Appendix

Intraocular Lens Opacification with Recombinant Tissue Plasminogen **Activator after Cataract Surgery**

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Introduction: Fibrinous uveitis in uneventful cataract surgery and intraocular lens (IOL) implantation occurs in less than 3% of cases.

Dramatic fibrinolysis has been observed with intracameral injection of recombinant tissue plasminogen activator (r-tPA), a highly potent fibrinolytic protein usually used for coronary thrombolysis. Reported complications of r-tPA include comeal oedema, band keratopathy, anterior chamber turbidity, and hyphaema. They are uncommon and the general consensus of previous work is that r-tPA is well tolerated in the anterior chamber.

Purpose: To report 5 cases of intraocular lens (IOL) opacification following treatment of fibrinous uveitis with recombinant tissue plasminogen activator (r-tPA) after cataract surgery.

Methods: .5 consecutive patients who developed intraocular intraocular Iens opacification at Whipps Cross University Hospital, London, between February 2008 and August 2009. All patients underwent uncomplicated cataract surgery and IOL implantation in the capsular bag. Fibrinous membranes developed between 1 to 4 weeks of surgery and were treated with intracameral injection of 10-25 micrograms of recombinant tissue plasminoger activator (r-tPA). Resolution of fibrin plaques occurred in all cases within 24 hours. IOL opacification was noted between 5 months to 7 years after r-tPA treatment with reduced visual acuity

Results

- Uneventful IOL exchange was carried out in 4 patients with a mean final visual acuity of 6.9.
- In-vivo OCT imaging demonstrated a central band shaped of echogenic deposits centrally located on the non-echogenic convex anterior IOL surface. (Figure 1)
- This corresponded to a band-shaped fine granular whitish material was observed in the central part of all explanted IOL optics. (Figure
- Light microscopic evaluation further revealed diffuse fine granular deposits, on the anterior surface of the optic and a parallel, linear granular layer, just below the anterior surface of the optic which diminished towards the periphery of the IOL optic. (Figure 3, 4)
- Both granular deposit layers stained positive with special stains for calcium (von-Kossa and alizarin red)
- The granular material was not observed or detected on the posterior region of the cut section, the haptics and the edge of the

Discussion:

Calcification of IOLs is an uncommon complication of IOL implantation, resulting in symptoms of visual loss or glare, and usually necessitating IOL explantation and exchange

IOL calcification, first reported in 1994 by Jenson et al, was initially thought to be associated Sodium Hyaluronate 1.4% (Healon GV) 29 It was hypothesized that the phosphate components in the viscoelastic preparation reacted with calcium in the irrigating solution and aqueous, to cause precipitation on the IOL surface.

'calcium-phosphate reaction' theory was further supported by the Bucher et al in 1995 who described a case of dystrophic calcification of the IOL and paracentesis site in a 80-year-old woman with chronic lymphatic leukemia. Disruption of calcium homeostasis in the aqueous as a resultant of systemic disease, intraocular surgery, inflammation or drug administration can and has been associated with dystrophic calcification, and furthermore band keratopathy was observed in one of our cases.

In our series, all patients had fibrinous uveitis and successful treatment with r-IPA within the first 24 hours. This increased cell lysis and the release of ionized calcium. The anterior chamber becomes saturated with both cellular aggregates and inflammatory debris, in ensuing weeks, thereby creating an ideal environment for binding of free calcium and precipitation of calcium salts. The scaffold, which has been formed by the network of fibrin on the anterior surface of the IOL, provides the site for initial calcium accumulation. This hypothesis is supported by our finding of calcification only involving the optic's anterior surface

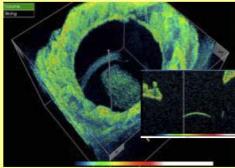


Figure 1. Central band shaped IOL deposits visible as echogenic particles posterior to iris ring by Topcon 3D-OCT imaging and as centrally located echogenic particles on non-echogenic convex IOL surface (insert).





Figure 3. (a) Alizarin Red Stain, IOL in 40X Magnification, (b) Cross section of IOL showing linear granular deposit just below anterior surface of IOL, (c) Alizarin Red Stain, IOL and capsular bag remnant in 4X magnification.



Figure 2. (a) Opacified IOL in-vivo, (b) explanted IOL

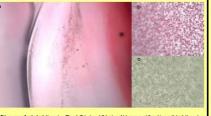


Figure 4. (a) Alizarin Red Stain, IOL in 4X magnification (b) Alizarin Red Stain, IOL in 10X magnification (b) Alizarin Red Stain, IOL in 10X magnification, (c) Optic glisenings - IOL in 10X magnification

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Conclusion: Intracameral r-tPA, though rapidly effective in the treatment of fibrinous membranes, may cause IOL opacification