Infectious crystalline keratopathy

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SUMMARY We present a patient who developed a crystalline keratopathy after a penetrating keratoplasty. This rare complication can be caused by bacterial infection, and the patient responded to the appropriate antibiotic therapy. The literature is reviewed and possible causes and mechanisms of the crystalline appearance are discussed.

A crystalline appearance within the stroma of the cornea may be caused by a variety of conditions including lipid and metabolic disorders such as cystinosis and monoclonal gammopathy in association with multiple myeloma. More unexpectedly it can occur as a complication of penetrating keratoplasty following either infection or rejection. We report here on a patient who developed a crystalline keratopathy following a graft. The cause of the keratopathy was considered to be infective and the condition resolved on antibacterial treatment.

Case reports

A 32-year-old man with advanced keratoconus underwent an uneventful penetrating keratoplasty in December 1984. A whole donor eye was used, and the graft was sutured in place with a continuous 10/0 nylon suture. The surgery was uncomplicated though technically difficult because of thinning of the host cornea peripherally. Six days later there was an aqueous leak, with hypotony. The anterior chamber was shallow, the suture loose, and the graft oedematous. Following placement of a single 10/0 nylon suture at the site of the leak the anterior chamber reformed and the leak was sealed; the cornea cleared, and there were no synechiae. Fifteen days later the continuous suture had loosened slightly between 8 and 10 o’clock at the site of the leak, and mucus had become adherent to it. This caused no problems, and no change in management was required save for the addition of 10% acetylcystine drops four times daily.

Ten months after surgery, in October 1985, the suture had loosened superiorly, and this section was removed. At this stage the corrected visual acuity was 6/5, and the patient was taking prednisolone (Predsol) twice daily in addition to the acetylcystine.

A few days after the removal of the suture the graft developed a superficial corneal crystalline stromal infiltrate (Fig. 1) at 9 o’clock, which appeared to be associated with a suture track. The epithelium was intact and the remainder of the graft clear; the anterior chamber contained occasional cells. Conjunctival swabs were taken, but no bacteria grew on blood agar plates. A corneal scraping was not carried out because of the intact epithelium.

Treatment with prednisolone was continued and intensive topical gentamicin and methicillin started. After five days, when the possibility of a streptococcal infection was realised in the light of the experience of others, treatment was changed to topical penicillin and corticosteroids. The lesion

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Fig. 2 The development of further crystalline deposits in February 1986.

regressed. After six weeks, in November 1985, the antibiotics were stopped.

In February 1986, three months after withdrawal of the antibiotics, the stromal lesion recurred and was associated with a crystalline opacity spreading into the graft at midstromal level. Topical penicillin and steroid was again started. A corneal scrape failed to grow any organisms when directly plated on to blood agar; a Gram stain was not performed. The eye initially worsened. It became painful, with the development of photophobia and redness, but the clinical signs were unchanged (Figs. 2, 3). Penicillin was stopped, and, because of the possibility of a more serious infection, the patient was given a subconjunctival injection of gentamicin and methicillin and was started on systemic treatment with the same antibiotics. The eye improved on this regimen, with a reduction in the area of opacification and no progression of the crystalline keratopathy. Two weeks after the acute episode the patient was using gentamicin and methicillin every two hours and prednisolone three times daily. The gentamicin was stopped one week later.

Three months later the crystals had markedly regressed. The patient at this time was taking prednisolone and methicillin twice daily, having received antibiotics for a total of three months. At follow-up in September 1986 there had been no recurrence, and the corrected visual acuity was 6/9. Slight stromal scarring persisted peripherally at 9 o'clock, but all crystalline appearances had regressed completely. Subsequent follow-up revealed no change (Fig. 4).

Discussion

Gorovoy et al. reported the first case of a crystal-like deposition associated with infection in a corneal graft. In his case, as in other reports, there was no sign of ocular inflammation. The crystalline appearance progressed over five months, and the patient eventually required a regraft. There is no mention of any culture being performed, and no antibacterial therapy was given. Analysis of the corneal button removed showed a localised ingrowth of epithelium associated with a suture, and from this area colonies of Gram-positive bacteria were seen extending between the stromal lamellae.

Meisler et al. presented an initial series of three

Fig. 3 Magnified view of the crystalline deposits in February 1986.

Fig. 4 The corneal appearance in February 1987. Note that central white area is light reflection.
patients with infectious crystalline keratopathy: two
developed after penetrating keratoplasty, one in a
herpetic eye. Two of the three patients grew an
α-haemolytic streptococcus either from a corneal
scrape or from a diagnostic keratectomy. All three of
his patients were treated with antibiotics. The lesions
resolved, leaving a variable amount of scarring or
corneal oedema.

Samples et al.\textsuperscript{2} reported on a patient, again show-
ing no sign of ocular inflammation, who was treated
for a presumed fungal infection. Diagnostic kera-
tectomy had failed to demonstrate any organisms.
The situation worsened so that a further graft had to
be performed. Examination of the corneal button
showed dense bacterial colonies beneath Bowman’s
membrane.

Reiss\textsuperscript{3} reported on a patient in whom Streptococcus
viridans had been cultured from a corneal scrape. A
repeated graft had to be performed, however, and
microscopy of the button again demonstrated the
presence of intrastromal bacteria.

The case reported in this paper follows a similar pattern to those reviewed above. The recurrence of
the lesion after a short course of antibiotics indicates
that topical treatment must be continued for some
months to eradicate the infection. The location of
the organism within the stroma, demonstrated by
electron microscopy\textsuperscript{415} not only makes it difficult to
obtain specimens to culture an organism but also
presumably lends protection to the bacteria from the
effect of topically applied antibiotic.

The way in which the bacteria penetrate the
corneal stroma and the reason for their growth in the
anterior part of the stroma is open to speculation. A
suture track would seem the most probable mode of
bacterial entry into the stroma, but any break in
Bowman’s membrane, no matter how caused, would
suffice. The immunosuppressive effect of topical
corticosteroids may also play a part. All but one of
the cases reported have occurred in patients with
corneal grafts, for whom prolonged steroid treatment
is usually required. There have been no reports of a
similar process occurring in cataract surgery, where
the period of steroid treatment is much shorter.
Samples et al.\textsuperscript{2} suggested that the predilection of
the organism for the anterior stroma reflects an
advantageous environment for growth at this depth
in the cornea.

The nature of the crystalline appearance itself is
also obscure. Reiss et al.\textsuperscript{3} suggested that it may be
formed by the bacterial colonies themselves as they
grow between the lamellae of the corneal stroma.

With the electron microscope Samples et al.\textsuperscript{2}
observed electron dense bodies with needle-like
projections and considered that they were respon-
sible for the crystalline appearance. The origin of
these bodies was uncertain.

It might be suggested that the crystals are the result
of the precipitation of immune complexes formed as
a result of an immunological response to intrastromal
bacteria. This would be akin to the suggested
aetiology of the crystals seen in graft rejection.\textsuperscript{6,7}
These have been reported as appearing at the deep
stromal level between five and 30 days after rejection
of the graft. The crystals differ from those seen in the
case of infectious crystalline keratopathy in that they
are found in the deep stroma and respond to steroid
treatment alone. The suggested cause of these
crystals is a precipitation of immune complexes
formed between host antibody and donor stromal
antigens. A further suggestion had been that the
crystals may be the result of lipid deposition.\textsuperscript{2} The
appearance is not, however, typical of that seen in
lipid keratopathy and it would not be expected to
resolve with antibiotic treatment.

CONCLUSION

Stromal infection of a corneal graft may present as a
superficial or midstromal crystalline keratopathy in a
quiet or minimally inflamed eye. It is associated with
the presence of intrastromal bacteria and must be
differentiated from the deep crystalline keratopathy
seen in graft rejection. Treatment should be with
thorough, prolonged application of antibiotics,
which is curative.

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