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Sir,

Post-operative saccular endophthalmitis caused by macrophage-associated staphylococci

An 83-year-old healthy man underwent extracapsular cataract extraction with placement of an intraocular lens (IOL) implant (PMMA) into the capsular bag. Pre-operative preparation included topical aqueous chlorhexidine. The incision was in the superior limbus, of size 14 mm. Surgery lasted 30 min. The patient received no antibiotic prophylaxis except Maxitrol drops (Alcon; dexamethasone 0.1%, neomycin 0.35% and polymyxin B 6000 U/ml) post-operatively.

On the first post-operative day the visual acuity (VA) was 6/60, which improved to 6/12 with a pinhole. The anterior chamber was quiet when a good view of the posterior pole was obtained. By the tenth day VA was 6/60, which improved to only 6/36 with a pinhole. There were a few cells in the anterior chamber suggesting mild anterior uveitis.

On the twenty-seventh day the patient complained of pain and impaired vision. VA was 6/36 with pinhole. There were keratic precipitates, cells and fibrin in the anterior chamber. Deposits on the IOL indicated an increase in the severity of the uveitis. The patient received topical dexamethasone 0.1% hourly and cyclopentolate 0.5% t.d.s.

After 49 days VA had dropped to < 6/60 with thickening of the capsular bag. There was fibrinous exudate in the anterior chamber but the fundal glow was reasonable. The patient was treated additionally with oral ciprofloxacin 500 mg b.d. for 2 weeks. The anterior chamber reaction reduced but VA did not recover because of capsular thickening. Vitreous tap failed to yield any bacteria.

Further inflammation occurred at 20 weeks, with VA reduced to perception of light, with increased keratic precipitates. Again the patient was treated with corticosteroids which resulted in reduced inflammation but no improvement in the VA.

The patient developed severe pain with hypopyon at 32 weeks (Fig. 1A). Faint fundal glow was visible. There was no relative afferent pupillary defect. Ultrasound examination showed clear vitreous with no evidence of retinal detachment. Anterior chamber tap was performed twice for investigation (Gram stain with culture) but no organisms were identified. A clinical diagnosis of saccular (within the 'bag') endophthalmitis was made and removal of the IOL was planned. The patient was given intravitreal vancomycin 1 mg together with oral co-trimoxazole, topical cefuroxime and further corticosteroids.

At 38 weeks, following resolution of the hyopyon with corticosteroids, the IOL and capsular bag were removed. Post-operatively the patient made a good recovery with a quiet, non-inflamed eye but retained little vision, due to a retinal detachment involving the macula.

Ocular pathological findings

The capsular fragment (Fig. 1B) was fixed in 1% glutaraldehyde for staining with haematoxylin and eosin (H&E) and Gram's stain and for electron microscopy. The IOL and another piece of the capsular fragment were placed in thioglycollate broth for culture.

Light and electron microscopic findings

The low-power view of the capsular fragment stained with PAS confirms the presence of lens material and the surrounding capsule (Fig. 1C). The high-power view (H&E) demonstrates many viable macrophages within the capsular fragment (Fig. 1D).

The low-power view stained with Gram's stain shows the presence of uniformly staining Gram-positive cocci within the macrophages but not extracellularly (Fig. 1E). The high-power view demonstrates morphology suggestive of actively multiplying coagulase-negative staphylococci (CNS) due to the large numbers of bacteria present within the cells (Fig. 1F).

Transmission electron microscopy (TEM) revealed macrophages within the capsular fragment (Fig. 1G) and, at high power, multiple intracellular bacteria with coccal morphology (Fig. 1H).

Comment

Late-onset pseudophakic endophthalmitis typically presents several months after cataract surgery, often as a hypopyon uveitis that has failed to respond to corticosteroids.[1] The term 'saccular endophthalmitis' denotes chronic uveitis associated with thickening of the lens capsule around the plastic IOL. It has been proposed (J. Dart, personal communication) that the causative bacteria are in a biofilm around the IOL and are consequently resistant to antibiotics. Progress of the disease may be responsive to treatment with high-dose cephalosporins given intravenously or intravitreally but often there is need for aggressive adjunctive surgery with removal of the IOL as well as excision of the remaining capsule.[1] The bacterium recorded most often is *Propionibacterium acnes*, but CNS have also been isolated. Inexplicably, however, bacteria have not been isolated on approximately 50% of occasions when the polymerase chain reaction (PCR) test has demonstrated their presence.[2,3] This typical clinical case, requiring removal of the IOL and capsular fragment, failed to yield bacterial growth from three taps (two anterior chamber and one vitreous).

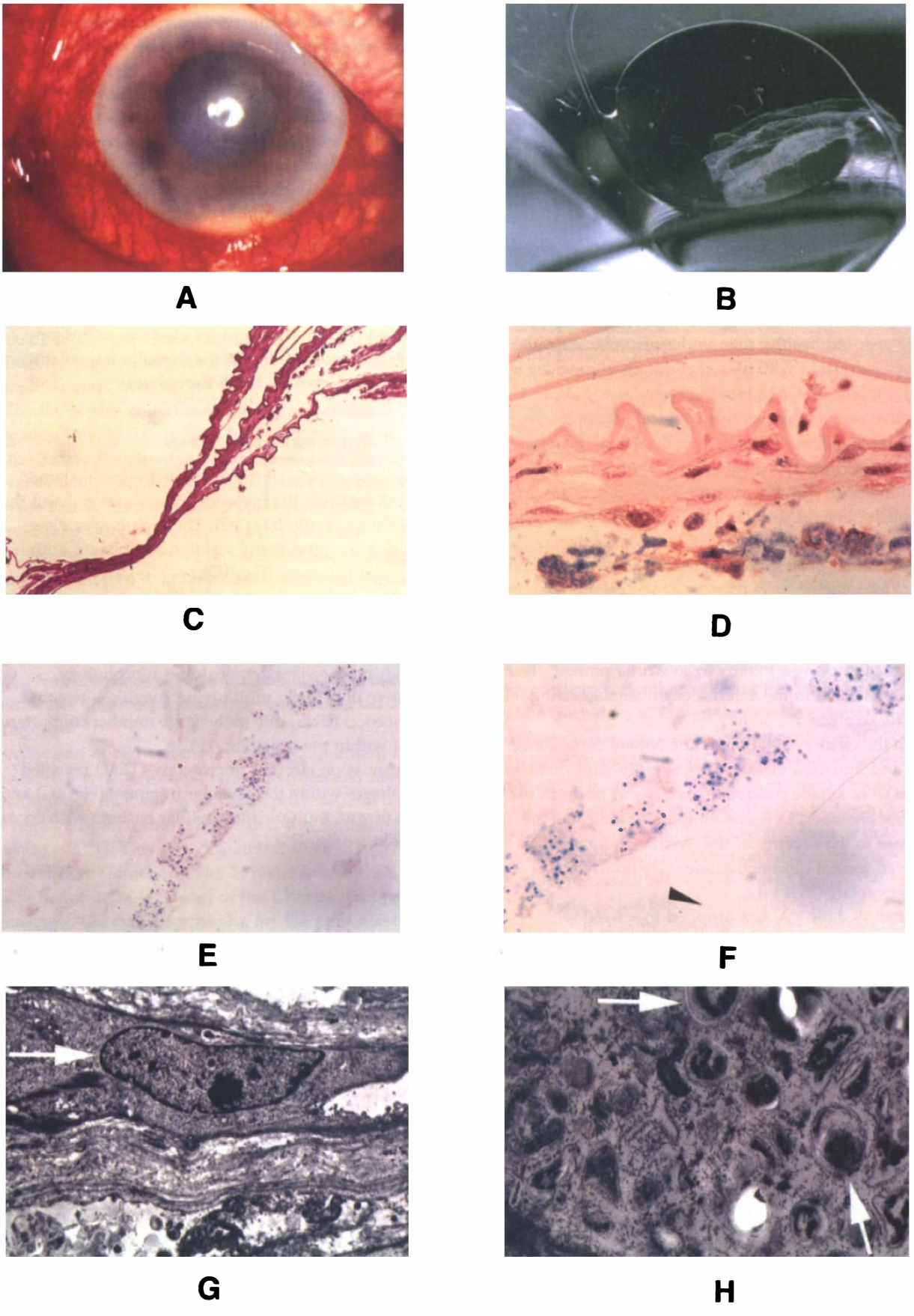

Fig. 1. *(A) Acute saccular endophthalmitis at 32 weeks. (B) IOL and capsular fragment after removal from the eye. (C) The folded posterior lens capsule is corrugated by a layer of fibrous tissue derived from metaplastic lens epithelium (×64, PAS). (D) The contractile spindle cells, adjacent to the posterior lens capsular remnants, are lined by a layer of macrophages containing basophilic inclusions (×160, H&E). (E) Bacteria are present in the mononuclear cells (×250, Gram). (F) The majority of organisms are intracytoplasmic (×400, Gram). (G) The fibrous membrane contains elongated spindle cells (arrow). The lower part of the figure contains a disintegrated macrophage (×3750, TEM). (H) Bacteria (arrows) within the cytoplasm of a macrophage (×11 500, TEM).*

The morphology has shown the presence of Gram-positive cocci within macrophages, but not polymorphonuclear cells. Such intracellular bacteria are sequestered away from systemic, topical and intracameral antibiotics. The outcome is 'parasitised' macrophages that have given rise to an inflammatory response, rather than a purulent one, which has been suppressed by corticosteroids. This finding is particularly important for satisfactory therapy because older antibiotics, such as cephalosporins and aminoglycosides, do not penetrate intracellularly.[4] The new azilide derivative of erythromycin, azithromycin, and the semi-synthetic macrolide, clarithromycin, are concentrated intracellularly up to 400 times more than cephalosporins.[4] They have been found highly effective against intracellular organisms such as *Chlamydia* sp. and *Legionella* sp.

Release of bacterial protein may not be the sole explanation for recurrent inflammation. Macrophages can be transformed into antigen presenting cells by IL (interleukin)-1, produced by B lymphocytes, polymorphonuclear cells or macrophages themselves. They can then process antigenic peptides, enzymatically degrading them to oligopeptides with an unfolded secondary structure. These peptides are expressed at their surface, bound to MHC class II molecules, for presentation to Th1 lymphocytes to stimulate a cell-mediated hypersensitivity response,[4] normally absent from the anterior chamber. This immunological response would be suppressed by corticosteroids. Our patient responded well to the removal of the IOL, and the associated capsular fragment, as described by others,[1] after the focus of antigen production within the eye had been excised. In addition, three similar cases have been reported recently when the IOL required to be removed and in which organisms were present (but not reported) within macrophages.[5]

The reason why bacteria did not multiply within the thioglycolate broth is not clear. It may be that the specimen should have been processed for the release of intracellular bacteria. Others have found it difficult to culture bacteria, in particular CNS, from plastic foreign-body specimens, when it has been suggested that a biofilm has been inhibitory for *in vitro* culture and prior ultrasonic shock (20 kHz for 10 min) has been advocated.[6] Our observations suggest that future culture of IOL and capsular fragment specimens should use techniques that will release intracellular bacteria. In addition, investigation is warranted by PCR.[2,3]

Late-onset, culture-negative pseudophakic saccular endophthalmitis has been demonstrated to be due to macrophage-associated Gram-positive cocci resembling staphylococci. The recognition that the inflammation is probably due to intracellular multiplication of bacteria is important, not only for possible expression of macrophage-processed antigen and immunological consequences, but also because cephalosporin and aminoglycoside antibiotics do not penetrate intracellularly. Use of the new macrolide antibiotics, in particular azithromycin and clarithromycin, is indicated as they penetrate phagocytic cells and macrophages and are highly active against Gram-positive bacteria.

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Sir,

Soemmering's ring presenting as an iris tumour

Soemmering's ring is a complication of cataract surgery first described by Soemmering in 1828.[1] It is a doughnut-shaped proliferation of lens epithelial cells in the periphery of the lens capsule, which have been left at the end of extracapsular cataract extraction. Electron microscopy shows it to consist of the fused remnants of the dissected anterior and posterior lens capsule, enclosing the equatorial part of the former lens which contains a proliferation of vacuolised, irregularly arranged lens epithelial cells in various stages of degeneration.[2] This proliferation is thought to be due to the protective effect of the anterior leaf of the lens capsule, which folds back upon itself to protect the remaining lens fibres from the lytic effects of aqueous humour.[3]

Posterior chamber lens implantation has been shown to decrease the formation of Soemmering's ring,[4] presumably by keeping the leaves of capsule separate and allowing aqueous to dissolve the remaining cells. Soemmering's ring must be differentiated from the now more commonly seen Elschnig's pearls, which are