

Traditional hydrogel soft contact lenses (SCL) have limited oxygen permeability. Recently introduced silicone hydrogel SCL have much higher oxygen transmissibility (Dk/t O2), allowing near normal oxygen supply to the cornea during extended lid closure, and are hoped by some to address most of the problems related to corneal hypoxia encountered with previous extended wear soft contact lenses. They have therefore been approved for up to 30 days of continuous wear in both Europe and Australia.

Figure 2  [A] Light micrograph shows pigmented cells, fibroblast-like cells, and collagen (Azan, original magnification ×100). Positive immunostaining for cytokeratin (B) and α-smooth muscle actin (C) is seen prominently in the membrane. (D) Positive staining for von Willebrand factor shows the vessels (peroxidase-anti-peroxidase, original magnification ×100).

Four cases of microbial keratitis in patients who were using silicone hydrogel SCL (either CibaVision Focus Night and Day lenses (Lotrafilcon A, fluorosiloxane hydrogel) or Bausch & Lomb PureVision lenses (Balafilcon A, silicone hydrogel)) on an extended wear basis are presented. The minimum amount of continuous wear was 24 hours. All cases were treated either in private or at the corneal clinic of the Royal Victorian Eye and Ear Hospital from December 2000 to February 2001. All the patients underwent a complete ophthalmic examination by a corneal specialist. Microbiological specimens were taken from all patients via cornea scrapings and were submitted for Gram and Blankophor staining, and bacterial and fungal cultures via direct inoculation onto sheep blood agar, chocolate agar, and Sabouraud agar plates. The contact lenses themselves were also sent for microbial cultures.

Each case is described in brief, and a summary presented in Table 1.

Case 1

This 22 year old man presented with a 2 day history of left ocular injection, pain, photophobia, and blurred vision. He was wearing CibaVision Focus Night and Day SCL continuously for 10 days at a time, discarding the lenses after a month of use. He had swum in the sea while wearing the same lenses 2 weeks before, after which he removed the lenses and disinfected them with “Remu” multipurpose solution (boric acid, edetate disodium, poloxamine, sodium borate, sodium chloride, and polyaminopropyl biguanide, manufactured and distributed by Bausch & Lomb, Greenville, SC, USA). Continuous wear was recommenced within a few hours.

Examination revealed an uncorrected visual acuity of 3/60 in both eyes, improving to 6/12 in both eyes with pinhole. A paracentral 1 mm epithelial defect with underlying dense infiltrate was noted in the left eye with anterior chamber inflammation of 1+ cells and multiple scattered KP (Fig 1).

Corneal scrapings revealed fungal elements on Gram and Blankophor staining. Cultures grew Acinetobacter species in the enrichment broth, sensitive to ciprofloxacin, chloramphenicol, and tobramycin. Penicillin was later grown on the Sabouraud agar slope. A yeast (not Candida albicans) was grown on Sabouraud agar from the left contact lens, with Penicillium species grown from the right.

Topical ciprofloxacin 0.3% was commenced hourly, after which his symptoms and signs markedly improved. The ciprofloxacin was tapered and changed to topical chloramphenicol 0.5% (Chlorosig, Sigma) 8 days after presentation.

Two weeks later, the epithelial defect had resolved but significant subepithelial scarring remained. His best corrected visual acuity was 6/6 right eye and 6/7 left eye.

Case 3

A 21 year old man was referred to MSL with a 2 day history of right eye injection, pain, photophobia, and decreased vision. He was wearing PureVision lenses on a daily wear basis, but changed to continuous wear 24 hours before the onset of his symptoms.
Examination revealed a visual acuity of 6/6 right eye and 6/5 left eye with his spectacle correction. Marked right eye ciliary injection and anterior chamber activity were noted with cells, flare, multiple scattered KPs, and a small peripheral infiltrate. The overlying epithelium was intact. Culture of the contact lenses was impossible as they had been discarded.

Treatment consisted of hourly topical ciprofloxacin 0.3%, topical fluoromethalone acetate 0.1% (Flarex, Alcon, Fort Worth, TX, USA) was added four times daily after clinical improvement. The overlying epithelium was intact.

Treatment was with hourly topical ciprofloxacin 0.3%, with tapering after 48 hours. Review 1 week later revealed a persisting subepithelial scar and a best corrected spectacle acuity of 6/7.5.

Comment
Extended wear of soft contact lenses for up to 6 days has been advocated in various forms since the 1980s with traditional hydrogel lenses. However, owing to the relatively high rates of associated microbial keratitis, this extended wear of soft contact lenses has not widespread use.

The advent of high oxygen permeability silicone hydrogel soft contact lenses has again made extended wear a viable option, as the increased oxygen permeability is thought to reduce the risk of development of a hypoxic epithelial defect, which can serve as a portal of entry. Pre-release extended wear studies did not reveal any cases of microbial keratitis but these studies were relatively small. Lenses with a Dk/t O2 greater than 50 × 10^-6 have also been shown to have a lesser affinity for P aeruginosa binding during extended wear, thus further decreasing the risk of microbial keratitis.

Our experience suggests that extended wear with even these newer soft hydrogel contact lenses is still a risk factor in the development of microbial keratitis. All four patients had central or paracentral infiltrates, with three patients presenting with an associated epithelial defect. All four patients also had a positive culture or Gram/Blankophor stain from the corneal scrapes and had residual scarring after resolution of the acute episode. Although Corynecoccus species are considered by some to be a non-pathogenic organism, it has been described as the causative organism in several cases of microbial keratitis.15 We therefore feel that it is very unlikely that any of these cases represent a more benign non-infectious contact lens complication such as CLPU (contact lens induced peripheral ulcer), CLARE (contact lens induced acute red eye), or IK (infiltrative keratitis), which are all described as being conditions that resolve after cessation of contact lens wear alone, without the development of residual corneal scarring.1,11

Previous studies have shown that the most important risk factor for the development of microbial keratitis in soft contact lens wearers is the duration of contact lens wear, where overnight wear in particular aggravates the relative hypoxia of the cornea.12 However, there are other risk factors such as hypercapnia, trauma, biofilm alterations/contamination, altered corneal sensation, altered tear volume, and composition.13-15 Only hypoxia and hypercapnia should be improved by increased contact lens gas permeability.

Three of the four patients described had swelling in their lenses within weeks of their presentation. This might be an important risk factor in the development of their microbial keratitis in association with their silicone hydrogel SCL (as it is with other SCL), although the organisms involved were not those typically associated with microbial keratitis from contaminated water exposure. All four of the patients were also males between the ages of 16 and 22 years. These two demographic factors have been linked to an increased risk of microbial keratitis in contact lens wearers.

Recent studies have shown that bacterial populations grown from silicone hydrogel SCL in asymptomatic wear were not statistically different in comparison with those grown from standard HEMA based SCL.16 This
suggests that a silicone hydrogel SCL can still be a means of contamination in the pathogenesis of SCL microbial keratitis. Certainly, some of the lenses in this small series did grow the same organisms as the corneal lesions themselves.

Our experience supports a multifactorial causality for the development of microbial keratitis in extended SCL wearers, rather than just corneal epithelial hypoxia, particularly in high risk groups such as the four patients described where high risk behaviour is also undertaken. Further investigation needs to be done on the effects these lenses have in extended wear with regard to the development of microbial keratitis before their long term safety can be assured.

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Accepted for publication 16 August 2001

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Serious corneoscleral complications after pterygium excision with mitomycin C

The use of topical mitomycin C (MMC) to prevent recurrence after pterygium surgery is increasing since its introduction by Kunitomo and Mori in Japan, and its subsequent popularisation in the United States by Singh and associates. Low dose MMC (0.02%) twice daily for 5 days after the operation has been prospectively studied with long term follow-up, and few serious side effects have been noted. Intraoperative MMC appeared to be an effective and safe adjunctive treatment of primary pterygium excision.

Case reports

We retrospectively analysed three patients who presented at the Haemek Medical Central, Afula, Israel with scleral melting which developed after pterygium excision between October and November 2000, with intraoperative application of MMC (0.02% for 3 minutes). The MMC was washed out immediately with an abundant amount of balanced salt solution for at least 3 minutes. During the past 10 years we performed over 300 pterygium excisions with intraoperative use of MMC in Haemek Medical Center with three cases having serious complications.

Case 1 (Fig 1)

A previously healthy 50 year old man underwent recurrent pterygium excision of the right eye using a bare sclera technique with intraoperative application of MMC 0.02% for 3 minutes, having undergone pterygium excision with MMC 10 months earlier in his right eye. Visual acuity was 6/9+ SC. Preoperative ophthalmological examination revealed a nasal flashoid wide lesion 4.5 mm over the limbus and inferior symblepharon, with the remainder of the examination being normal. He was released on the same day, following surgery at which time there were no complications. On the first (postoperative day 1) and second (postoperative day 7) follow ups no complaints or complications were noted. However, on postoperative day 30, corneal limbal perforation and iris incarceration in the wound was noted. Immediately, he underwent right eye corneal tectonic graft surgery. At his last follow up (12 weeks after the pterygium excision with MMC), the best corrected visual acuity was 6/24 CPH, the graft has good adaptation, no gap and no rejection signs.

Case 2 (Fig 2)

A previously healthy 37 year old man underwent pterygium excision of the left eye using a bare sclera technique with intraoperative application of MMC 0.02% for 3 minutes. His presenting symptoms were cosmetic only. Visual acuity was 6/6 partial SC. Preoperative ophthalmological examination revealed nasal flashoid wide lesion 2.8 mm over the limbus with the remainder of the examination being normal. Two years previously he had undergone pterygium excision of the right eye using a bare sclera technique with intraoperative application of MMC 0.02% for 3 minutes. The right eye procedure had been successful and was performed in the same institute. Three weeks after the surgery, on routine follow up scleral melting and necrosis were noted. The scleral defect was unresponsive to ocular lubricants, topical antibiotics, topical steroids, and patching. Ten weeks after the left eye pterygium excision and MMC application, he underwent autologous conjunctival graft surgery to repair the defect. Follow up 2 weeks later showed that the graft has good adaptation and re-epithelialisation was noted.

Case 3

A previously healthy 70 year old man underwent pterygium excision of the right eye using a bare sclera technique with intraoperative application of MMC 0.02% for 3 minutes. On preoperative examination, visual acuity was 6/24 partial SC in the right eye and 6/60 SC in the left, anterior segment was quiet except flashoid temporal pterygium 7 mm over the limbus partially covering the pupil axis in the right eye. The procedure of the right eye pterygium excision with MMC was successful and performed in the same institute. No complaints or complications were noted at the first two follow ups; however, 3 weeks postoperatively right eye temporal scleral melting and ecdasis was seen (3 mm × 3 mm in size). Conservative topical treatment with antibiotics, topical anti-inflammatory agents, and steroids failed to resolve the situation. Consequently, 8 weeks after the initial right eye surgery he underwent right eye conjunctival flap grafting over the area of scleral melting. At his last examination best corrected visual acuity was 6/36 partial; blood vessel growth was noted towards the bare sclera and re-epithelialisation with minimal staining. He is still being treated with topical antibiotics with some improvement.

Figure 1

Figure 2
Table 1

<table>
<thead>
<tr>
<th>No</th>
<th>Age/sex/race</th>
<th>Presenting symptom</th>
<th>Clinical finding</th>
<th>Treatment</th>
<th>Preop VA ν postop</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>50/M/white</td>
<td>Blurred vision, dust sensation</td>
<td>Limbal perforation with iris incarceration in the wound</td>
<td>Tectonic corneal graft</td>
<td>6/9+ SC 6/24</td>
<td>Good graft adaptation. No recurrence of pterygium after 12 weeks</td>
</tr>
<tr>
<td>2</td>
<td>37/M/white</td>
<td>Cosmetic disturbance</td>
<td>Scleral nasal melting (3 mm x 2 mm)</td>
<td>Trial at conservative topical treatment failure. Autologous conjunctival graft</td>
<td>6/9+ SC 6/12+</td>
<td>Good graft adaptation at last follow up</td>
</tr>
<tr>
<td>3</td>
<td>70/M/white</td>
<td>Pterygium covering the pupil visual axis</td>
<td>Scleral temporal melting (3 mm x 3 mm)</td>
<td>Trial at conservative topical treatment failure. Conjunctival flap</td>
<td>6/24 pt CC 6/36 pt CC</td>
<td>Blood vessels growth towards the bare sclera with re-epithelialisation. No recurrence of pterygium after 12 weeks</td>
</tr>
</tbody>
</table>

Comment

Mitomycin C is an antineoplastic antibiotic agent isolated from the fermentation filtrate of Streptomyces caespi tus. Its action is similar to alkylating agents; it alkylates and crosslinks DNA and, in addition, may generate superoxide and hydroxyl radicals in solution. It also inhibits DNA, RNA, and protein synthesis. These combined effects may result in a long-term influence on cellular proliferation.

Scleral melting occurring after pterygium surgery with adjunctive treatment has been well reported. However, no serious complications were noted in the study by Frucht-Pery and Ilsar with postoperative use of 0.1 mg/ml MMC twice daily for 5 days (with a mean follow up period of 15.3 months) or in intraoperative MMC treated eyes. A common element in toxicity with MMC is a relatively large cumulative dose. Therefore, most ophthalmologists believe that a single intraoperative exposure to MMC would reduce the complication rate of MMC eye drop regimen.

In the current series, all patients underwent pterygium excision in the bare sclera technique with the low concentration of 0.02% of MMC and a short application of 3 minutes. Among our patients one had corneal perforation that was treated by tectonic keratoplasty and the other two had severe deep scleral melting that required conjunctival flaps or autologous grafts. Our patients were all healthy, without conditions predisposing to ulceration or poor wound healing such as Sjögren syndrome, severe keratoconjunctivitis sicca, acne rosacea, atopic keratoconjunctivitis, or herpes keratitis (Table 1). We suspected that the MMC concentration was not appropriate during that period. We checked the concentration and it was difficult to obtain precise results after a waiting period, owing to the degradation of the material.

This report raises serious questions regarding routine use of MMC. Recently, some investigators have evaluated the safety and efficacy of low dose MMC (0.02%) for an even shorter time (30 seconds). All ophthalmologists should be aware of the possibility of vision-threatening complications and avoid routine and broad use of mitomycin in all fields.

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Accepted for publication 22 August 2001

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Extrasceral extension of a choroidal melanoma after argon photoacoagulation and transsypillary thermotherapy

The optimal management of small posterior choroidal melanomas remains controversial, especially for tumours located near the optic disc and fovea. Although with increasing rarity, argon laser photoacoagulation continues to be used in the primary treatment of small tumours, despite data suggesting that other therapeutic methods may be more successful. More recently, transsypillary thermotherapy (TTT) has emerged as a therapeutic option for the primary treatment of small choroidal melanomas. Initial results are promising, but like any new treatments, more widespread use and longer follow up are needed for a thorough assessment of its efficacy. As a cautionary reminder that additional study is required to define the potential complications of these treatments, we present a case of choroidal melanoma in which treatment with primary argon photoacoagulation followed by TTT was associated with extrasceral extension of the tumour.

Case report

A 38 year old woman presented with decreased visual acuity in her right eye. An ophthalmologist noted a pigmented choroidal lesion with associated subretinal fluid. The lesion was initially treated with argon laser photoacoagulation, but within a month the decision was made to re-treat the lesion with TTT. Over the next 7 months, visual acuity deteriorated to 2/200. The lesion exhibited persistent elevation and subretinal fluid. By ultrasonad, a change in the retinoscleral echogenicity was observed, precipitating referral to an ophthalmic oncologist whereupon a diagnosis of choroidal melanoma with extrasceral extension was made. The patient was then referred to UCSF for consideration of proton beam therapy.

On examination, all abnormal findings were confined to the right eye. The patient’s visual acuity was counting fingers at 2 feet. Funduscopy examination revealed a raised pigmented tumour centred on the fovea, measuring 7 mm vertically by 10 mm horizontally, extending to within 2.3 mm of the disc. Subretinal fluid was present and extended over the nasal aspect of the tumour (Fig 1A). A flat choroidal angiography demonstrates irregular choroidal vessels within the tumour that are bright in the early arterial phase and show late leakage with punctate hot spots.
naevus 2 mm in diameter was also noted inferiorty (not shown). Fluorescein angiography was remarkable for an irregular plexus of choroidal vessels within the tumour noted in the early arterial phase, mid-phase leakage from retinal veins overlying the tumour, and late leakage with punctate hot spots at the tumour margin (Fig 1B). B-scan ultrasonography revealed choroidal excavation, an acoustic quiet zone, and orbital shadowing (Fig 2A). A-scan demonstrated spontaneous pulsation, low to medium internal reflectivity, and a sharp posterior spike (Fig 2B). The intraocular thickness was 3.0 mm, with 7.7 mm of extraocular extension. These findings are consistent with choroidal melanoma with posterior extraocular extension. Systematic evaluation revealed no signs of metastasis. The potential for orbital contamination by tumour made focal therapy by proton beam a less desirable alternative. Therefore, enucleation with en bloc resection of the extrascleral tumour was recommended and subsequently performed. Pathological examination confirmed the diagnosis of malignant choroidal melanoma, mixed cell type, with extensive extrascleral extension and focal vascular invasion. The patient elected to undergo adjuvant post-surgical external beam irradiation to reduce the rate of orbital recurrence, with the understanding that this treatment, while not definitively harmful, is of unproven benefit. She was also referred to the medical oncology service for systemic therapy and has begun an experimental treatment protocol using interferon alfa. Systemic chemotherapy is currently under consideration.

Comment
Options for the management of choroidal melanoma include observation, laser photocoagulation, transpupillary thermotherapy, charged particle radiotherapy, brachytherapy, local resection, and enucleation. Argon laser photocoagulation is typically used as an adjunct to other treatments, but in select cases has been used as primary therapy for choroidal melanoma. Typically, photocoagulation is reserved for small tumours (less than 3–4 mm in thickness and less than 10 mm in diameter) that are close to the fovea and/or the optic disc in eyes with good vision. Because the level of tumour necrosis with laser photocoagulation is shallow (0.2–0.8 mm), multiple treatments are often necessary. Therefore, the greatest challenge to successful photocoagulative therapy in choroidal melanomas is determining when the tumour has been fully ablated.

TTT shares the advantage that photocoagulation has over radiotherapy, including the more rapid visible reduction of tumour size, the relative sparing of adjacent normal tissue, and the convenience and economy of an outpatient procedure. In contrast with the shallow penetration of the argon laser, however, TTT employs near infrared light to produce up to a 3.9 mm depth of tumour necrosis. The premise of this technique is to squared irradiation into its use as a primary treatment for small posterior choroidal melanomas with encouraging early results. It has been reported that recurrences occurring follow apparently successful photocoagulation or TTT because invisible nests of malignant cells can infiltrate the sclera, a histologically documented phenomenon. The presented case signifies a reminder that this possibility is not trivial. Extrascleral extension, presumably from tumour out of reach of initial argon phototherapy and subsequent TTT, resulted in a requirement for aggressive local surgical therapy, photocoagulation, and adjuvant systemic therapy to reduce the risk of metastatic disease. The unusual degree of extrascleral extension for a small melanoma also raises the possibility that either photocoagulation or, more likely, TTT produced some reduction in scleral integrity allowing focal egress of tumour cells. Reports of complications following argon laser therapy are likely to become rarer because advances in modern radiotherapy have made primary photocoagulation an uncommon treatment. The use and investigation of TTT, however, continue to increase and the risks for extrascleral extension remain undefined.

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Accepted for publication 29 August 2001

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Macular infarction after intravitreal amikacin: mounting evidence against amikacin
Retinal toxicity attributable to intravitreal use of aminoglycosides for endophthalmitis has been reported. Campochiaro and Conway reported 101 cases of retinal damage due to intravitreal aminoglycosides. Amikacin, an aminoglycoside, is in widespread use in the United Kingdom for the treatment of Gram negative organisms in endophthalmitis. We report a case of macular toxicity following the use of intravitreal amikacin for postoperative endophthalmitis, outlining mechanisms of retinal toxicity, and offer alternatives to amikacin. We believe that enough evidence now exists to support a change in the current Royal College of Ophthalmologists’ endophthalmitis treatment guidelines that are based on the Endophthalmitis Vitrectomy Study. The patient was a 69 year old white woman presented 1 day after uneventful right phacoemulsification and intraocular lens implantation with a vision of counting fingers (CF), a relative afferent pupil defect, hypopyon with anterior chamber fibrin, and normal intraocular pressure. We were unable to visualise the fundus although a red reflex was noted. Ultrasound examination showed patchy increased vitreous reflectivity with a flat retina and choroid. Pars plana vitreous tap of 0.2 ml was performed followed by injection of 1 ml 0.1% of vancomycin and 0.4 mg/0.1 ml of amikacin. Sterile dilution was conducted with typed ophir written instructions. The age never became tense. The oculi inflammation resolved on a daily regimen of oral prednisolone 60 mg, oral ciprofloxacin 750 mg four times daily, topical eflornithine 3% hourly, topical dexamethasone 0.1% hourly, and topical atropine 1% once daily. Vision however remained CF because of angiographically proved macular ischaemia and vascular occlusion (Figs 1 and 2). There was no microbiological growth from the vitreous sample.
we support a change in current UK treatment guidelines. Choices will remain controversial until the incidence of toxicity for both amikacin and ceftazidime is determined by a prospective randomised controlled study; however, on the evidence currently available we suggest that ceftazidime should replace amikacin as the first line agent of choice against Gram negative organisms in postoperative endophthalmitis.

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Accepted for publication 22 August 2001

References


Spontaneous involution of retinal and intracranial arteriovenous malformation in Bonnet-Dechaume-Blanc syndrome

Intracranial arteriovenous malformations are capable of spontaneous regression. There are also numerous recorded events of vascular remodelling, thrombosis, and autoinvolution in retinal arteriovenous malformations. This report documents a self obliterated retinal arteriovenous malformation in a patient with Bonnet-Dechaume-Blanc syndrome who developed neurological symptoms due to spontaneous regression of the intracranial component of the angiomatous malformation.

Case report

A 32 year old man from Guam was evaluated for a history of right parietal headaches for several months and acquired temporal hemianopia in the left eye. He had a history of blindness in the right eye from early childhood, and had recently become aware of a temporal hemianopia in the left eye.

The rationale for amikacin use relates to the relatively high incidence of Gram negative isolates in endophthalmitis (6.4–26.2%) and the broad spectrum of action with low resistance offered by this agent. Amikacin has largely superseded gentamicin because of its perceived safety profile. Our case and others reported in the literature serve to notify clinicians of the serious retinal toxicity occurring with amikacin use, which is possibly a class related phenomenon.

Hypotheses for toxicity include dilution errors, raised post-injection intraocular pressure, concomitant use of high concentrations of subconjunctival amikacin, and variations in vitreous concentration. Local variation in concentration may play a part if the agent is directly injected into the posterior vitreous space instead of the gel itself. Another possibility for macular predilection is that this is the dependent part in the supine patient during pars plana injection.

Large studies offer alternatives to aminoglycosides on the basis of culture sensitivities. Suggestions include ceftazidime, cefotaxime, and ciprofloxacin. Sensitivities of Gram negative organisms to ceftazidime range from 61% to 100% according to published studies. It appears that in most studies 2 mg (0.1 ml of 20 mg/ml solution) of ceftazidime has in vitro effectiveness equivalent to or greater than 0.4 mg amikacin. Primate studies have shown that intravitreal ceftazidime is non-toxic at doses of 2.25 mg. Ceftazidime is already in clinical use in the United Kingdom. There have been no reported cases of retinal toxicity with intravitreal ceftazidime use in humans.

With mounting evidence against amikacin we support a change in current UK treatment
regional oedema on magnetic resonance imaging, suggested a recent obstruction of vascular flow within the angiomatous malformation.

Comment

The syndrome of unilateral retinocephalic arteriovenous malformation was first described in 1937 by Bonnet et al. Six years later, Wyburn-Mason published his report in the English language. These congenital unilateral retinocephalic arteriovenous malformations may involve the visual pathways from the retina to optic nerve to the ipsilateral occipital cortex, and may involve the chiasm, hypothalamus, basal ganglia, midbrain, and cerebellum. Since these arteriovenous malformations are high flow systems in which veins are exposed to arterial blood pressures, they are susceptible to turbulent blood flow and to vessel wall damage which can lead to thrombosis and occlusion. Over time, components of an angiomatic malformation can grow, haemorrhage, sclerose, thrombose, and involute.

Our patient had longstanding involution of his retinal arteriovenous malformation, with new neurological symptoms resulting from thrombosis of the intracranial component of the tumour. Spontaneous occlusion of the major venous drainage within the deep cerebral hemisphere and optic chiasm may have caused headaches by producing regional oedema or by diverting flow to other venous structures. Since the major venous drainage within the malformation was already occluded at the time of presentation, no treatment was advised. The complex evolution of clinical signs in our patient underscores the need to distinguish disease progression from spontaneous involution in symptomatic patients with Bonnet-Dechaume-Blanc syndrome.

Acknowledgement

Supported in part by a grant from Research to Prevent Blindness, Inc.

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Accepted for publication 29 August 2001

References


NOTICES

Glaucuma

The latest issue of Community Eye Health (No 39) discusses the glaucomas, with an editorial by Professor Gordon J Johnson, director of the International Centre for Eye Health. Further information please contact: Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7676 6910; email: eyeresource@ucl.ac.uk; website: www.jech.co.uk). Annual subscription (4 issues) UK£25/US$40. Free to workers in developing countries.

International Centre for Eye Health

The International Centre for Eye Health has published a new edition of the Standard List of Medicines, Equipment, Instruments and Optical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7676 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blindness in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, is regularly sending volunteers to India. More information can be found at the charity website (www.secondsight.org.uk) or by contacting Dr Lucy Mather (lucymather@yahoo.com).

Specific Eye ConditionS (SPECS)

Specific Eye Conditions (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups of any condition or syndrome with an integral eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups from developing countries. It is compiled by the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7676 6910; email: eyeresource@ucl.ac.uk).

International Society for Behçet’s Disease

The 10th International Congress on Behçet’s Disease will be held in Berlin 27–29 June 2002. Further details: Professor Ch Zouboulis (zoubbere@zedat.fu-berlin.de).

Singapore National Eye Centre 5th International Meeting

The Singapore National Eye Centre 5th International Meeting will be held on 3–5 August 2002 in Singapore. Further details: Ms Amy Lim, Organising Secretariat, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751 (tel: (65) 322 8374; fax: (65) 227 7290; email: Amy_Lim@snec.com.sg).

BEAVRS Meeting

The next BEAVRS meeting will be held in the Dalmahoy Hotel near Edinburgh on 31 October to 1 November 2002. Further details: Susan Campbell, Medical Secretary, Gartnavel General Hospital (email: susan.j.campbell.wg@northglasgow.scot.nhs.uk).