Original Article

Clinical characteristics and outcomes of band keratopathy: a 10-year retrospective analysis

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ABSTRACT

Background: Band keratopathy is a chronic, degenerative corneal disease resulting from gradual calcium deposition in the superficial cornea. Herein, we report the spectrum of causes, treatment outcomes, and recurrence rates of band keratopathy at a tertiary referral center throughout one decade.

Methods: This retrospective study included patients with clinical diagnoses of band keratopathy who were treated with combined ethylenediaminetetraacetic acid (EDTA) and superficial keratectomy with or without amniotic membrane transplantation (AMT). Patient medical records were reviewed, and detailed demographic and ophthalmological data, such as baseline and last follow-up best-corrected distance visual acuity (BCDVA), ocular or medical comorbidities, type of intervention, postoperative follow-up duration, relevant complications, and recurrence were recorded.

Results: A total of 32 eyes of 29 patients with 3 (10.3%) bilateral and 26 (89.7%) unilateral cases of treatment-requiring bank keratopathy were included. The mean (standard deviation [SD]) (range) age was 39.4 (22.4) (2–74) years, and most patients were female. The most common secondary cause was previous vitreoretinal surgery with silicone oil tamponade (15.6%); however, idiopathic cases were the most common (18.8%). Systemic comorbidities were present in 27.6% of patients, consisting of hypertension, diabetes mellitus, epilepsy, coronary artery disease, Behcet's disease, and juvenile idiopathic arthritis; however, none of the patients had systemic diseases associated with hypercalcemia. Two of the 3 patients with bilateral involvement had chronic uveitis secondary to systemic rheumatological disease. The mean (SD) follow-up duration was 5.6 (4.0) years, and no serious postoperative complications occurred. The mean (SD) baseline and final BCDVA in logarithm of the minimum angle of resolution (logMAR) were 1.98 (1.0) and 1.7 (1.0), respectively ($P > 0.05$). Combined EDTA chelation and superficial keratectomy with and without AMT were performed in 12.5% and 87.5% of eyes, respectively. Recurrence was observed in 37.5% of eyes within the mean (SD) (range) follow-up of 9.4 (9.1) (1–32) months. Seven of the 12 eyes with recurrence underwent re-EDTA chelation combined with superficial keratectomy and AMT; however, 5 patients managed conservatively.

Conclusions: In this study, band keratopathy requiring intervention more commonly affected female individuals and was unilateral. Most cases were idiopathic. Systemic comorbidities were present in approximately one-third of cases. Managing band keratopathy using a combination of EDTA chelation and superficial keratectomy with or without AMT could be a potential treatment modality. Further large-scale studies are required to provide robust conclusions regarding the efficacy and safety of this management approach.

KEYWORDS

band keratopathy, corneal degeneration, ethylenedinitrilotetraacetic acid, chelation therapies, keratectomies, amniotic membrane, visual acuities, recurrences

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INTRODUCTION

Band keratopathy is a corneal degeneration characterized by the chronic deposition of calcium salts in the basement membrane of the corneal epithelium, Bowman's layer, and anterior stroma. Corneal deposition begins in the interpalpebral area, close to the limbus. Because of the absence of Bowman's layer in the peripheral cornea, a gap between the limbus and calcific band is evident [1-3]. Clinically, band keratopathy appears as a superficial grayish-white corneal opacity with a frosted or ground-glass appearance [1]. The lesion progresses toward the center of the cornea and thickens in its anterior and posterior dimensions, resulting in an opacified whitish nodularity. Calcium deposits may compromise the integrity of the overlying epithelium, resulting in spontaneous and recurrent corneal epithelial erosions [1-4].

Band keratopathy may be isolated or associated with ocular or systemic diseases such as uveitis and systemic hypercalcemia [5]. Patients may be asymptomatic, especially in the early stages; however, with progression, vision deteriorates [6]. Although clinical diagnosis is usually straightforward, the use of anterior segment optical coherence tomography, confocal microscopy, and immunohistochemical staining has facilitated the identification of degeneration [6].

In advanced cases with vision loss or severe ocular discomfort, removal of calcium opacities and restoration of a smooth ocular surface are crucial [1-3]. Earlier, this was achieved through mechanical debridement; however, the most common treatment modality is now chelation with ethylenediaminetetraacetic acid (EDTA) alone or in combination with superficial keratectomy (using manual or excimer laser) with or without amniotic membrane transplantation (AMT) [1, 7, 8]. Patients with ocular comorbidities, such as limbal stem cell deficiency, severe dry eye, or neurotrophic keratopathy, could be treated conservatively or using additional methods to accelerate epithelial healing [7, 8] and restore a stable corneal epithelium [1, 7, 8].

We evaluated the spectrum of causes, treatment outcomes, and recurrence rates of treatment-requiring band keratopathy at our tertiary referral center over a period of one decade.

METHODS

In this retrospective case series, we included patients with clinical diagnoses of band keratopathy who were treated between January 2011 and December 2022 at a tertiary referral center, the Ege University Department of Ophthalmology, Izmir, Turkey. The study was approved by the Ege University Institutional Ethics Review Board and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients or their legal guardians.

Patient medical records were retrospectively reviewed. In addition to demographic data such as age and sex, we recorded detailed ophthalmological findings such as best-corrected distance visual acuity (BCDVA), the presence of systemic or ocular comorbidities, drug history, type of intervention for band keratopathy, postoperative follow-up duration, recurrence, relevant complications, and history of other ocular interventions.

All included patients had a documented detailed ophthalmological examination, including measurement of BCDVA using a Snellen chart (Nidek model CP-770 chart projector; Nidek Co., Ltd., Tokyo, Japan) with measurements recorded in logarithm of the minimum angle of resolution (logMAR) notation, intraocular pressure measurement (Goldmann applanation tonometer, Haag-Streit Group, Koniz, Sweden), detailed slit-lamp examination (Topcon DC-4, Topcon Healthcare, Tokyo, Japan) of the anterior and posterior segments, and anterior segment photography with images processed using Topcon IMAGEnet® i-base imaging software (Topcon Healthcare) at the preoperative and each postoperative visit.

All procedures were performed by a single clinician (O.B.S.). EDTA chelation with superficial keratectomy or EDTA chelation with superficial keratectomy and AMT were performed depending on the patient's clinical condition. For EDTA chelation with superficial keratectomy, following epithelium removal, EDTA (0.125 M) (Ataman Chemicals, Istanbul, Turkey) was applied to the area of band keratopathy until the calcium impaction dissolved. Superficial keratectomy was then performed using a 15-0 Bard–Parker blade [9]. For EDTA chelation with superficial keratectomy and AMT, following EDTA chelation and superficial keratectomy, the AMT covering was applied using an inlay or overlay technique depending on the patient's clinical condition. Inlay grafts were cut to fit the size of the keratectomy area [10]. The grafts were placed with the epithelial basement membrane side up and were secured to the edge of the defect using interrupted 10-0 nylon sutures (Visionary Medical Supplies, Inc., Madison, Wisconsin, USA). Overlay grafts, approximately 12–14 mm in diameter, were applied to cover the entire corneal, limbal, and perilimbal surfaces. The overlay AMT was placed with the epithelial basement membrane side up and were secured to the surrounding conjunctiva using interrupted sutures [11].

Postoperatively, topical moxifloxacin (0.5%) + dexamethasone (0.1%) combination eye drops (Moxidexa®, Abdi Ibrahim Pharmaceuticals, Istanbul, Turkey), preservative-free artificial tears (Novaqua 1.4% + 0.6% single-dose eye drops, Deva, Istanbul, Turkey), and topical cyclosporine A 0.05% eye drops (Depores single-dose eye drops, Deva) were administered and adjusted in subsequent follow-ups, using an individualized approach.

Statistical analyses were performed using SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as mean (standard deviation [SD]) or frequency (percentage). The Shapiro–Wilk test was used to assess the normality of data distribution, and the paired samples *t*-test was used to compare the baseline and final BCDVA. A *P*-value < 0.05 indicated statistical significance.

RESULTS

A total of 32 eyes of 29 patients, with 3 (10.3%) patients having bilateral and 26 (89.7%) having unilateral treatment-requiring band keratopathy, were included. The mean (SD) (range) age was 39.4 (22.4) (2–74) years, and participants included 12 men (41.4%) and 17 women (58.6%) (Table 1). Tables 1 and 2 summarize the clinical and demographic characteristics of the study participants and the underlying causes of band keratopathy, respectively.

The most common secondary cause of band keratopathy was previous vitreoretinal surgery with silicone oil tamponade (n = 5 eyes, 15.6%), and 6 eyes (18.8%) had idiopathic band keratopathy (Table 2). Systemic comorbidities were present in 8 (27.6%) patients, consisting of hypertension, diabetes mellitus, epilepsy, coronary artery disease, Behcet's disease, and juvenile idiopathic arthritis (Table 1); however, no participant had a systemic disease associated with hypercalcemia. Two of the 3 patients with bilateral involvement had chronic uveitis secondary to systemic rheumatological disease (Behcet's disease and juvenile idiopathic arthritis). Both patients received systemic methotrexate therapy (Metoart Con; Kocak Farma Drug and Chemical Industry, A.S., Istanbul, Turkey).

The mean (SD) (range) follow-up duration was 5.6 (4.0) (1–12) years (Table 1), and no serious postoperative complications were documented. Mean (SD) (range) baseline and final BCDVAs were 1.98 (1.0) (0.3–3.2) and 1.7 (1.0) (0.3–3.2) logMAR, respectively (Table 1) (P = 0.576). Combined EDTA chelation and superficial keratectomy was performed in 28 (87.5%) eyes, while combined EDTA chelation and superficial keratectomy with AMT (2 with inlay and 2 with overlay techniques) was performed in 4 (12.5%) eyes (Table 1 and Figure 1). Recurrence was observed in 12 (37.5%) eyes (Table 1) within a mean (SD) (range) follow-up of 9.4 (9.1) (1–32) months. Seven of the 12 eyes with recurrence underwent re-EDTA chelation combined with superficial keratectomy and AMT; however, the other 5 patients abandoned further intervention and were managed conservatively because of systemic comorbidities or poor visual prognosis. In these cases, treatment was followed with symptomatic supportive treatment using preservative-free artificial tears and topical 0.05% cyclosporine A at an individualized frequency based on the patient's clinical features at each follow-up.

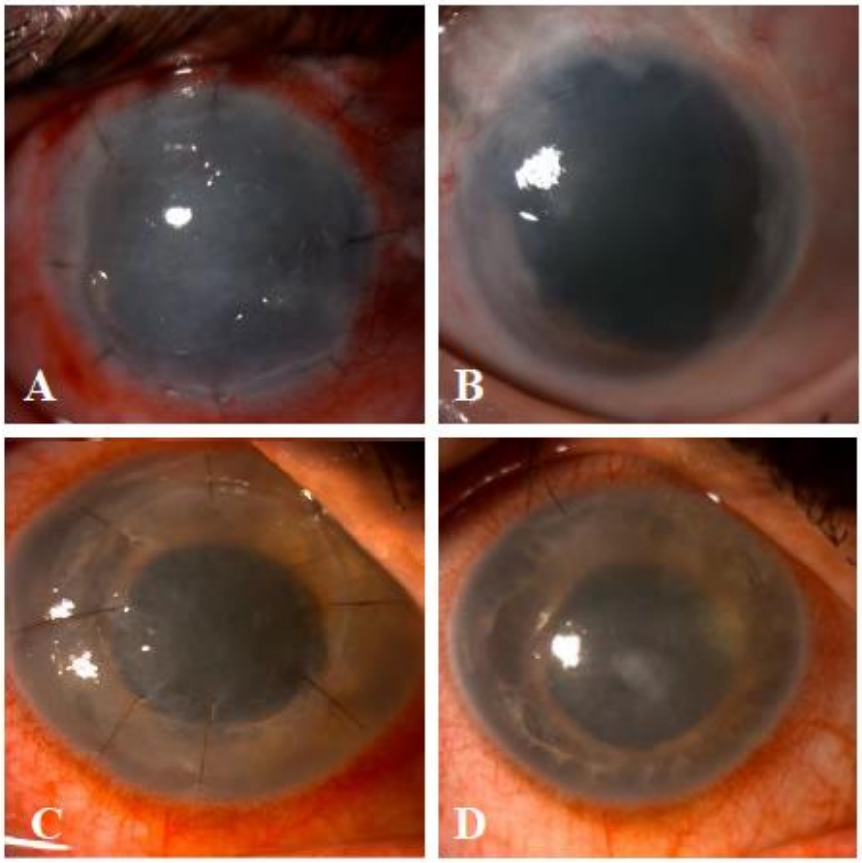

Figure 1. Early (A) and late (B) postoperative anterior segment photographs of the right eye of a 65-year-old man with band keratopathy secondary to an alkaline chemical burn who underwent ethylenediaminetetraacetic acid (EDTA) chelation (0.125 M) (Ataman Chemicals, Istanbul, Turkey) with superficial keratectomy and amniotic membrane transplantation secured using 8 interrupted 10-0 nylon sutures (Visionary Medical Supplies Inc., Madison, Wisconsin, USA) at (A) 1 week and (B) 2 months after intervention. Early (C) and late (D) postoperative anterior segment photographs of the right eye of a 36-year-old woman with band keratopathy secondary to vitreoretinal surgery with silicone oil tamponade who underwent EDTA chelation with superficial keratectomy and amniotic membrane transplantation secured with 8 interrupted 10-0 nylon sutures at (C) 1 week and (D) 2 months after intervention.

Table 1. Clinical and demographic characteristics of study participants

Variable	Value
Age (y), Mean ± SD (Range)	39.4 ± 22.4 (2 to 74)
Sex (Male / Female), n (%)	12 (41.4) / 17 (58.6)
Laterality (Monocular / Binocular), n (%)	26 (89.7) / 3 (10.3)
Nationality (Turkish), n (%)	29 (100)
Previous ocular history	
Medical causes, n (%)	15 (46.9)
Surgical causes, n (%)	11 (34.4)
Idiopathic, n (%)	6 (18.8)
Systemic comorbidities	
Diabetes mellitus, n (%)	2 (6.9)
Hypertension, n (%)	2 (6.9)
Coronary artery disease, n (%)	1 (3.4)
Epilepsy, n (%)	1 (3.4)
Behcet's disease	1 (3.4)
Juvenile idiopathic arthritis, n (%)	1 (3.4)
None, n (%)	21 (72.4)
Mean BCDVA at presentation (logMAR), Mean ± SD (Range)	1.98 ± 1.00 (0.3 to 3.2)
Mean BCDVA at final follow up (logMAR), Mean ± SD (Range)	1.70 ± 1.00 (0.3 to 3.2)
Type of intervention	
EDTA chelation + superficial keratectomy, n (%)	28 (87.5)
EDTA chelation + superficial keratectomy + AMT, n (%)	4 (12.5)
Follow up duration (y), Mean ± SD (Range)	5.6 ± 4.0 (1 to 12)
Recurrence rate (Yes / No), n (%)	12 (37.5) / 20 (62.5)

Abbreviations: y, years; SD, standard deviation; n, number; %, percentage; BCDVA, best-corrected distance visual acuity; logMAR, logarithm of the minimum angle of resolution; EDTA, ethylenediaminetetraacetic acid; AMT, amniotic membrane transplantation.

Table 2. Causes of band keratopathy in study participants

Etiology	n (%)
Vitreoretinal surgery with silicone oil tamponade	5 (15.6)
Pseudophakic bullous keratopathy	4 (12.5)
Penetrating eye injury	3 (9.4)
Congenital glaucoma	3 (9.4)
Non-infectious anterior uveitis	2 (6.3)
Non-infectious panuveitis	2 (6.3)
Aphakic glaucoma	2 (6.3)
Corneal alkaline-chemical injury	2 (6.3)
Exogenous bacterial endophthalmitis	1 (3.1)
Vernal keratoconjunctivitis	1 (3.1)
Bacterial keratitis	1 (3.1)
Idiopathic	6 (18.8)
Total	32 (100.0)

Abbreviations: n, number of eyes; %, percentage.

DISCUSSION

In a review spanning one decade, we included 32 eyes of 29 patients requiring treatment for band keratopathy at a single tertiary referral center. The mean (SD) age was 39.4 (22.4) years, and most patients were female with unilateral involvement. The most common secondary cause was prior vitreoretinal surgery with silicone oil tamponade (15.6%); however, most cases were idiopathic (18.8%). Systemic comorbidities were present in 8 patients (27.6%). Despite uneventful surgical interventions, the final BCDVA did not differ significantly from the baseline value at a mean (SD) follow-up of 5.6 (4.0) years. Recurrence was observed in 12 (37.5%) eyes within a mean (SD) follow-up duration of 9.4 (9.1) months, and 7 of these underwent retreatment.

In a prior decade-long retrospective case series conducted at Wills Eye Hospital, Philadelphia, PA, USA [12], the most common cause of band keratopathy was chronic corneal edema (28%), followed by idiopathic (25.9%). All eyes were treated using EDTA chelation. Most patients experienced 2 or more lines of statistically significant improvement in visual acuity at 1 month (33.3%) or at the last follow-up (35.2%). The recurrence rate was 17.8% during a mean (range) time of 17.7 (1–26) years [12]. We retrospectively reviewed the clinical profiles of eyes with treatment-requiring band keratopathy over a similar 10-year period and found that idiopathic cases were the most common (18.8%), followed by secondary cases after silicone oil tamponade [13] and posterior vitrectomy (15.6%). In contrast to the findings of Najjar et al. [12], corneal edema secondary to bullous keratopathy accounted for only 12.5% of our cases and was the third most common cause.

Overall, during a shorter mean follow-up time (5.6 years), we did not detect a significant improvement in BCDVA of treated eyes, while Najjar et al. [12] documented a significant improvement during a longer mean follow-up time of 17.7 years [12]. The observed disparity between the outcomes of our series and those of Najjar et al. [12] could be due to differences in inclusion criteria, underlying etiologies, follow-up durations, or the combined treatment procedures used in the current study; however, other undetermined causes are possible.

In a large-scale study of patients from a multi-tier ophthalmology hospital network in India, Das et al. [14] found that most patients were male (62.87%) with unilateral involvement [14]. During a similar time interval, most patients in our series were female (58.6%) with unilateral lesions (89.7%). This observed discrepancy in the sex ratio may be due to our inclusion of only the treatment-requiring cases, whereas Das et al. included all cases with a diagnosis of band keratopathy [14]. As in our study, the most common ocular comorbidity was prior vitreoretinal surgery (20.55%) [14], which was present in (15.6%) in our series. Similarly, the most common intervention was EDTA chelation [14], which we applied in all cases requiring treatment. Das et al. documented the socioeconomic status of participants and found that most participants belonged to higher socioeconomic strata from urban geography [14]. However, we did not record these further characteristics of our participants; thus, comparison between studies in this context is impractical.

Only 8 patients in our series (27.6%) had systemic comorbidities, including hypertension, diabetes mellitus, coronary artery disease, epilepsy, Behcet's disease, and juvenile idiopathic arthritis, yet most had no systemic comorbidities (72.4%). Two of the 3 patients with bilateral band keratopathy secondary to chronic uveitis had systemic comorbidities (Behcet's disease and juvenile idiopathic arthritis). However, we encountered no cases of band keratopathy secondary to hypercalcemia-related diseases such as hyperparathyroidism, sarcoidosis, or renal disease [15, 16]. Das et al. [14] found that the most common systemic comorbidity was hypertension (4.98%), followed by diabetes mellitus (3.77%), arthritis (0.72%), coronary heart disease (0.67%), and renal disease (0.26%). Similarly, they reported no cases of band keratopathy secondary to hyperparathyroidism or sarcoidosis [14].

Bilateral band keratopathy mostly results from an underlying systemic disease [2]. We detected bilateral band keratopathy in 10.3% of our series, and the patients with bilateral involvement had systemic comorbidities. In contrast, the most common cause of bilateral band keratopathy, which accounted for 24% of patients in the study of Najjar et al. [12], was idiopathic (43%), followed by chronic corneal edema (21.4%), uveitis (12.5%), and chronic renal failure (7.1%). They detected hypercalcemia (1.7% of patients) along with other secondary causes [12]; however, we encountered no cases of hypercalcemia-related band keratopathy.

Idiopathic band keratopathy accounted for the highest number of cases in our series, whereby 18.8% had no underlying ocular or systemic comorbidities. We did not encounter any serious postoperative complications in eyes treated with combined EDTA and superficial keratectomy, with or without AMT. However, 37.5% of patients experienced recurrence during a mean follow-up of 9.4 months. We retreated 58.3% of eyes with recurrent band keratopathy using combined EDTA chelation and superficial keratectomy; however, the remaining patients abandoned repeated surgical interventions and were treated conservatively in view of low visual prognosis, poor general condition, or associated comorbidities. In a 6-year retrospective review of patients with symptomatic band keratopathy treated with EDTA chelation, Al-Hity et al. [17] found that idiopathic cases (36.6%) were the most common. They found that EDTA chelation was a safe and effective treatment modality with an overall retreatment rate of 4.5% [17].

Although EDTA chelation is a safe and cost-effective modality [1], combined treatment with EDTA chelation and AMT can accelerate epithelial healing and reduce postoperative discomfort when managing band keratopathy [1, 18]. Phototherapeutic keratectomy is another effective combined treatment modality for band keratopathy [19-21]. We managed all cases with EDTA chelation combined with superficial keratectomy with or without AMT, which was uneventful. However, EDTA chelation combined with phototherapeutic keratectomy was not used in our study.

This series presents the treatment outcomes of corneal degenerative disease in a tertiary referral center over the last decade, supporting the safety of combined EDTA chelation and superficial keratectomy with or without AMT in managing treatment-requiring band keratopathy. However, as this was a retrospective case series, the generalizability of our results is limited. Using paraclinical investigations along with clinical assessment could further validate the working diagnosis and outcomes; however, we failed to apply methods such as anterior segment optical coherence tomography before and after treatment. Given the scarcity of data on this topic from our region, a future multicenter national study addressing these limitations could provide a real perspective on the magnitude of the problem, precise association with systemic disease, and safety and efficacy of available combined treatment modalities in managing this debilitating corneal degenerative disease.

CONCLUSIONS

Our findings show that treatment-requiring band keratopathy commonly affects female individuals and is unilateral. In the present study, idiopathic band keratopathy had the highest frequency. Systemic comorbidities were detected in approximately one-third of cases. Managing band keratopathy using a combination of EDTA chelation and superficial keratectomy with or without AMT could be a potential treatment modality. Further large-scale studies could provide robust conclusions regarding the efficacy and safety of this management approach.

ETHICAL DECLARATIONS

Ethical approval: The study was approved by the Ege University Institutional Ethics Review Board and was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients or their legal guardians.
Conflict of interest: None.

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