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B Cvenkel

Eye Clinic
University Medical Centre Ljubljana
Zaloska 29 a, 1000 Ljubljana, Slovenia

Correspondence: B Cvenkel
Tel: +44 386 1 522 1728
Fax: +44 386 1 522 1960
E-mail: barbara.cvenkel@kclj.si

Sir,

Chronic postoperative uveitis—a clinicopathological case report

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The management of chronic postoperative uveitis following uneventful cataract surgery is challenging because of difficulties in isolating low-grade microorganisms from such eyes.[1,2] Often, the initial response to conventional treatment may be poorly sustained, needing more aggressive intervention. With timely intervention, the prognosis can be favourable compared to acute infective endophthalmitis.

Case report

A 72-year-old lady underwent uncomplicated phacoemulsification cataract surgery with implantation of a 6 mm optic Acrysof Intraocular lens (IOL) in her left eye. She was prescribed prednisolone acetate 1% drops and fusidic ointment, and was 'discharged' 6 weeks later with a best visual acuity of 6/12. At 2 months postoperatively, she presented with symptoms and signs of uveitis in the operated eye. The visual acuity was 6/12, and the eye was red with 10–15 cells per high power field (HPF) in the anterior chamber without flare or hypopyon. The patient was recommenced on topical prednisolone acetate 1% drops every 4 h. After 1 week, the inflammation had subsided and the treatment was discontinued. The patient had recurrent episodes of uveitis and was treated at various stages with topical, orbital floor, and systemic steroids. She was referred to our uveitis clinic 5 months following surgery. The visual acuity was 6/36 and N18 with 10–15 cells per HPF in the anterior chamber. Vitreous cells were evident. Clinically, the capsular bag was clear and free of plaques. Fundus fluorescein angiography revealed gross disc oedema and cystoid macular oedema. A vitreous biopsy was carried out together with an intravitreal injection of 2 mg vancomycin. The vitreous biopsy was sterile and the anterior chamber sample showed only inflammatory cells. She was maintained on twice daily topical prednisolone acetate 1% drops. At 12 months postsurgery, she presented with a 6 mm hypopyon. The visual acuity had deteriorated to perception of light. The capsular bag was removed *in toto* together with the IOL. Intravitreal vancomycin 2 mg and ceftazidime 1 mg were injected. The anterior chamber tap revealed Gram positive cocci and bacilli. The histology specimen was made up of a capsular bag ($9 \times 5 \times 3\,mm^3$) enclosing an IOL. The capsular tissues comprised a lens capsule, degenerative cortical lens fibres, an area of capsular fibrosis, and a focus of acute inflammation. This reaction appeared to be located towards the lens equator, in association with one of the IOL haptics, and consisted largely of calcified degenerated polymorphs, calcified material, a microabscess, and some fibrous tissue (Figure 1). No microorganisms were seen. The anterior chamber became quiet within a week. After 12 months, the eye remains free of inflammation with no medication. The visual acuity is 6/36 with an aphakic correction. The view of the fundus is clear, revealing a fine epiretinal membrane secondary to long-standing macular oedema.

Comment

Chronic postoperative endophthalmitis is defined as any inflammation that presents more than 6 weeks after surgery. This definition is arbitrary as the time of onset may be influenced by the postoperative use of steroids and the virulence of the microorganisms involved. Whereas the Endophthalmitis Vitrectomy Study has produced a protocol for treating acute infective endophthalmitis,[3] the management of chronic cases is less certain. Obtaining samples from the anterior chamber and vitreous and intraocular injection of wide-spectrum antibiotics is commonly employed to treat these cases.[4] Further difficulty in the management of these cases arises if there is no response to repeat intraocular antibiotic administration[4,5] and/or microorganisms are not isolated by conventional methods.[6] Identification may need special culture media and prolonged incubation time because of the slow-growing nature of microorganisms such as *Propionibacterium acnes* and *Corynebacterium* species. The persistence of active chronic inflammation also raises the

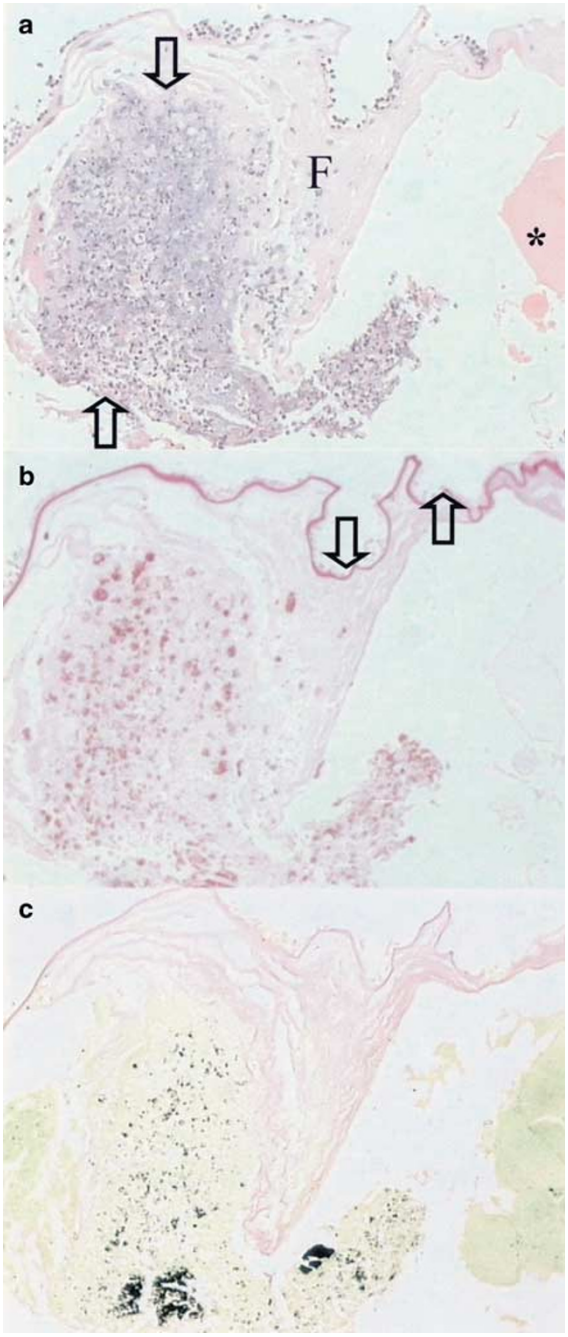

Figure 1 Sections through the periphery of the specimen stained with (a) haematoxylin and eosin, (b) PAS, and (c) von Kossa methods. In (a), cortical lens remnants are seen (asterisk) adjacent to the microabscess (arrows). Fibrous tissue (F) is also present (b) PAS stain delineates the lens capsule remnant (arrows). The von Kossa stain demonstrates calcification, seen in black in the microabscess.

possibility of microorganisms being trapped within a biofilm in the posterior capsular bag or at the interface of the bag and the haptics of the IOL implant. Under certain circumstances, bacteria secrete and reside in an extrapolysaccharide glycoglycan polymer that gives shelter from the immune system and antibiotics. These bacteria trapped in a biofilm are up to 1000 times less sensitive to antibiotics. Partial or total removal of the posterior capsule and implant[7] is advocated in such situations. The pathology report, in our case, confirmed the presence of a microabscess within the equator of the capsular bag that was not visible clinically. The lack of a macrophage response to cortical remnant argues against a reaction to lens material as a cause of the chronic uveitis. Rather, the microabscess was consistent with a bacterial aetiology, despite a specific agent not being identified. *P. acnes* gives rise to a syndrome of indolent granulomatous uveitis weeks to months after cataract surgery. A characteristic clinical feature is the presence of a white intracapsular plaque that has been shown histologically to be composed of sequestrated microorganisms inside the peripheral capsular bag. Although we were unable to demonstrate unequivocally *P. acnes*, the aqueous humour sample did contain a mixture of Gram positive cocci and bacilli with no growth on cultures. *P acnes* is an anaerobic, Gram positive, pleomorphic, bacillus that demonstrates extremely slow growth characteristics on culture media. PCR technology aids in identifying low-grade microorganisms but was, unfortunately, not available locally during both surgical episodes.

In summary, all cases of chronic postoperative uveitis need to be treated as infective in origin. In situations where the inflammation continues or recurs despite vitreous biopsy and intravitreal injection, the whole bag needs to be explanted to remove the sequestered focus of infection. The final visual recovery in our patient was compromised by irreversible macular changes. Yet, she retains an acuity of 6/36 following a florid, hypopyon postoperative uveitis 12 months following surgery. Early aggressive intervention in chronic endophthalmitis can result in a relatively favourable prognosis compared to acute infective endophthalmitis.

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JA Gonzalez-Martin[1], P Hiscott[2] and P Palimar[1]

[1]Warrington Hospital
Kendrick Wing Lovely Lane
Warrington
Cheshire WA5 1QG, UK
[2]Royal Liverpool University Hospital
Prescot Road
Liverpool, UK

Correspondence: P Palimar
Tel/Fax: +44 1925 662 395
E-mail: palimar@tinyonline.co.uk

Sir,

Cytarabine-induced corneal toxicity

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Cytarabine (cytosine arabinoside) is a powerful antimetabolite used in the treatment of acute myeloid leukaemia (AML). Corneal toxicity from high-dose intravenous cytarabine therapy has been described in the literature[1] and routine prophylaxis with topical steroids is now an established part of the treatment protocol.[2] Only two cases have been reported of corneal toxicity occurring at low doses. One case occurred with an intermittent subcutaneous regimen.[3] A second case was reported with a continuous intravenous regimen.[4] The cytotoxic activity of cytarabine is related to the concentration and duration of exposure, both of which vary with different modes of administration. There are no reports of corneal toxicity in patients receiving an intermittent, intravenous low-dose regimen, and currently no recommendations have been made for prophylaxis in these cases.

Figure 1 Corneal epithelial microcysts visible with direct slit-beam illumination.

Case report

A 39-year-old male presented with a 1-day history of blurred vision, severe discomfort and photophobia following a 10-day course of intermittent low-dose intravenous cytarabine therapy for AML. He had received 200 mg/m^2 every 12 h for 9 days prior to the onset of symptoms and had not been using topical steroid prophylaxis. On examination he had an uncorrected visual acuity of 6/9 in each eye. Severe blepharospasm and moderate conjunctival inflammation were present. Bilateral corneal epithelial microcysts, more densely distributed in the centre of the cornea than in the midperiphery were noted, with a clear zone of about 1.5 mm in the corneal periphery (Figure 1). The anterior chamber in both eyes was free of inflammation and the intraocular pressure was normal. Treatment was commenced with G. dexamethasone 0.1% 2 hourly and the symptoms resolved completely within 3 days. The microcysts disappeared after 7 days and the steroid drops were subsequently tapered and then stopped over the following week.

Comment

Cytarabine corneal toxicity has mainly been associated with high-dose intravenous therapy (>1 g/m^2). This drug is known to penetrate the blood–brain barrier after intravenous infusion and is also found in the aqueous and tears. Typically, corneal toxicity occurs after 5–7 days of treatment and can be prevented by using topical corticosteroids.[1,2] In this patient, because of the relatively low-dose regimen, prophylactic steroid therapy was not used and typical corneal toxicity occurred as a consequence.

The mechanism of cytarabine-induced microcyst formation is not currently known. Rapid cycling cells are most sensitive to the actions of cytarabine. Corneal