Case Report

Taiwan J Ophthalmol 2022;12:487-490

Access this article online

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Website:
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DOI:
10.4103/tjo.tjo_11_21

Acute onset of deep calcareous degeneration treated with keratoplasty procedures: Two cases report

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Abstract:

There are two types of corneal calcium deposition, one is calcific band keratopathy and another is calcareous degeneration. We report two cases of acute onset of calcareous degeneration after using topical eye drops for their corneal wounds. The calcification in both the cases developed within 1 month. Due to the deeper stromal opacity, calcareous degeneration was impressed. In our cases, the deposits were too deep that they required keratoplasty procedures as better treatment options. One of the cases was treated with penetrating keratoplasty and another case was treated with deep anterior lamellar keratoplasty. Both of our cases had stable corneal grafts, and there were no ocular inflammation and no recurrence of calcification at least for 6 months.

Keywords:

Calcareous degeneration, calcific band keratopathy, deep anterior lamellar keratoplasty, penetrating keratoplasty, steroid-phosphate preparations

Introduction

Calcium deposition in the cornea typically occurs as deposition of calcium phosphate. There are two types of corneal calcium deposition.[1] One is calcific band keratopathy, which is more common and the calcium salts precipitate in the basement membrane, Bowman's membrane, and the superficial stroma.[2] Another type is calcareous degeneration and the calcium deposition involves the deeper stroma including Descemet's membrane, which is relatively rare.[3] Both have been discussed in the patients with severe dry eye condition, serum hypercalcemic states, severe anterior segment inflammatory conditions, inherited and systemic diseases, or usage of some kinds of eye drops with preservatives.[4,5] Although most cases are classified as calcific band keratopathy, we report two interesting cases of acute onset of calcareous degeneration treated with deep anterior lamellar keratoplasty (DALK) or penetrating keratoplasty (PK).

Case Reports

Case 1

A 67-year-old man who denied any underlying disease complained about right eye redness and pain for 2 weeks. Due to previous corneal epithelial defect history, central neurotrophic ulcer of the right eye was diagnosed at a local clinic and he was treated with sulfamethoxazole (Sulmezole Eye Drops 4%, Medicine Co., Ltd., Taoyuan, Taiwan), dexamethasone phosphate 0.1%+neomycin sulfate 0.35% (Delone Eye Drops, Sinphar Pharmaceutical Co., Ltd., Yilan, Taiwan), and carbomer (Vidisic Gel, Gerhard Mann Gmbh., Berlin, Germany) four times per day. After 1 month, his symptoms had no improvement, so he was referred to our outpatient department. He denied dry eye syndrome or traumatic history. Ophthalmic examination showed that his best-corrected visual

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Submission: 28-01-2021
Accepted: 08-03-2021
Published: 20-05-2021

How to cite this article: Ou YC, Hu CC. Acute onset of deep calcareous degeneration treated with keratoplasty procedures: Two cases report. Taiwan J Ophthalmol 2022;12:487-90.

acuity (BVCA) (Snellen) was counting fingers at 0.5 m in the right eye and 20/20 in the left. Slit-lamp examination revealed a quiet and deep anterior chamber, mild conjunctival inflammation, and a whitish plaque over the central cornea of the right eye [Figure 1a]. Calcific band keratopathy was impressed at first and his laboratory parameters revealed normal serum calcium and phosphate level. Superficial keratectomy was arranged and performed for him. However, the stromal opacity was too deep to be fully removed [Figure 1b]. Part of the removed whitish plaque was sent for the analysis by Fourier Transform Infrared Spectroscopy (FT/IR-4100, Jasco, Japan), which was proved to be calcium phosphate ($Ca_3(PO_4)_2$).[6]

Due to the deeper stromal opacity, calcareous degeneration was impressed and PK was performed for his right eye with amniotic membrane covered [Figure 1c]. The removed cornea button was sent for histopathological examination. Paraffin sections were further processed with hematoxylin and eosin (H and E). Sections showed corneal tissue with deep stromal fibrosis and basophilic deposits of calcification stained with H and E [Figure 1d]. Post transplantation, we prescribed chloramphenicol (Chloramphenicol Eye Drop 0.25%, Sinphar Pharmaceutical Co., Ltd., Yilan, Taiwan), prednisolone acetate (Pred Forte, Allergan, Westport, Ireland), and balanced salt solution (BSS, Alcon Couvreur N.V., Puurs, Belgium). After 6 month of outpatient department followed up and cataract surgery, his right eye BCVA improved to 20/100 and the cornea was still transparent. No sign of inflammation or reappearance of the deposits in the corneal graft was observed [Figure 2].

Case 2

A 62-year-old woman had underlying diseases of type two diabetes mellitus, hypertension, and gouty arthritis under medications of metformin, amlodipine, and allopurinol. She had ocular disease of dry eye syndrome under lubricants treatment. This time she complained about progressively blurred vision of the right eye for a year. Right eye cataract was impressed and she received phacoemulsification with intraocular lens implantation of the right eye. A central epithelial defect of the right eye cornea was noted after a week of the operation. According to her family, the defect was made by touching with post-operation eye drops bottles. Topical chloramphenicol (Chloramphenicol Eye Drop 0.25%, Sinphar Pharmaceutical Co., Ltd., Yilan, Taiwan) and dexamethasone phosphate 0.1%+neomycin sulfate 0.35% (Delone Eye Drops, Sinphar Pharmaceutical Co., Ltd., Yilan, Taiwan) were prescribed and used every 2 hours daily. Three weeks later at our outpatient department, her BVCA was 20/1200 in the right eye and 20/20 in the left. Slit-lamp examination revealed a quiet and deep anterior chamber but band-shaped corneal deposits over the central cornea of the right eye [Figure 3]. Anterior segment optic coherence tomography (AS-OCT) images showed hyperintense signal involving entire anterior stroma [Figure 4]. Laboratory parameter only revealed a high blood glucose level. Serum calcium and phosphate levels were normal.

DALK was then performed in the right eye for him. There was no complication reported during the procedure. Post transplantation, we prescribed chloramphenicol, prednisolone acetate, and BSS for her. One-year postoperative BCVA was 20/60. No signs of inflammation, rejection, or reappearance of the deposits in the corneal graft were observed [Figure 5].

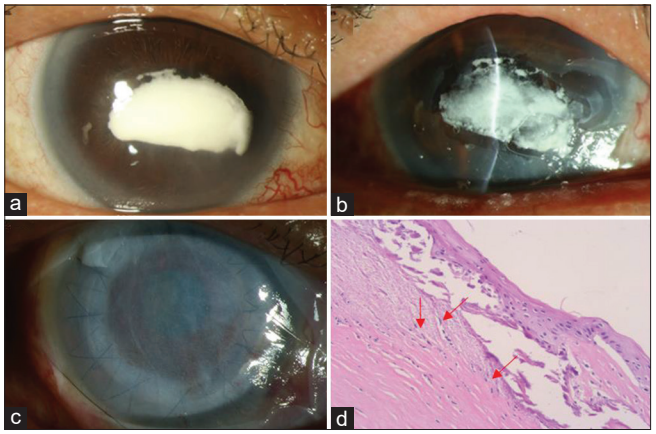

Figure 1: (a) Right eye biomicroscopy: A whitish plaque over the central cornea. (b) Slit-lamp examination of the right eye: After performing superficial keratectomy, the stromal opacity and calcification were too deep to be fully removed. (c) Right eye biomicroscopy: 3 days after performing penetrating keratoplasty and covering with amniotic membrane graft. (d) Histopathology (H and E): Corneal tissue with deep stromal fibrosis and basophilic deposits of calcification stained with H and E (red arrows). (original magnification ×100)

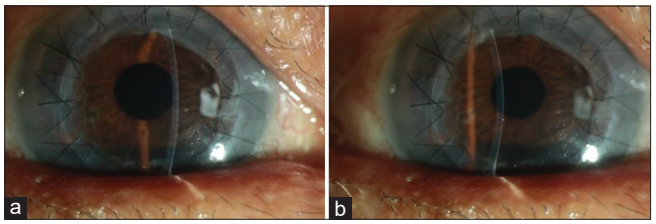

Figure 2: Slit-lamp examination of the right eye: The cornea was still transparent after penetrating keratoplasty for 6 months. There were no signs of inflammation, rejection, or reappearance of the deposits in the corneal graft

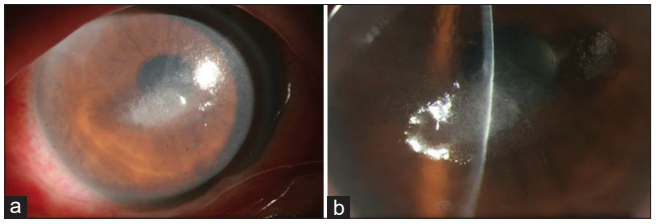

Figure 3: (a) Right eye biomicroscopy: Band-shaped corneal deposits over the central cornea. (b) Slit-lamp examination of the right eye: The deposits involved deep into the stroma

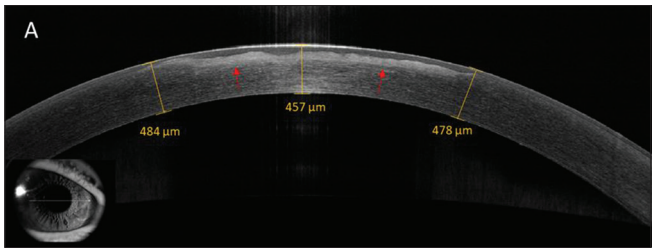

Figure 4: Anterior segment optic coherence tomography images showed hyperintense signal involving the entire anterior stroma (red arrows)signal involving the entire anterior stroma (red arrows)

Discussion

There are similarities and differences between calcific band keratopathy and calcareous degeneration. Corneal calcification occurs more common as calcific band keratopathy that is caused by systemic illnesses (such as renal disease), chronic ocular inflammation (such as dry eye disease), using of topical medications, or after surgical procedures. There is typically a band-shaped, horizontal opacity in calcific band keratopathy that grows from the peripheral cornea toward the central. The calcium usually deposits in the subepithelium, Bowman's layer, and the superficial stroma of the cornea. In contrast, a rare condition called calcareous degeneration can involve all corneal layers. It can be metastatic or dystrophic. Metastatic calcification occurs in the presence of abnormal serum calcium or phosphate level, which was not seen in our patients.[7] Dystrophic calcification is secondary to local tissue damage in chronic ocular inflammation which may occur in eyes with trauma history, persistent corneal ulcers, or after surgical procedures.[8]

Topical medications have been implicated in corneal calcium deposition which can be superficial or deep into the stroma. Previous reports suspected that the preservatives such as phenylmercuric nitrate and thiomersal,[8,9] retinoic acid,[10] lubricants,[4] and topical use of steroid-phosphate preparations with or without beta-blockers[11,12] may contribute to corneal calcification. Due to that both of our cases have a history of using topical steroid-phosphate eye drops, the potential complication of steroid-phosphate preparations may play a role in forming corneal calcification. Using steroid-phosphate medications can be attributed to high phosphate concentrations in tears or interstitial fluid. Due to the reason that calcareous calcification involves the deeper stroma and Descemet's membrane, a compromised epithelium and the absence of Bowman's layer are considered as risk factors for deeper calcification.[13] Ophthalmic inflammatory condition such as dry eye disease could also aggravate calcium deposition. Once these patients have persistent corneal ulcer or extensive trauma history and use phosphate-based medications,

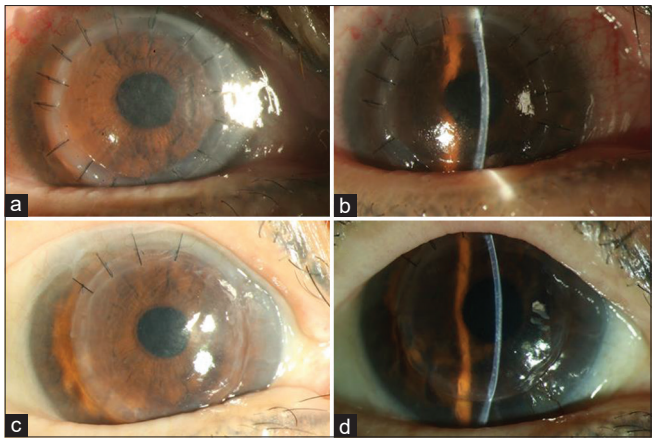

Figure 5: (a and b) Biomicroscopy and slit-lamp examination of the right eye 3 days after deep anterior lamellar keratoplasty: the cornea was intact but mild edema. (c and d) One year after deep anterior lamellar keratoplasty: the cornea was still transparent. There were no signs of inflammation, rejection, or reappearance of the deposits in the corneal graft

they have the chance of developing the rapid onset of deep stroma calcification, like our patients. Popiela and Hawksworth present a reference list of phosphate-based ophthalmic drugs.[14] Eye drops containing steroids like dexamethasone and some intraocular pressure-reducing drops were found to be predominantly phosphate containing. Prednisolone acetate (Predforte, Allergan), which was mentioned not containing phosphates, was prescribed for our patients after the transplantation surgery.

Calcareous degeneration can occur fairly rapidly in the cornea with an epithelial defect which developed within a month in our cases. It is very important to distinguish calcareous degeneration from band keratopathy to indicate the correct treatment. Bordin *et al.* suggested that AS-OCT was helpful to investigate and establish the proper diagnosis.[15] Superficial keratectomy with or without ethylenediaminetetraacetic acid chelation is reported to have an excellent effect for the treatment of calcific band keratopathy.[16] However for calcareous degeneration, there are few reports discussing the treatment. In our experience, the deposits are too deep that it requires DALK or PK as better treatment options. After the surgery, both of our two cases had stable corneal grafts. There were no ocular inflammation and no recurrence of calcification after adjusting the topical medications at least for 6 months.

Declaration of patient consent

We have obtained all appropriate patient consent forms. In the form, the patients have given their consent for images and other clinical information to be reported in the journal. The patients understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Acknowledgments

The authors are grateful to Su-Han Huang for excellent histotechnical assistance.

Financial support and sponsorship

Nil.

Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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