Original Article

Postkeratoplasty Corneal Plaques: A Case Series

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Abstract

Purpose: To assess the risk factors and management of corneal plaques formed after keratoplasty.

Methods: In this retrospective study, medical records of all eyes with plaques formed on top of corneal grafts performed in the period between January 2014 and January 2022 were reviewed. The retrieved data included prekeratoplasty corneal pathology, ocular risk factors, operative data and complications, plaque management, and chemical composition of the plaques using infrared spectrometer.

Results: Thirteen eyes were included in this study. Predisposing ocular comorbidities included ocular surface disorders with variable degrees of dry eye in nine patients, rheumatoid arthritis in three patients, history of herpetic keratitis in two eyes, and cicatrizing conjunctivitis in two patients. Surgical excision and amniotic membrane transplantation (AMT) were performed in 12 eyes. Postoperatively, five eyes showed recurrence after excision, two eyes developed graft vascularization and scarring, and one eye showed persistent epithelial defect and graft scarring, whereas four eyes showed complete epithelialization with mild haze. Rekeratoplasty and AMT were performed in two eyes with no plaque recurrence. Chemical analysis using infrared spectrometry showed that the plaques consisted of ammonium magnesium phosphate and calcium phosphate carbonate in 9 (75%) cases and pure mucus in 3 (25%) cases.

Conclusions: Postkeratoplasty corneal plaque formation is an underestimated complication of keratoplasty that may occur after persistent epithelial defects. Ocular surface disorders are the primary predisposing risk factors. In our experience, the prognosis after medical treatment or surgical scraping is guarded, and regrafting can be the only solution to restore graft clarity.

Keywords: Corneal deposits, Corneal plaques, Keratoplasty, Postkeratoplasty complications

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Introduction

Corneal plaques have been previously described in various corneal disorders, such as keratoconjunctivitis sicca, herpes zoster ophthalmicus, microbial keratitis, and vernal keratoconjunctivitis. However, the pathogenic mechanisms responsible for corneal plaque formation remain unclear. It has been postulated to be due to abnormal tear secretion, exposure, denervation, or systemic pathologies. Corneal plaques vary in size, shape, pattern, and constituents, with mucous and degenerated epithelial cells being dominant components.[1-6]

Keratoplasty, whether lamellar or penetrating, is the most common solid organ transplantation performed worldwide. Keratoplasty is a highly successful procedure, with a 90% success in low-risk cases.[7] Corneal plaques are a rare cause of visual impairment after corneal transplantation and may contribute to corneal graft failure.

Herein, we report a case series of plaques formed in corneal grafts following surgery to detect the risk factors and outcomes.

Methods

We retrospectively reviewed the medical records of all eyes that underwent keratoplasty between January 2014 and January 2022 at Alexandria Main University Hospital. Patients with

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eyes complicated by corneal plaque formation were included in this study.

This study was conducted in accordance with the tenets of the Declaration of Helsinki and approved by the Ethics Committee of the Faculty of Medicine, Alexandria University. All patients had given written informed consent for the surgery. The retrieved data included preoperative corneal pathology, drug history, underlying systemic diseases, and other ocular comorbidities. Operative data included type of keratoplasty (lamellar or penetrating) and intraoperative complications. Postoperative data included corneal plaque onset, medications used at the time of onset, plaque management, and final best-corrected visual acuity.

Surgical removal of the plaque and amniotic membrane transplantation (AMT) were performed in most cases.

A 26G hypodermic needle was used to create a plane of dissection under the tightly adherent plaque, where the needle was introduced with the bevel facing downward and gradually advanced and swept sideways to create the required plane. Dissection was then continued gently to remove the plaque in one mass or sometimes it broke, and the process was repeated to end with multiple excised pieces. The raw surface was then covered with AM, with the stroma facing downward [Figure 1a-d].

Excised plaques were analyzed microbiologically, histopathologically, and using an infrared spectrometer to detect plaque composition.

Data were fed to the computer and analyzed using IBM SPSS software package (version 20.0) (Armonk, NY, USA: IBM Corp). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum) and mean.

Results

The records of 1879 eyes that underwent keratoplasty were reviewed. Corneal plaque formation was detected in 13 eyes of 13 patients (9 females and 4 males) with a mean age of 51.8 years (range, 12–80 years). Eleven eyes had corneal plaques after penetrating keratoplasty, while two eyes had plaques formed after deep anterior lamellar keratoplasty. Indications for keratoplasty were corneal scarring postmicrobial keratitis ($n = 9$), advanced keratoconus ($n = 2$), previous graft failure ($n = 1$), and corneal degeneration ($n = 1$) [Table 1].

Plaque formation occurred early (in the first 2 months postoperatively) in seven eyes, after 1 year in three eyes, and between 2 months and 1 year in three eyes. A persistent epithelial defect in the graft was present in all the eyes prior to plaque formation. In four patients, no ocular surface abnormalities were identified, and plaque formation in these patients was considered idiopathic. Ocular surface disorders with variable degrees of dry eye were present in nine eyes (69.2%). Cicatrizing conjunctivitis with shallow fornices and absent plica was present in two eyes. Rheumatoid arthritis, a cause of ocular surface disorders, was present in three patients, two of whom were on biological treatment before keratoplasty. Two of the patients had a history of herpetic keratitis [Figure 2a-d].

All patients were on topical medications in the form of preservative-free antibiotics, steroids, and lubricants, because of the presence of epithelial defects prior to plaque formation. An off-label preparation of topical N-acetylcysteine 10% was added once the plaque started to form. The plaques were tough and chalky white in color, with variable extension into the underlying corneal stroma and surrounding epithelial defect.

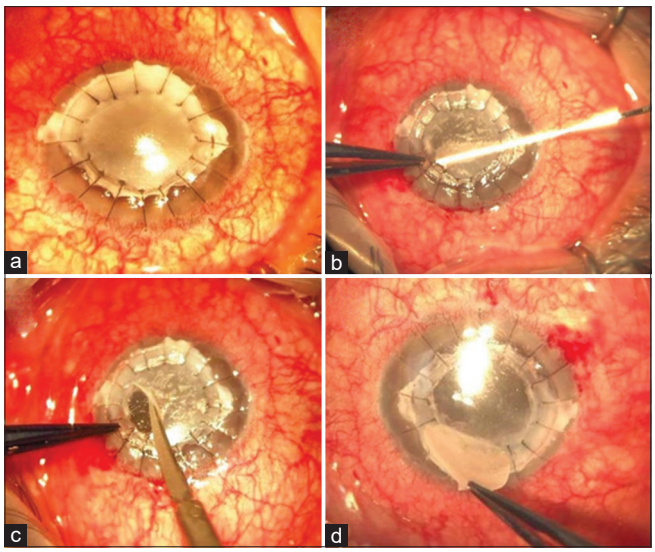

Figure 1: (a) Intraoperative photo of the plaque covering the entire graft (surgeon's view), (b) Introducing the hypodermic needle under the plaque edge to create a plane of dissection, (c) Gradually lifting the plaque edge, (d) Near-total peeling of the plaque over the graft

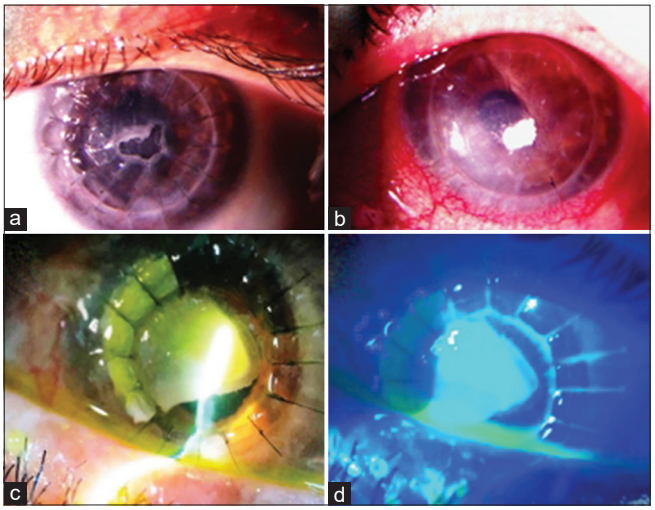

Figure 2: Postkeratoplasty plaques of variable extensions. (a) Late plaque occurrence in a patient with history of herpetic keratitis, (b) Late occurrence of corneal plaque in a patient with rheumatoid arthritis, (c) Early corneal plaque formation after penetrating keratoplasty (idiopathic), (d) Same patient, notice the epithelial defect overlying the plaque

Table 1: Postkeratoplasty corneal plaques

Case number	Age	Sex	Ocular risk factors	Indication for keratoplasty	Type of keratoplasty	Date of surgery	Date of plaque occurrence	Response to scrapping	Chemical composition
1	31	♂	HK	Opacity	PK	March 2007	April 2020	Recurrence, corneal melting, and atrophia bulbi occurred after 6 months	Ammonium magnesium phosphate 85% Calcium phosphate carbonate 15%
2	62	♀	RA	Opacity	PK	January 2016	January 2020	Did not recur after 2nd scrapping	100% mucous
3	53	♀	Cicatrizing conjunctivitis	Opacity	PK	April 2017	May 2020	Mild haze	100% mucous
4	70	♂	None	Opacity	PK	December 2018	December 2019	Patient refused scrapping	
5	80	♀	Cicatrizing conjunctivitis	Opacity	PK	December 2019	February 2020	Recurrence	Calcium phosphate carbonate 85% Ammonium magnesium phosphate 15%
6	36	♀	None	Advanced KC	DALK	January 2020	March 2020	Mild haze	100% mucous
7	12	♀	None	Opacity	PK	February 2020	April 2020	Graft opacity and vascularization	Ammonium magnesium phosphate 85% Calcium phosphate carbonate 15%
8	48	♂	HK	Rejected graft	PK with AMT	March 2020	April 2020	Recurrence, corneal melting after 3 months, atrophia bulbi occurred	Ammonium magnesium phosphate 85% Calcium phosphate carbonate 15%
9	68	♀	Dry eye	Opacity	PK with cataract extraction	November 2020	November 2020	Recurrence, regrafting done (successful)	Ammonium magnesium phosphate 80% Calcium phosphate carbonate 20%
10	58	♂	Dry eye	Corneal degeneration	PK with secondary IOL implantation	December 2020	December 2020	Stromal graft opacity, regrafting done (successful)	Calcium phosphate carbonate 70% Ammonium magnesium phosphate 30%
11	36	♀	None	Advanced KC	DALK	January 2021	December 2021	Persistent epithelial defect, graft scarring	Calcium phosphate carbonate 85% Ammonium magnesium phosphate 15%
12	66	♀	RA	Opacity	PK with cataract extraction	January 2021	February 2021	Recurrence	Calcium phosphate carbonate 60% Ammonium magnesium phosphate 40%
13	54	♀	RA	Opacity	PK	September 2021	November 2021	Mild corneal haze	Ammonium magnesium phosphate 80% Calcium phosphate carbonate 20%

HK: Herpetic keratitis, PK: Penetrating keratoplasty, RA: Rheumatoid arthritis, KC: Keratoconus, DALK: Deep anterior lamellar keratoplasty, IOL: Intraocular lens, AMT: Amniotic membrane transplantation

None of the eyes showed any response to topical medication. Surgical removal of the plaque, together with AMT, was performed in 12 eyes, and 1 patient refused further intervention. One month postoperatively, four eyes (33.3%) showed complete epithelialization and mild corneal haze, five eyes showed recurrence of the plaque, two eyes developed stromal scarring and vascularization, and one eye had persistent epithelial defect with graft scarring [Figure 3a-d]. Regrafting with AMT was performed in two eyes. In both cases, a clear graft was achieved, with complete epithelial healing and no plaque recurrence throughout an 18-month follow-up period. Two eyes with recurrent plaques developed corneal melting 3 and 6 months after surgery, which ended in atrophia bulbi.

Microbiological evaluation of the excised plaques revealed no microorganism growth. Histopathological analysis revealed nonspecific degenerated inflammatory cell aggregation with keratinization. Chemical analysis using infrared

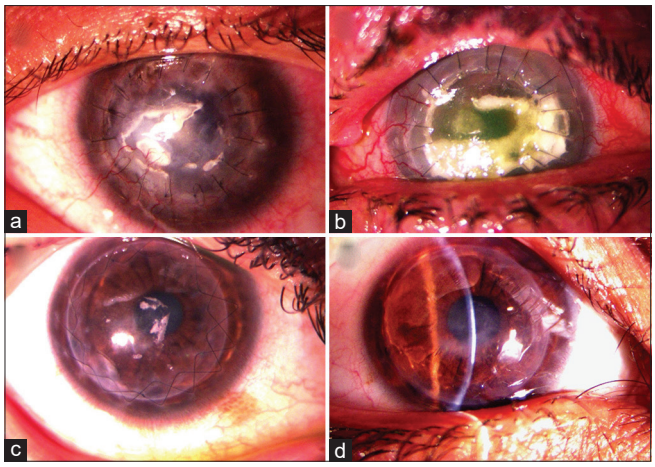

Figure 3: Outcomes of plaque scrapping. (a) Plaque recurrence with vascularization after scrapping, (b) Aggressive plaque recurrence after scrapping, (c) Minimal plaque recurrence with acceptable visual outcome, (d) Complete plaque resolution after scarping with residual superficial stromal haze

spectrophotometry revealed ammonium magnesium phosphate with calcium phosphate carbonate in nine eyes (75%) and mucus only in three eyes (25%).

Discussion

This case series shows that corneal plaque formation is a detrimental, yet infrequently reported complication that can occur after keratoplasty. Corneal plaques have previously been reported in patients with vernal keratoconjunctivitis, keratoconjunctivitis sicca, herpes zoster ophthalmicus, and infectious keratitis.[1-3,5,6,8] To our knowledge, this is the first study to discuss postkeratoplasty corneal plaques.

In all cases, plaques formed on top of a persistent epithelial defect, and were tightly adherent to the underlying stroma. Most of our patients had predisposing ocular surface problems. The presence of ocular surface and tear film abnormalities can invite plaque deposition on top of these persistent defects.

Chemical analysis of the plaques revealed pure mucus in three cases. These cases did not respond to medical treatment including topical N-acetylcysteine probably due to thick, deep, and large nature of the plaques. However, they showed a relatively favorable response to surgical scrapping with no plaque recurrence and only mild graft haze. The remaining plaques were composed of a combination of calcium and ammonium salts in different ratios, raising the possibility of alterations in the chemical composition of the tear film. It has been previously reported that dry eye disorders are associated with an increase in both tear film osmolarity and the concentration of some electrolytes, including calcium, bicarbonate, and magnesium.[9] Moreover, tear film pH is more alkaline in patients with dry eye.[10] Consequently, the combination of an increase in tear film electrolytes and alkaline pH could be a possible etiopathologic factor for plaque formation.

Most corneal plaques reported in the literature showed a favorable response to medical treatment with topical N-acetylcysteine or surgical scraping.[3,6,8,11,12] However, we did not encounter such a favorable response in our cases. Medical treatment failed in all our cases. Surgical scraping and AMT were not effective in some cases because the plaques were tightly and deeply adherent to the underlying stroma, which may lead to stromal scarring. We believe that this difference in plaque behavior is mainly due to different chemical composition, where most of our cases had plaques formed of calcium and ammonium salts whereas most corneal plaques reported in literature were formed mainly of mucus.

Bernauer *et al*. reported calcific corneal plaque formation after using preservative-free tear formulations rich in phosphate buffer. They reported rapid plaque occurrence in five cases with ocular surface disease after frequent use of these drops. We revised the prescribed artificial tears that our patients used and contacted the manufacturers; none of them used phosphate buffers in their formulations.[13]

AM was added after scraping and regrafting to promote epithelialization and prevent plaque recurrence. AM is well known for its nutritive, anti-inflammatory, and anti-scarring nature on the ocular surface. It is reported to have a thick basement membrane that facilitates epithelial cell migration, adhesion, and differentiation, and hinders epithelial apoptosis.[14-18] In our series, four cases showed favorable response after scrapping and AMT. We believe that AM played an important role in promoting epithelial healing in these cases. Moreover, AMT prevented plaque recurrence and enhanced epithelial healing after regrafting performed in two of our cases.

In conclusion, postkeratoplasty corneal plaque formation is an underestimated complication of keratoplasty that may occur after persistent epithelial defects. Ocular surface disorders are the primary predisposing risk factors. In our experience, the prognosis after medical treatment or surgical scraping is guarded, and regrafting can be the only solution to restore graft clarity.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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