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Overview of sclerocornea

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Abstract:

Sclerocornea is a rare non-progressive, non-inflammatory usually bilateral congenital corneal opacity that can be associated with both ocular and systemic abnormalities. It could be inherited in 50% of cases. Ill-defined limbal architecture and vascularization in association with ocular comorbidities results in poor outcomes with corneal transplantation. This narrative review summarizes the current literature on etiology and clinical presentation in sclerocornea. With regards to keratoplasty, it focusses on key elements in decision making, highlights the role of investigations and discusses practical surgical pearls to enhance outcome of keratoplasty in these eyes.

Keywords:

Cornea plana, investigations, penetrating keratoplasty, sclerocornea, systemic associations

Introduction

Sclerocornea is a relatively uncommon cause of congenital corneal opacity and is a nonprogressive, noninflammatory disorder, in which the entire cornea (total) or a part of it acquires scleral characteristics with or without central corneal flattening.[1] Surgical outcomes with keratoplasty are considered poor due to multiple ocular comorbidities. The purpose of this review is to summarize the current literature on etiology and clinical presentation in sclerocornea, key elements in decision-making, role of investigations, and practical surgical pearls to enhance the outcomes of keratoplasty in these eyes.

Methodology

A PubMed search of the literature was undertaken in February 2023 without dates of exclusion. All papers in English related to sclerocornea were included in the study. The search terms used were sclerocornea, clinical features and associations, genetics, histopathology and penetrating keratoplasty (PK) in sclerocornea, and various combinations of these terms. This article is based on the previous literature. Informed consent was obtained for the publication of images from patients.

Clinical Features

Sclerocornea occurs bilaterally and could be asymmetric although rarely described unilaterally.[2] Clinical spectrum is wide from mild form to total opacification. The corneal involvement can be peripheral or central. In peripheral type, the affected peripheral cornea is vascularized by the superficial episcleral and conjunctival vessels with no lucid zone between the opacity and the limbus, whereas in the total type, the opacity involves the entire cornea variably[3] [Figures 1 and 2].

Sclerocornea has been classified initially into four types, as described by Waring and Rodrigues.[4]

1. Isolated peripheral sclerocornea
2. Plana sclerocornea
3. Sclerocornea associated with anterior segment alterations
4. Diffuse sclerocornea

Ocular Associations

It may be an isolated anomaly or can occur in association with other ocular conditions such as nystagmus, strabismus,

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cornea plana, horizontally oval cornea, blepharoptosis, cataract, shallow anterior chamber, anterior synechiae, posterior embryotoxon, microphthalmos, enophthalmos, congenital staphyloma and glaucoma- most common being cornea plana in 80% of cases, resulting in high hyperopia[3,5] [Figure 3]. Glaucoma associated with sclerocornea is thought to be due to goniodysgenesis related to the abnormal neural crest development.[6]

Systemic Associations

Sclerocornea can also be a part of a systemic disorder with concomitant systemic anomalies.[7] Polydactyly, craniofacial abnormalities, deformities of the ears, mental retardation, cardiovascular malformations, and genitourinary malformations are some described.[3] Syndromes that feature sclerocornea include PHACES syndrome, Dandy–Walker, Hurler, and Hallermann–Streiff syndrome.[8]

Genetics

It may be autosomal dominant or recessive in 50% of cases or sporadic, with no gender prediction.[2,3,9] When inherited, the recessive form typically demonstrates a more severe phenotype than the dominant form.[2,9,10] Associated genetic loci that have been reported include Xp22.31 when sclerocornea is present with microphthalmia and dermal aplasia as a part of the MIDAS syndrome;[11] 18q21.3 in a 12 years old child with autism, anophthalmia, microphthalmia, and sclerocornea and a mutation in the *RAX* gene,[12] and 6p22-24 in a dysmorphic infant with an interstitial deletion[13] has also been described. Binenbaum *et al*. have suggested that sclerocornea should be added to the clinical manifestations of the 22q11.2 deletion syndrome, and ophthalmologists diagnosing sclerocornea in children with systemic findings, suggestive of 22q11.2 deletion should ensure appropriate genetic referral.[1]

Embryology

It is believed to occur due to the absence of normal migration of the neural crest cells between the 7th and 10th week of gestation, resulting in failure of the formation of the limbal anlage, leading to the absence of limbus, lack of differentiation between the scleral and corneal architecture, and the development of corneal opacity and flattening.[13-15]

Histopathology

The previous studies of sclerocornea have reported a marked disorganization of stromal lamellae and collagen fibrils that are generally much larger than normal. The architecture of the anterior scleralized cornea was noted to have a disorganized stroma, vascularization, abnormal Bowman's layer, abnormal Descemet's membrane, and endothelium.[8]

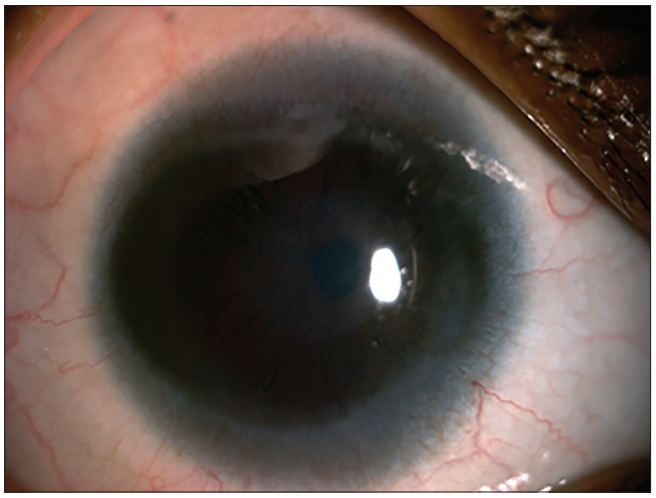

Figure 1: Slit-lamp image of sclerocornea with peripheral corneal opacification and vascularization and a central corneal haze

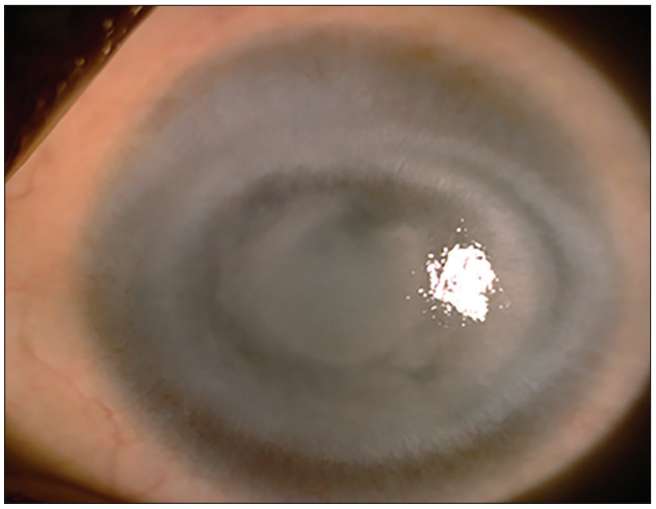

Figure 2: Slit-lamp image of sclerocornea with corneal opacity involving the entire cornea

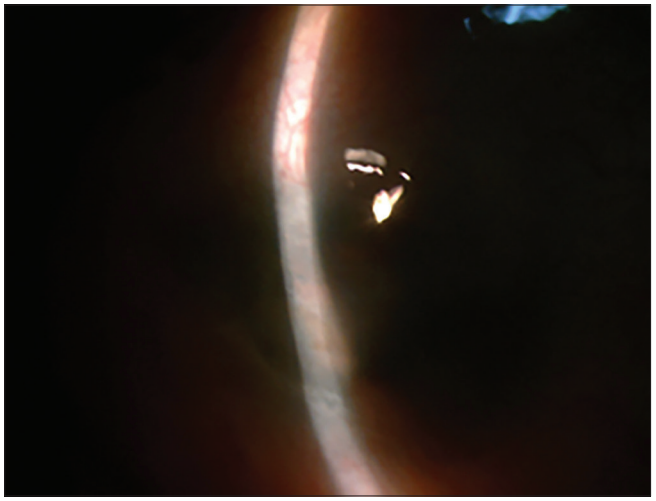

Figure 3: Slit-lamp examination (slit view) of sclerocornea showing cornea plana

However, Young *et al*. have demonstrated that sclerocornea expresses proteoglycans with keratan sulfation that resemble those in cornea, rather than those in sclera.[16] The presence of cytokeratin 3 and 12 and the absence of cytokeratin 13.19 and goblet cell mucin in MUC5AC in scleralized corneas has been demonstrated using immunoconfocal microscopy indicating that the scleralized cornea preserves the corneal phenotype rather than the conjunctival phenotype[17] [Figure 4a and b].

Approach to a Patient with Sclerocornea

Decision-making

Vision is affected depending on the degree of scleralization and the extent of central corneal involvement. Surgical outcomes in sclerocornea are usually poor due to risks associated with small-sized graft, peripheral vascularization, and glaucoma. Visual rehabilitation can be considered with refractive correction or optical iridectomy in select cases. Key elements in decision-making with respect to corneal transplantation in these eyes include age at presentation, laterality, extent of central corneal involvement, and associated ocular and systemic comorbidities. Systemic associations could make them high risk for repeated anesthesia postoperatively and should be factored in decision–making, especially in eyes with very guarded prognosis.

Preoperative concerns and role of investigations

External evaluation should include examination for anomalies, brow ptosis besides nystagmus and fixation preference as in any pediatric assessment.

A comprehensive evaluation is recommended under general anesthesia in children and should include the use of handheld slit lamp besides other investigations detailed below.

Laterality

Considering the guarded prognosis with PK in these eyes, it may be prudent to defer keratoplasty in unilateral cases, especially with ocular comorbidities. However, as these are quite often bilateral, PK may need to be considered, especially when central cornea is significantly involved.

Corneal evaluation

Sclerocornea can be associated with a normal corneal diameter or microcornea. Clinically, it is difficult to discern the exact location of the limbus. Corneal diameter can be assessed using anterior segment optical coherence tomography (ASOCT). Examination should include the assessment of type and extent of corneal involvement. Cornea plana associated central corneal flattening and depth of corneal involvement, which is usually full thickness, can also be estimated with ASOCT [Figure 5].

Limbal architecture

The limbal architecture is usually ill-defined and seldom, limbal palisades can be seen. Extent of vascularization should be assessed.

Anterior segment evaluation

ASOCT/ultrasound biomicroscopy helps in providing the structural details of the anterior chamber structures, angle, depth of the anterior chamber, presence and extent of peripheral synechiae and of lens status, and aids in complementing clinical diagnosis [Figure 6].

Clinically, while both sclerocornea and Peters share the some common features of anterior segment dysgenesis including anterior synechiae, posterior embryotoxon, prominent iris processes, or congenital glaucoma, central corneal involvement with clear periphery is usually a feature of Peters, whereas peripheral corneal scleralization with vascularization with or without central involvement is a feature of sclerocornea.[18]

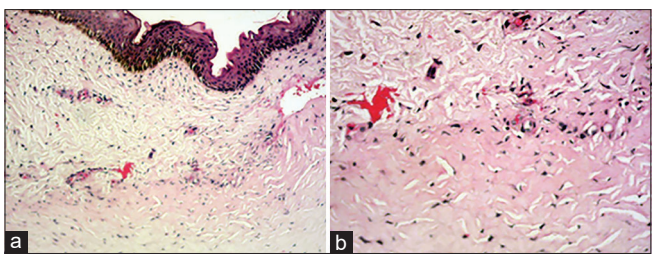

Figure 4: (a) Microphotograph of the corneal button showing multilayered stratified squamous epithelium, loss of Bowman's membrane along with thick collagen fibers with scattered fibroblasts, below corneal collagen fibers. (×100, H and E), (b) Microphotograph in higher magnification of scleral collagen fibers with scattered fibrocytes and vascular channels (×300, H and E)

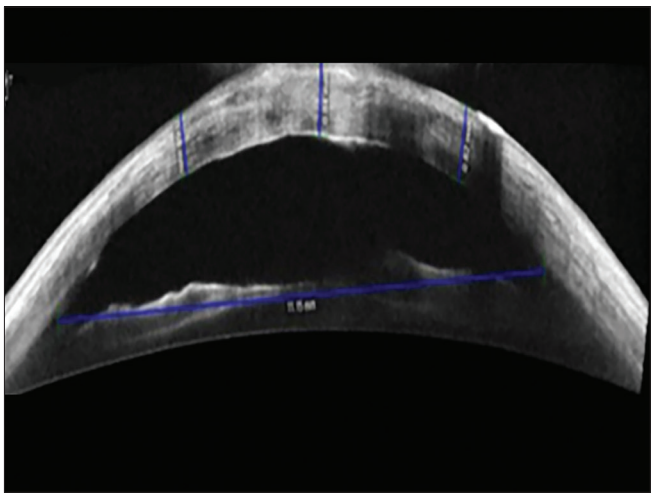

Figure 5: Anterior segment optical coherence tomography image of sclerocornea to estimate corneal diameter and demonstrating increased corneal thickness

Intraocular pressure estimation

Glaucoma in sclerocornea could be congenital/developmental following anterior segment dysgenesis. Central flattening and shallow chambers are attributed to further increase the risk of glaucoma. Corneal scarring and flattening can influence the measurement of intraocular pressure (IOP) in these eyes. Hence, a combination of methods including applanation tonometer and digital IOP estimation can be considered. Tonopen can aid in better clinical judgment as its measurement is independent of the corneal thickness.

Ultrasound

Sclerocornea can be associated with microphthalmos and congenital staphyloma, and hence in patients with central corneal involvement with limited visualization, ultrasound should be considered to determine both axial length and retinal status.

Intraoperative factors

Most of the intraoperative risks are common in all pediatric cases and result from increased elasticity of the cornea and sclera in infants, shallow anterior chamber, anterior displacement of lens-iris diaphragm, smaller size of the eye, and increased postoperative fibrin.

Careful peritomy and dissection of the conjunctiva over cornea must be done to preserve the limited limbal stem cell reserve. Conjunctiva must be retracted for adequate limbal exposure, and this enables to determine graft size also [Figure 7]. Smaller size graft is preferred in view of the peripheral vascularization. Careful trephining should be done, especially in patients with associated cornea plana.

Postoperative concerns

In sclerocornea, following PK, the risks of persistent epithelial defect and resultant graft melt are higher due to limited limbal reserve. Hence, it is recommended that the reflected conjunctiva is reposited back atraumatically to preserve it [Figure 8]. Amniotic membrane can aid in epithelial healing, especially in the early postoperative period. Postoperative care should include periodic IOP monitoring besides graft clarity.

Discussion and Review of Literature

Sensory deprivation especially in sclerocornea with central corneal involvement and in bilateral cases can be severe and hence the need for early intervention in these eyes. In patients with peripheral sclerocornea with minimal central corneal involvement, visual rehabilitation with refractive correction or optical iridectomy based on the density and extent of central corneal involvement should be considered keeping in mind the guarded outcomes with PK in these eyes due to glaucoma and peripheral corneal vascularization,

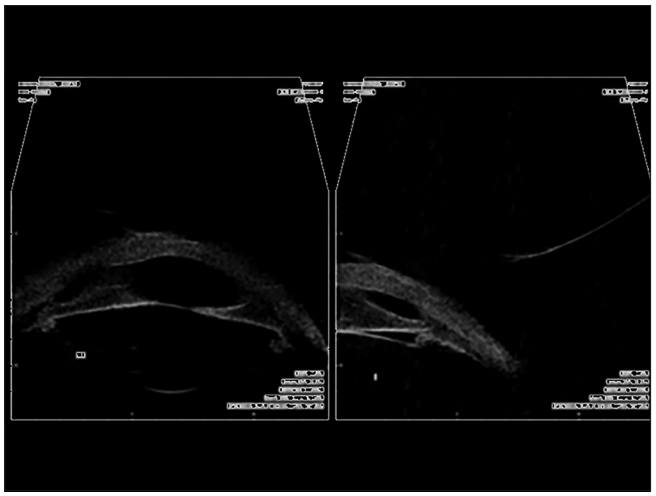

Figure 6: Ultrasound biomicroscopy image of sclerocornea showing thickened cornea, shallow anterior chamber, and peripheral anterior synechiae

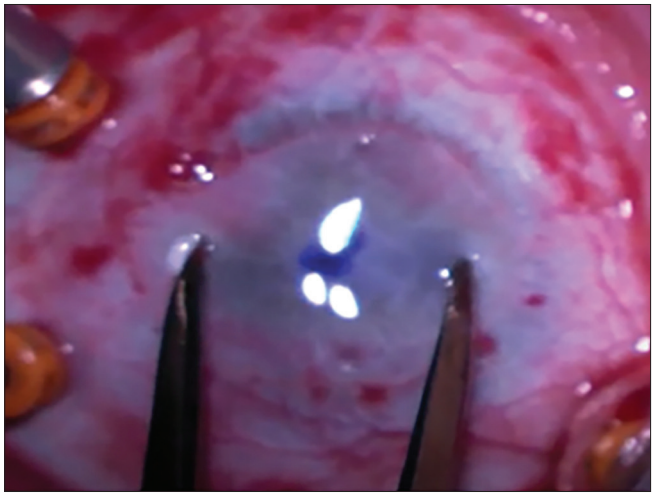

Figure 7: Intraoperative image showing the retraction of the conjunctiva for adequate limbal visualization and sizing of the graft

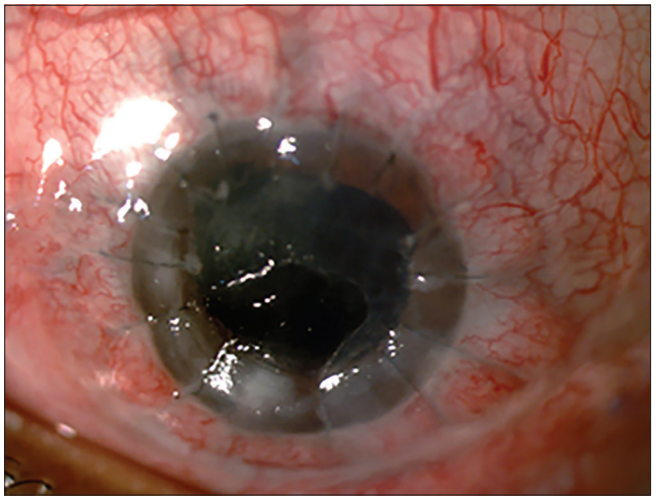

Figure 8: Postoperative image of a patient with sclerocornea who underwent penetrating keratoplasty showing persistent epithelial defect

resulting in graft rejection. Michaeli *et al*. noted that, while the overall success rate for graft clarity was 78% for children undergoing transplants for congenitally opaque corneas, sclerocornea and congenital glaucoma carried only a 50% chance of success, with repeated transplants needed for many eyes.[7] Frueh and Brown reported an overall success of 70% following PK in eyes with sclerocornea. They also described an operative technique of recessing conjunctiva 2–3 mm from the limbus and removing the subconjunctival tissue so that the conjunctiva remained recessed without sutures.[19] Rezende *et al*. reported limited success with failure of six of the eight grafts done for sclerocornea.[20] Young *et al*. compared outcomes of PK in patients 5 years or younger in Peters versus sclerocornea and found that the survival time and rate were significantly better in Peters and attributed this to the presence of opacity or vascularization at the limbus and in the peripheral cornea. Smaller diameter of recipient cornea was correlated significantly with graft failure.[16] They have suggested that the frequent use of topical steroids or a combination of systemic steroids or immunosuppressive might help in graft survival. Ho *et al*. described a successful 6-year outcome in a 12-year-old boy with sclerocornea and PHACES syndrome, highlighting the importance of preservation of the limbus intraoperatively by careful lamellar dissection and posterior recession of inferior limbus to minimize vascularization, thereby achieving a stable postoperative surface.[8]

Conclusion

Corneal transplants in sclerocornea carry a high risk of rejection. Pediatric age and coincident ocular factors including vascularization, altered limbal architecture, small graft size, and glaucoma are some important factors attributed to the guarded prognosis. The presence of systemic abnormalities could increase the risks with repeated anesthesia. However, despite these limitations, corneal transplants have to be performed in select cases, especially in patients with bilateral significant involvement of the visual axis. Genetic counseling is recommended as a part of evaluation. Despite careful planning, meticulous surgery, and close follow-ups, outcomes could be guarded.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her/his consent for her/his images and other clinical information to be reported in the journal. The patient understands that her/his name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Nil.

Conflicts of interest

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

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