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Infectious crystalline keratopathy: the clinical utility of periodic acid–Schiff stain

Sir,

Infectious crystalline keratopathy (ICK) describes a pattern of chronic corneal infection characterised by needle-shaped colonies of microorganisms growing between collagen lamella with disproportionately little inflammation.¹ The condition arises when microorganisms gain access to the corneal stroma of patients whose local immune response has been suppressed by topical corticosteroids. The majority of infections are caused by low virulence bacteria, but fungi and acanthamoeba have been reported.¹ We describe a patient with ICK due to periodic acid–Schiff (PAS)-positive bacteria who developed post-operative endophthalmitis more than a month after penetrating keratoplasty. Delayed onset post-operative endophthalmitis is an uncommon but serious complication of intraocular surgery. Knowledge that PAS-positive bacteria are putative contaminants in this clinical setting can alter management.

A man in his late eighties underwent a penetrating keratoplasty to restore vision that had declined to 'hand motions' from a failed corneal transplant (Descemet's stripping endothelial automated keratoplasty) 6 years earlier for Fuchs' dystrophy. For 9 months prior to penetrating keratoplasty the patient was treated with topical prednisolone acetate 1% (varying from hourly to four times per day). During this time the cornea was diffusely oedematous and focally 'cloudy'. Surgery was uncomplicated; no tissue was submitted for culture. The clinicians were alerted days after surgery that the cornea was infected (see below). Topical moxifloxacin, started after surgery, was discontinued on post-operative day 22. Recovery remained uneventful until post-operative day 42 when the patient developed anterior chamber inflammation and elevated intraocular pressure. He was started on topical prednisolone acetate 1% for non-specific 'uveitis' and

pressure lowering medications (dorzolamide 2%/timolol 0.5%). On post-operative day 50, inflammation substantially worsened so oral valtrex was begun on the presumptive diagnosis of herpes uveitis (there was no previous history of ocular herpes infection or any characteristic findings, e.g., epithelial dendrite, etc.). Inflammation worsened until post-operative day 93 at which time cultures from aqueous and vitreous humours were taken; both grew *Corynebacterium striatum* with greater colony counts from the anterior chamber. Intravitreal antibiotics (ceftazidime 2.25 mg/0.1 mL; vancomycin 1 mg/0.1 mL) were injected the day the samples were obtained; intraocular inflammation progressively improved over several weeks. Final visual acuity was 20/400.

On microscopic examination, the central cornea was superficially ulcerated. Innumerable bacteria were growing in stroma between collagen lamellae forming spindle shaped colonies (Fig. 1). There was modest focal acute inflammation around the outer edge of bacterial colonies. Deeper stroma and Descemet's membrane (earlier graft tissue) were separated from anterior stroma. Descemet's membrane was covered on its posterior surface with fibrin and degenerating neutrophils. Gram stain showed mostly Gram-positive cocci and small non-branching Gram-positive rods (Fig. 1C). The bacteria stained strongly with PAS after diastase and were acid-fast negative with Ziehl–Neelsen and Fite stains. A Gomori methenamine silver (GMS) stain was negative for fungus.

The histopathological findings in this case were diagnostic of ICK, namely the biofilm-like proliferation of bacteria between collagen lamellae with disproportionately little inflammatory response. Secondary endophthalmitis is an anticipated complication after contaminated intraocular surgery, but in this case endophthalmitis was unusual in that the signs of intraocular inflammation were delayed more than a month after surgery.^{2,3} Delayed onset endophthalmitis is a manifestation of a limited subset of low-virulence organisms. The putative bacterial contaminants found in this case were PAS-positive which also limits possible pathogens. PAS-positive bacteria include *Bacillus cereus*, *Klebsiella pneumoniae*, *Micrococcus luteus*, *Propionibacterium*, *Corynebacterium*, *Tropheryma whippelii*, *Actinomyces*, and atypical mycobacteria.^{4,5} In context of this case, GMS and AFB stains along with morphological findings excluded atypical mycobacteria and actinomycetes. *Bacillus cereus* and *Klebsiella pneumoniae* are highly virulent ocular pathogens and cause rapidly progressive endophthalmitis.⁶ *Micrococcus luteus* and *Tropheryma whippelii* have not been implicated in post-operative endophthalmitis. To our knowledge, only two PAS-positive bacteria have been associated with chronic (e.g., delayed onset) endophthalmitis: propionibacterium and corynebacterium.^{7,8}

Corynebacterium spp., are Gram-positive bacilli that are part of the normal flora of the skin and eyelid. Most members of this genus are regarded as laboratory contaminants that rarely cause human infection. *Corynebacterium striatum*, however, may be different. It has been implicated in cases of endocarditis, meningitis, bacteraemia, and respiratory infection.^{9,10} In the context of this case, *C. striatum* appears as both a low grade pathogen and an opportunistic organism that has colonised corneal stroma. The patient had no systemic immune-compromising conditions (other than age) but the structural integrity of his eye was compromised by the complications of past surgery.

Fig. 1 (A) Removed corneal button with anterior stroma filled with PAS-positive bacteria and relatively minimal inflammation. The space between anterior three-fourths stroma (*) and posterior fourth represents the non-union of host and donor tissues from transplant performed 6 years earlier. (B) Higher magnification showing myriad PAS-positive bacteria in near absence of inflammatory cells. (C) Gram stains showing a minority of bacteria as Gram-positive cocci and some small rods. (D) PAS stain at edge of colony showing small cocci and small rod-shaped organisms. The density and intensity of staining precluded good morphological detail of bacteria.

Unlike most cases of post-operative bacterial endophthalmitis that show signs of intraocular inflammation within days to a week of surgery, several low virulence organisms can result in delayed clinical manifestations. In the setting of contaminated surgery from PAS-positive bacteria, the exclusion of actinomyces and atypical mycobacteria by GMS and AFB stains and morphology narrows the possible causes of post-operative infection to high and low virulent bacteria. Intraocular infections with *B. cereus* and *K. pneumoniae* have rapidly progressive clinical courses often resulting in loss of the eye within days.⁶ Knowledge that a potential bacterial contaminant of intraocular surgery is PAS-positive provides useful information by narrowing the list of possible pathogens. That list includes several capable of causing delayed onset endophthalmitis.

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