Infectious Crystalline Keratopathy: A Case Series

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ABSTRACT

This is the case series of three patients of infectious crystalline keratopathy (ICK) presented to us after undergoing penetrating keratoplasty between 2010 to 2020. The lesions showed classical crystalline patterns and clinical diagnosis was made. The patients were treated by broad spectrum antibiotics till the complete resolution of the lesions. The cases highlight the clinical features, diagnosis and management of this rare and resistant disease.

Key words: Infectious crystalline keratopathy, Penetrating keratoplasty, Streptococcus viridans.

INTRODUCTION

Infectious Crystalline Keratopathy (ICK) is characterised by an indolent infectious keratitis in which needle-like, branching crystalline opacities are seen within the corneal stroma, in the absence of appreciable corneal or anterior segment inflammation.

A crystalline appearance within the stroma of cornea may be caused by a variety of conditions. The causative substances might include lipids and products of metabolic disorders such as cystinosis or monoclonal gammopathy in association with multiple myeloma. It rarely occurs as a complication of penetrating keratoplasty following either infection or rejection (Davis 1987; Georgiou 2002).

We report three patients of penetrating keratoplasty who developed ICK in their graft in the past ten years (2010 – 2020). The cause of keratopathy was considered to be infective in these patients and it resolved on antibacterial treatment.

CASE REPORT 1:

A 44-year-old woman with right eye leucomatous corneal opacity underwent an uneventful optical Penetrating Keratoplasty in November 2010. The postoperative examination revealed

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an epithelial defect that healed within 48 hours. Anterior chamber was well maintained and all interrupted sutures were in situ and buried. Patient was in regular follow up and at 4 months postoperative follow up she came with loose sutures at 3 o'clock and 7 o'clock which were removed.

In the 9th month, patient came with complaints of foreign body sensation, diminution of vision and some white opacification in graft. The decrease in the vision was very gradual, painless and progressive. Past history did not reveal any significant fact. The patient was using topical prednisolone eye drops (once) and lubricant eye drops (twice).

On examination the best corrected visual acuity (BCVA) of the patient reduced from 6/12 to 5/60 on Snellen's chart. Slit lamp examination showed white eye i.e. no congestion with a large area of localised non-suppurative intrastromal white opacities (3.1 /4.8 mm^2) in branching pattern with crystalline deposits along the branches (**Figure 1**). The lesion extended from the graft-host interface at 3 o'clock to 5 o'clock corresponding to the area of previous sutures removal. Its extension was noted towards the centre and at approximately 60% of stromal depth. The epithelium was intact and the anterior chamber had occasional cells and flare (Grade 1).

Differential diagnosis of following diseases were made:

1. Herpes simplex keratitis due to branching pattern. But the crystalline nature of the opacity was against this differential. Moreover, fluorescein dye showed negative staining and corneal sensation was not drastically reduced at the uninvolved cornea
2. Graft rejection was another diagnosis due to differential corneal edema. But minimal cells and no congestion (white eyes) ruled out the diagnosis.

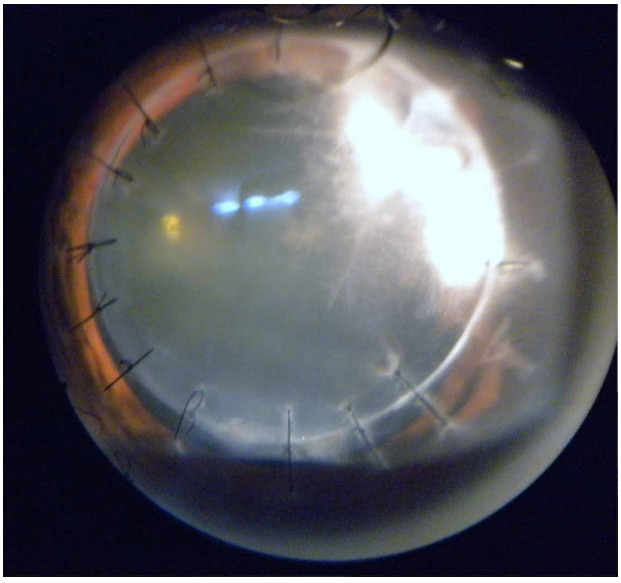

Figure 1: ICK lesion at presentation on day one in first case.

3. Clinically the diagnosis of crystalline keratopathy was made due to typical crystalline opacities in branching pattern.

The scraping / biopsy of the lesion could not be taken as the epithelium was intact and the pupillary area was clear. Moreover, suture can't be removed for biopsy as it was already removed from that area on the last follow up.

So, she was put on broad spectrum antibiotics based on classical clinical picture and infectious etiology being the most common cause. Streptococcus viridans is the most common organism implicated[2], so Azithromycin (1%) ophthalmic drops, fortified Tobramycin (1.3%) and Vancomycin (5%) were started every 2 hourly. Topical prednisolone was stopped and topical Fluorometholone eye drop once daily was added . Topical homatropine (2%), three times daily was also added and lubricants were continued. The patient was kept under strict follow up by monitoring her symptoms, the size of the lesion, direction & orientation of crystals by slit lamp examination and photographs. Initially the lesion did not show any regression although it did not increase either. The medications were continued in view of the resistant nature of the disease. At 2 weeks follow up the patient showed some response to the treatment and improved symptomatically. On slit lamp examination, the density and length of the lesion decreased although size remained the same (**Figure 2**).

The continued treatment showed reduced crystals size at 2 months follow up. The course of treatment was uneventful with no worsening of symptoms or any signs of rejection. The ICK resolved in 5 months and 15 days duration (**Figure 3**). Topical antibiotics were tapered as

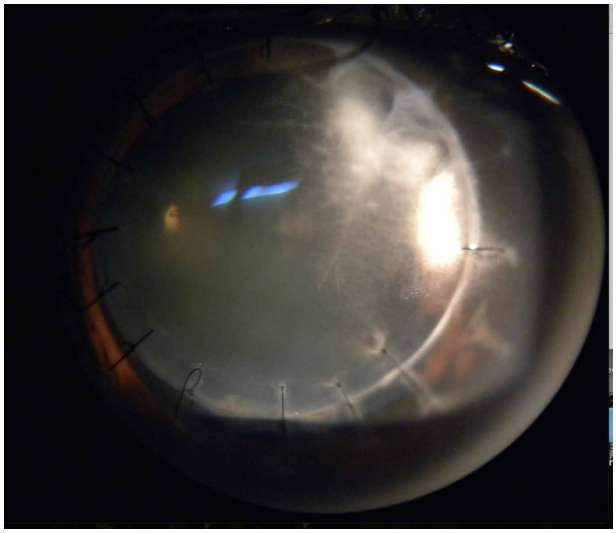

Figure 2: Reduced density of lesion at 2 weeks of treatment in first case.

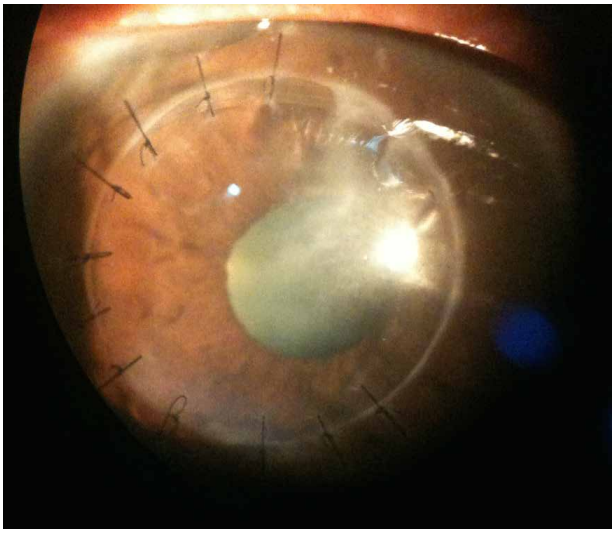

Figure 3: Resolved lesion at 6 months with corneal opacity.

per the clinical response during the follow up period. The BCVA was restored to 6/36 as there was increased astigmatism of -3.00D cylinder at 40° due to corneal opacity and cataract. So a cataract surgery by Phacoemulsification and toric posterior chamber intraocular lens implant was planned. Surgery went as planned and was uneventful. On the first day post surgery the media was clear, the anterior chamber was well defined with no cells, lens implant was in place, fundal glow was good. The final BCVA was 6/9 with -0.5 D of sphere.

CASE REPORT 2:

Sixty years old male patient underwent penetrating keratoplasty for pseudophakic bullous keratopathy (PBK) & corneal scarring of 6 months duration. The BCVA was 6/9 on Snellen's chart. He was doing well with topical prednisolone eye drops once daily when he presented with diminution of vision at 11 months of follow up.

The BCVA was 6/18 with controlled IOP. Slit lamp examination revealed a small lesion (1.5 mm diameter) at the centre of cornea involving the nasal edge of the pupil. The lesion showed typical crystalline nature and a presumptive diagnosis of ICK was kept. Patient was treated on the same lines as the case one. Complete resolution of the lesion was achieved at 5 and half months follow up (**Figure 4**). The BCVA improved from 6/18 to 6/9 on refraction of + 1.0D sph and – 3.5 D of cyl.

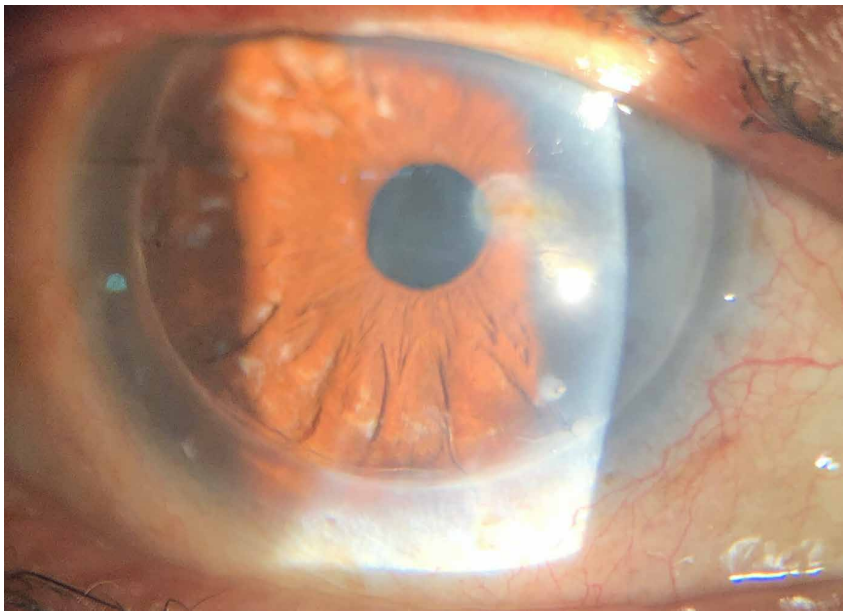

Figure 4: Resolved case 2 after 5 and half months.

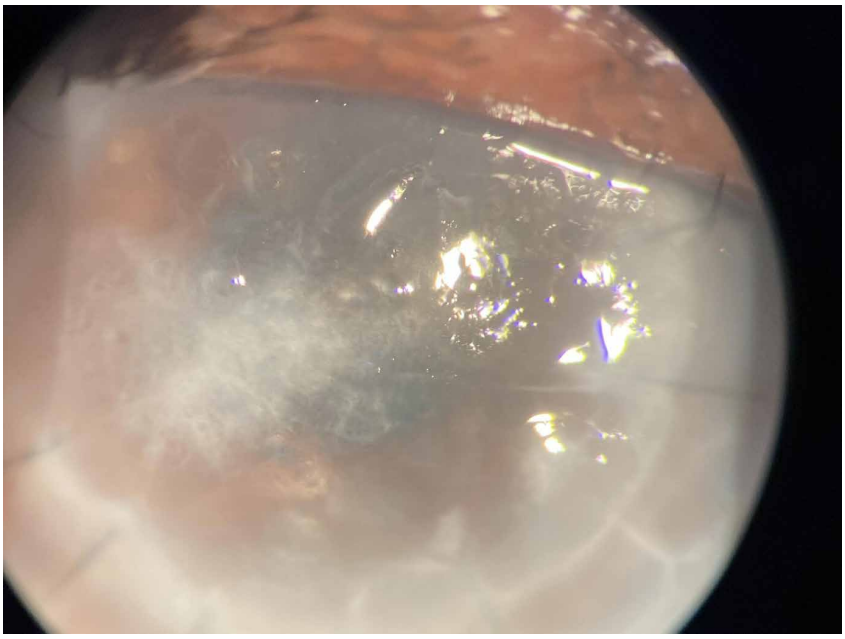

Figure 5: Branching patterned lesion seen at temporal part of graft with surrounding graft edema.

CASE REPORT 3:

This was a 55-year-old female patient who was doing well after keratoplasty for a failed graft when she complained of foreign body sensation in the temporal part of the eye. On examination there were branching opacities in the temporal part of graft which did not take up stain with Fluorescein **(Figure 5)**. Same treatment protocol was followed as case one in the patient and she responded well to treatment. Although she underwent regrafting due to extensive healed opacification in the graft that involved the visual axis too.

DISCUSSION

ICK may occur with a bacterial infection. The infection can arise de novo or as a squeal of surgical procedures, such as refractive surgery and corneal transplants or if the cornea is traumatized chemically or mechanically. ICK is a rare complication typically following penetrating keratoplasty, but it can occur in an ungrafted cornea too in patients with Herpes simplex, Herpes zoster, *Acanthamoeba*, or local anesthetic abuse (Georgiou 2002; Osakabe 2006). It was first described by Gorovoy et al (1983) in patients of corneal transplant who received prolonged corticosteroids.

The various predisposing factors are penetrating keratoplasty on long term steroid, previous HSV keratitis, neurotrophic keratopathy, topical anaesthetic abuse, persistent epithelial defects, loose sutures, contact lenses, radial keratotomy scars, post LASIK etc (Davis et al, 1987).

Many organisms have been isolated in cases of ICK, but the most common are gram positive aerobic streptococci which have been reported in 42% of cases, of which *S. viridans* is the most common (Davis et al,1987; Meisler et al,1984). Another 12% of cases are reported with Staphylococci as the organism isolated, including *Staphylococcus aureus* and *S. haemolyticus*. Fungi have been implicated in 8% of cases, including *Candida tropicalis*, *albicans*, and *parapsilosis*, and *Alternaria*. Additional organisms that have been isolated include *Mycobacterium fortuitum*, *Peptostreptococcus*, *Corynebacterium*, *Pseudomonas* and *Acanthamoeba* (Sharma et al,2000). Often, multiple organisms are isolated. Eyes undergoing refractive surgery are at higher risk for infections with atypical organisms such as mycobacteria (acid-fast bacteria) and *Alternaria* (fungi). With the increasing number of patients undergoing refractive surgery and the relevance of early intervention, it is important to recognize ICK. The organisms gain access along the suture track or through the micro defects in epithelium and form a biofilm that prevents proper penetration of antibiotics (Georgiou et al, 2002).

Infection-related crystalline deposits have a fine branch-like shape, develop over time and may be associated with inflammation. Diagnosis can be clinical after observing the typical crystalline branching pattern. Diagnostic testing such as gram staining, acid-fast staining, routine bacterial and fungal cultures, as well as mycobacterial cultures, should be obtained whenever feasible (Sharma et al, 2000).

The treatment of choice for ICK is with intensive topical antibiotics. Most treating surgeons use cocktail of "fortified" antibiotics such as cefazolin, vancomycin or tobramycin(Meisler et al 1984, Sharma et al 2000).When the organism has not been identified, broad-spectrum antibiotics should be used (Gorovoy et al, 1983). The antibiotics as per sensitivity should be switched and tailored once the organism and antibiotic sensitivities have been obtained. If symptoms do not resolve, it is reasonable to expand coverage or one can start systemic antibiotics. It is common for treatment of ICK to be continued for weeks or even months. In some cases it does not regress at all and compel the surgeon to repeat the keratoplasty.

CONCLUSION

The idea behind presenting these case scenarios was to describe the diagnosis & management strategy in such a situation where confirmatory diagnosis might not be possible due to intact epithelium / clear graft in pupillary area / inability of corneal scraping to reveal any organism.

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