Bilateral Corneal Ghost Vessels in an Otherwise Healthy Child

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We report a rare case of bilateral corneal ghost vessels in a 6-year-old child with an unremarkable past ocular and past medical history. This study was a single observational case report. A 6-year-old girl was referred to our clinic for further evaluation, due to suboptimal visual acuity in both eyes. Her past medical and ocular history revealed no systemic, inflammatory, infectious, or degenerative disorders. Slit-lamp examination revealed regressed blood vessels (“ghost vessels”) in the anterior and mid-corneal stroma as the only pathologic finding. Confocal scanning microscopy of both corneas demonstrated scattered branching railroad-shaped ghost vessels at the level of the middle and anterior stroma. Complete systemic workup was performed for the patient. No identifiable risk factor for the development of corneal vascularization was found. According to our findings, we assume that in our patient, vasculogenesis occurred due to angioblast invasion to the presumptive cornea due to disequilibrium in mechanisms involved in vascular patterning during embryonic development.

ABSTRACT

We report a rare case of bilateral corneal ghost vessels in a 6-year-old child with an unremarkable past ocular and past medical history. This study was a single observational case report. A 6-year-old girl was referred to our clinic for further evaluation, due to suboptimal visual acuity in both eyes. Her past medical and ocular history revealed no systemic, inflammatory, infectious, or degenerative disorders. Slit-lamp examination revealed regressed blood vessels (“ghost vessels”) in the anterior and mid-corneal stroma as the only pathologic finding. Confocal scanning microscopy of both corneas demonstrated scattered branching railroad-shaped ghost vessels at the level of the middle and anterior stroma. Complete systemic workup was performed for the patient. No identifiable risk factor for the development of corneal vascularization was found. According to our findings, we assume that in our patient, vasculogenesis occurred due to angioblast invasion to the presumptive cornea due to disequilibrium in mechanisms involved in vascular patterning during embryonic development.

Introduction

The cornea is completely avascular and Corneal Neovascularization (CNV) is always considered a pathologic condition [1]. The etiology of CNV is not completely understood and a wide range of inflammatory, infectious, degenerative, conditions may induce CNV [2]. Two possibly fundamental mechanisms may play a role in the development of neovascularization of the cornea: vasculogenesis (the de novo formation of new blood vessels by differentiation of circulating bone marrow-derived mesodermal precursors, largely during embryogenesis), and angiogenesis (the formation of new blood vessels from sprouting or splitting of preexisting vasculature). These two aforementioned mechanisms may have overlap with each other [3]. Herein, we report an interesting case of the bilateral and almost symmetric pattern of regressed deep corneal stromal neovascularization in a 6-year-old girl with...
A 6-year-old girl who was referred to the ophthalmologist due to suboptimal visual acuity in her pre-school screening program was presented to the cornea service for further evaluation. The best-corrected visual acuity was 20/40 in both eyes. Slit-lamp examination revealed regressed blood vessels (“ghost vessels”) in the anterior and mid-corneal stroma. Some lumens were large and carried a few red blood cells in the peripheral of the cornea, anterior to the limbus in both eyes (Figure 1). There was no corneal opacity, and corneal thickness was within the normal range in both eyes. Other examinations of anterior and posterior segments were normal. Confocal scanning microscopy of both corneas demonstrated scattered branching railroad-shaped ghost vessels at the level of the middle and anterior stroma. Endothelium, posterior stroma, and epithelium were unremarkable (Figure 2). She was born full-term, with normal vaginal delivery and normal developmental milestones. Her mother’s obstetric history was unremarkable. Full systemic workup revealed no systemic, inflammatory, infectious, or degenerative disorders.

**Discussion**

Corneal avascularity is required for the preservation of corneal transparency and vision clarity [4]. CNV may occur due to disrupted balance between angiogenic and antiangiogenic factors, which may cause invasion of new vascular structures into the cornea from the limbus that can lead to corneal scarring, lipid deposition, and inflammation that may significantly alter visual acuity [5, 6].

Several inflammatory (such as keratoconjunctivitis, stevens-johnson syndrome, etc.), infectious (herpes simplex, herpes zoster, etc.), degenerative (pterygium, Terrien’s marginal degeneration, aniridia, etc.), and traumatic-iatrogenic disorders (contact lens, stem cell deficiency, etc.) are associated with CNV and the aforementioned balance may tilt towards angiogenesis [2].

The cornea remains avascular despite the formation of large arteries and vascular networks in the periocu-
lar region during the embryonic developmental period. After taking an extensive history and examination, we discovered that this patient had an unremarkable past medical history of certain risk factors, such as inflammatory and infectious diseases after her birth. We assume that any insult during pregnancy may be involved in the formation of CNV in our patient through exacerbation of vasculogenesis processes.

Previous experimental studies have identified potential pro- and anti-angiogenic factors in the anterior eye of the developing avian embryos that may play a role in ocular vasculogenesis and corneal avascularity during embryonic development for the first time. Angiogenesis occurs when a disequilibrium between proangiogenic and antiangiogenic factors stimuli results in an up-regulation of proangiogenic factors, such as VEGF-A (Vascular Endothelial Growth Factor), FGF1 (Fibroblast Growth Factor 1), and FGF2 (Fibroblast Growth Factor 2), and a down-regulation in antiangiogenic agents, such as Sema3E (Semaphorin 3E), Sema3G (Semaphorin 3G), Netrin1, Netrin4, and sFlt1 (soluble fms-like tyrosine kinase 1) [3].

To determine when corneal avascularity is established, Kwiatkowski et al. visualized the vascular patterning of the anterior eye using transgenic quail embryos. On an embryonic day 3, angioblasts and primitive blood vessels are present in the periocular region but prevented from the formation of tubular temporal and nasal ciliary arteries and a “vascular ring” around the cornea periphery [4]. By embryonic day 10 angioblasts form a stream of blood vessels that approaches the limbus region and connects to the conjunctival vasculature to form the limbal vasculature. The angiostatic function of the limbus has been proposed as a mechanism for corneal avascularity [6, 7].

Although the interaction between these factors in the cornea is not completely understood, soluble VEGF receptor-1 (sVEGFR1; also known as sFlt-1), which sequesters VEGF-A, is suggested as a key modulator inhibiting VEGF-driven angiogenesis [8].

In addition, as noted by McKenna et al., loss of Nrp1/ Sema signaling in the presence of functional Nrp1/VEGF signaling results in angioblast invasion to the presumptive cornea and subsequent vascularization of the developing cornea, which induces mechanisms involved in vascular patterning during embryonic development [9].

There is no physical barrier between the periocular mesenchyme and presumptive cornea. Thus, we attributed the corneal vascularization in the present case to an intrauterine insult such as transient exposure to toxic materials, hypoxia, or inflammation during pregnancy with consequent destruction of the balance between pro-angiogenic and anti-angiogenic factors, resulting in the attraction of angioblasts into the developing cornea in the present case, which was regressed after elimination of the inciting mechanism.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Conflict of interest

The authors declared no conflict of interest.

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