Chapter 7

Ophthalmic Manifestations

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Introduction

Ophthalmic manifestations have been reported in approximately 40% of individuals with dyskeratosis congenita (DC) [1, 2]. Most studies of eye-related complications have been reported in individuals with classic DC, Revesz syndrome, Hoyeraal-Hreidarsson syndrome (HH), or Coats plus. Some of these complications have also been reported in individuals with Telomere Biology Disorders (TBDs), in general, but quantitative data are limited. Ophthalmic complications can be divided into changes affecting the anterior segment and adnexa (eyelids, eye lashes and lacrimal [tear duct] system) and those affecting the retina.

Anterior Segment and Adnexa

Changes to the anterior segment and adnexa include punctal atresia and nasolacrimal duct obstruction, trichiasis (mis-directed eyelashes), loss of eyelashes, entropion (in-turning of the eyelids and eyelashes), ectropion (out-turning of the eyelids and eyelashes), conjunctivitis (infection of the conjunctiva), corneal scarring, corneal ulceration (erosion of the outer surface of the eye) and perforation, and cataracts [1, 3-9].

The most common finding in individuals with TBDs is obliteration of the lacrimal drainage system, which can present with either absent punctae or nasolacrimal duct obstruction. The individual might experience constant tearing, frequent episodes of conjunctivitis, episodes of blepharitis (inflammation of the eyelids), or corneal ulcers. Treatment of tear flow obstruction is surgical, by either dacryocystorhinostomy (DCR), whereby an opening is created between the lacrimal sac and the nasal cavity, or by insertion of Jones tubes, glass implants placed to allow direct drainage from the conjunctival fornix into the nose.

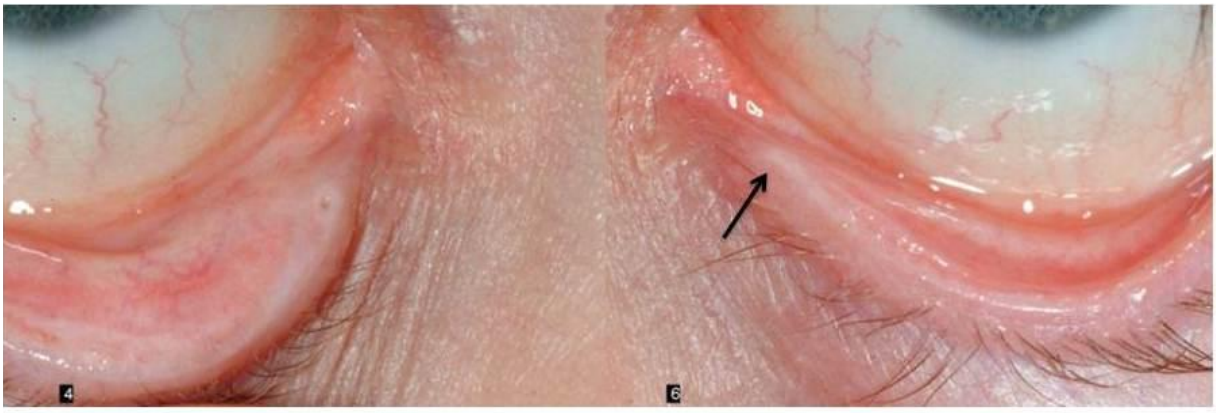

Figure 1. Photograph of a patient with dyskeratosis congenita demonstrating an absent punctum in the left eye (arrow).

Entropion, ectropion, and trichiasis may be secondary to epithelial abnormalities of the skin and mucous membranes of the eye, and can lead to recurrent blepharitis,

conjunctivitis, keratitis, corneal scarring, and eventually to decreased vision if untreated. Entropion and ectropion can be surgically repaired, and misdirected eyelashes seen in trichiasis can be either temporarily or permanently removed. Early recognition of these potentially significant complications of TBDs leads to optimal management and outcomes.

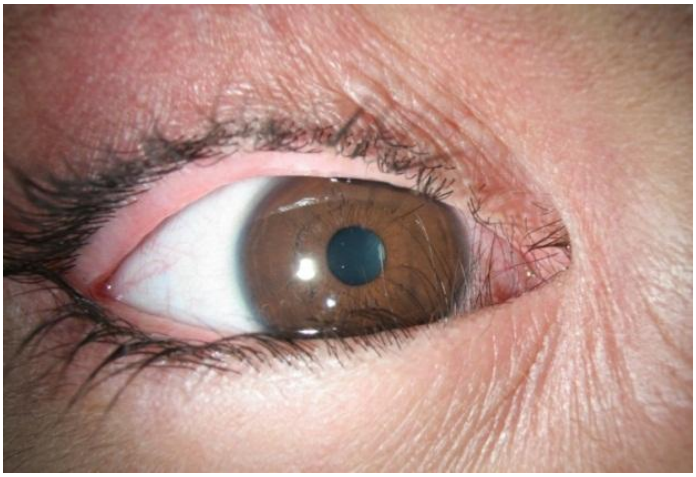

Figure 2. Entropion and trichiasis in an individual with dyskeratosis congenita.

Posterior Segment

Optic nerve atrophy [3, 10, 11] and retinal vascular changes have been described in patients with DC/TBDs. Retinal changes can include hemorrhages, areas of non-perfusion, retinal neovascularization, exudative retinopathy, and retinal detachment [2, 9, 10, 12-20] These changes require early recognition and management to avoid the potentially devastating complication of vision loss if untreated. Fluorescein angiography, ideally widefield, is indicated if any significant vascular abnormalities are identified during the retinal exam of a patient with DC/TBD. Treatment may include laser photocoagulation, or vitreoretinal surgery in advanced cases.

Two clinical variants of TBDs are associated with a greater risk of retinal abnormalities. Individuals with Revesz Syndrome develop exudative retinopathy, in addition to aplastic

anemia and central nervous system abnormalities [17-19]. Individuals with HH can also display an increased frequency of retinal neovascularization. However, the prevalence of retinopathy is likely underappreciated. Widefield fluorescein angiography on individuals with DC/TBDs has shown that the vast majority of individuals will likely harbor retinal vascular alterations [21].

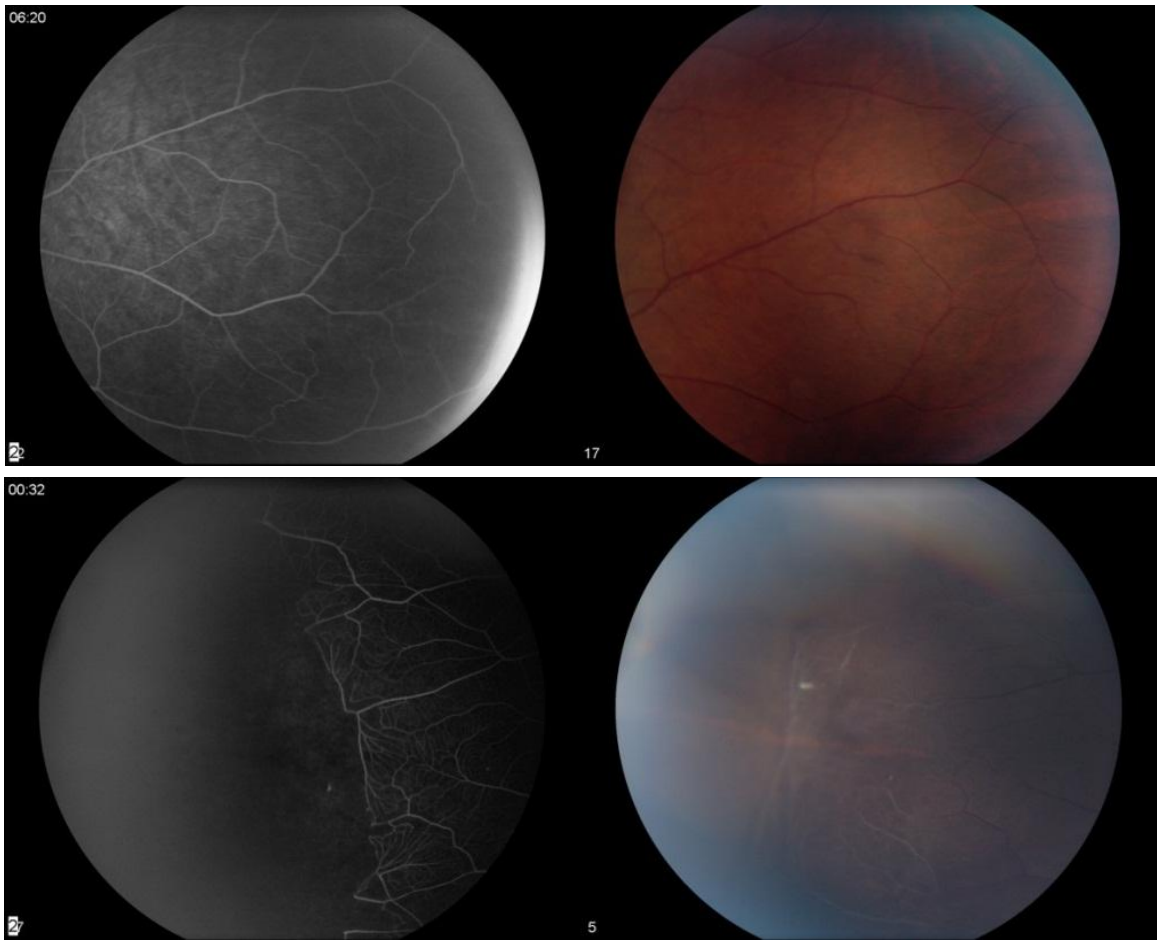

Figure 3. Fluorescein angiography (top left) and fundus photograph (top right) of normal retina. Fluorescein angiography (bottom left) and fundus photograph (bottom right) of a patient with dyskeratosis congenita, demonstrating sclerotic vasculature and non-perfusion.

Additional Complications

In addition to the syndrome-specific manifestations of TBDs, side effects of treatment required for other TBD-associated manifestations can result in other ocular complications. Therapeutic radiation can cause radiation retinopathy, and systemic corticosteroid therapy associated with hematopoietic cell transplantation (HCT) may cause glaucoma or cataract. Patients undergoing HCT require a detailed eye examination and follow-up monitoring to identify potential problems.

Recommendations

A baseline ophthalmic evaluation should be part of the initial evaluation of every patient with TBDs, and subsequent periodic examinations should be part of routine care.

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