

## Sight-threatening Complication of Cicatricial Ectropion in a Patient with Lamellar Ichthyosis – Case Report

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**ABSTRACT** We report a case of lamellar ichthyosis and sight-threatening complications of cicatricial ectropion in an adult male patient which was surgically managed with tectonic penetrating keratoplasty. We present a case of autosomal-recessive lamellar ichthyosis in a 47-year-old man who was referred to our outpatient eye clinic for treatment of primary keratouveitis of the right eye with keratolysis and exudation in the anterior chamber. A diagnosis of cicatricial ectropion with serious lagophthalmos was established on examination. The patient underwent tectonic penetrating keratoplasty, cataract extraction, and intra-ocular lens placement with no perioperative complications. The patient was subsequently treated with oral fluconazole 200 mg once daily for 12 days due to a positive fungal culture for *Candida albicans* and systemic oral acyclovir 250 mg 3 times per day for 12 days as prophylaxis for a labial herpetic infection. Post-operative complications included corneal rejection and nonhealing neurotropic epithelial defect of the graft. Long-term treatment with topical cyclosporine (Ikervis<sup>®</sup>) and dexamethasone led to resolution of the corneal rejection. Lubrication with artificial tears containing hyaluronic acid, perfluorohexyl octane (Evotears<sup>®</sup>), and vitamin A ointment led to symptomatic relief of dry eye disease. The patient was referred to a dermatologist and was started on systemic retinoid acitretin at a dose of 0.5 mg/kg per day. Ten months after surgery, the patient's visual acuity was 0.1 based on the Snellen chart and the corneal graft was stable. Infection in the cornea can rapidly progress to corneal melting in patients with severe cicatricial ectropion. A good patient outcome depends on the interdisciplinary approach to patient management by the ophthalmologist, dermatologist, and plastic surgeon.

**KEY WORDS:** ichthyosis, corneal perforation, ectropion, penetrating keratoplasty

### INTRODUCTION

Lamellar ichthyosis (LI) is an autosomal recessive condition characterized by hyperkeratosis and scaling. This hereditary disorder generally manifests at birth as a colloidal membrane of hyperkeratotic cells encasing the entire body of the newborn. The most

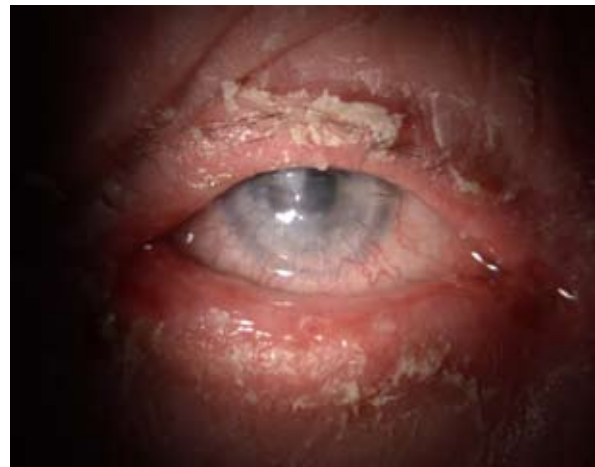
common ocular manifestations are cicatricial ectropion, dry eye disease, and exposure keratopathy (1,3-6). The goal of this article is to summarize the sight-threatening complications of cicatricial ectropion in an adult patient with progressive lamellar ichthyosis.



**Figure 1.** Clinical findings at the time of first evaluation – hyperkeratotic scales on the eyelids, mucopurulent discharge, secondary infected corneal ulcer with imminent perforation.

### CASE REPORT

A 47-year-old male patient with lamellar ichthyosis was referred to our outpatient eye clinic due to an infected corneal ulcer of the right eye, with imminent risk of perforation and inflammatory reaction of the anterior chamber (Figure 1). At the time he was not receiving any systemic therapy for his LI and was not monitored in a dermatology clinic specializing in ichthyosis syndromes. In the two weeks before presenting at our eye clinic, he was treated by an ophthalmologist for his corneal ulcer and glaucoma of the right eye. During the exam, the patient reported rapid reduction of pain and worsening of vision that occurred when he pressed on the orbit with his fingers. Physical exam showed bilateral cicatricial ectropion, lagophthalmos with positive Bell's phenomenon, severe narrowing of the palpebral fissures, and eyelids covered with hyperkeratotic skin. We observed signs of Meibomian gland dysfunction which is often found in association with evaporative dry eye disease (1). As previously noted, the right eye had a corneal ulcer with melting as well as a descemetocoele formation 8×5 mm in size, uveal prolapse, and hypopyon. Visual acuity was limited to hand motion. Corneal scrapings for bacterial and fungal cultivation were obtained. The patient underwent a three-part procedure consisting of tectonic penetrating keratoplasty, cataract extraction through phacoemulsification, and posterior chamber intraocular lens implantation under general anesthesia. There were no complications during the



**Figure 2.** The right eye after tectonic corneal transplantation – note the superficial vascularization following corneal sutures on corneal graft. Sharp scales from the eyelids can erode the corneal epithelium.

procedure. Immediately after the surgery, the patient was prescribed topical levofloxacin and dexamethasone eye drops, both 5 times per day. The patient was treated with oral fluconazole 200 mg once daily for 12 days in addition to topical natamycin eye drops due to a positive fungal culture growing *Candida albicans*. He received oral acyclovir 5 mg/kg 3 times per day for 12 days as prophylaxis for a labial herpes. Systemic corticosteroids and immunosuppressants were not used because of the risk of secondary skin infections. The patient developed corneal rejection in the early post-operative period and was treated with increased dosage of local dexamethasone eye drops as well as artificial tears containing hyaluronic acid, perfluorohexyl octane (Evotears®), and vitamin A ointment. Because of the narrowing of the palpebral fissure and stricture, the use of therapeutic contact lenses was not an option. To reduce the risk of corneal toxicity, we reduced the dose of fluoroquinolone eyedrops (2) and discontinued the use of natamycin, an antifungal drug. The patient was released from the hospital on postoperative day 12. During the patient's outpatient visit 3 days later, he mentioned injuring his cornea with an eye drop applicator. The blunt-force traumatic injury moved the temporal edge of the graft downward and caused dehiscence at the graft junction, with resulting iridocorneal adhesions. During our examination there was no leaking from the anterior chamber and the Seidel test was negative. Therefore, we did not recommend re-suturing the graft or releasing of the iridocorneal adhesions.

Two months after surgery, the patient developed neurotrophic and exposure keratopathy with persistent epithelial defect in the corneal graft, possibly



**Figure 3.** Hyperkeratotic scales on the eyelids, cicatricial ectropion, and lagophthalmos positive for Bell's phenomenon.

caused by a sharp edge on the patient's hyperkeratotic eyelid scratching the graft (Figure 2). To promote more rapid healing of the epithelium, we reduced the dose of local steroids from 5 times per day to a 3 times per day. Reduction in steroids led to acute corneal rejection; we therefore started treatment with local cyclosporine eye drops (Ikervis®) applied once a day, and gradually the rejection resolved. Corneal neovascularization developed near the host-graft interface, both superficially and in deeper tissue. Concurrently with addressing the patient's most urgent ocular complications, he was referred to a dermatologist specializing in the treatment of ichthyotic conditions. The dermatologist started the patient on retinoids; after 2 months of treatment with acitretin 0.5 mg/kg/day we observed reduction of the ectropion, the eyelid erythema, and the periocular scaling. DNA analysis confirmed the patient was heterozygous for the transglutaminase-1 (TGM-1) mutation. We then consulted a plastic surgeon who recommended autograft surgery to correct the ectropion; however, the patient repeatedly declined surgery (Figure 3). As of this writing the corneal graft is stable and partially transparent.

## DISCUSSION

The term ichthyosis covers a range of genetically transmitted disorders that affect normal keratinocyte differentiation and maturation, leading to hyperkeratosis and scaling of most if not all the patient's skin (3). The word is derived from the Greek word *ichthys*

meaning fish scales (4). The ichthyoses range in severity from mild forms such as ichthyosis vulgaris to the potential lethal form of harlequin-type ichthyosis (3). The classification of ichthyosis disorders is based on clinical findings and is divided into syndromic and non-syndromic conditions. In non-syndromic ichthyoses, the phenotypic expression of the genetic defect is confined to the skin, while other organs may be involved in syndromic ichthyoses. The range of genetic defects is broad, and mutations can be found on the X-chromosome or on the somatic chromosomes (5).

Ichthyosis vulgaris, autosomal-recessive ichthyoses, X-linked ichthyoses and keratinopathic ichthyoses are considered non-syndromic conditions or disorders. Syndromic ichthyoses include autosomal-recessive ichthyoses and X-linked ichthyoses, including the autosomal recessive, neurocutaneous Sjögren-Larsson syndrome. The genetic defect is located on chromosome 17, causing a deficiency in the fatty aldehyde dehydrogenase enzyme. Another syndromic ichthyosis is trichothiodystrophy, characterized by brittle hair due to lack of sulfur; other organs are affected in more severe cases (3).

Lamellar ichthyosis (LI) is a non-syndromic form of ichthyosis, inherited as an autosomal-recessive condition. It is detectable at birth due to the collodion membrane covering the skin surface of the newborn. Ectropion and eclabium can be present. These patients have defects in genes TGM1, NIPA, ALOX12B, and AOXE3 loci on 12p11.2-q13 genes. The disease may range from mild to severe, and treatment is not curative. LI is characterized by the presence of thick brownish to dark scales, possibly erythema and moderate to severe hypohidrosis. Other findings can include alopecia and short stature. Phenotypic expression of the disease can vary over time based on the patient's response to treatment (3).

Both syndromic and non-syndromic ichthyoses show involvement of the eyes, notably the eyelids and the cornea. The most prominent of these findings include cicatricial ectropion, with subsequent development of lagophthalmos. Lagophthalmos can lead to exposure keratopathy and development of neurotropic corneal ulcer, which can become infected and lead to sight-threatening corneal perforation (1,4,6). Other, rarer findings have been published in the literature and include posterior embryotoxon (7), megalocornea (8), and spontaneous subconjunctival abscess. Absence or dysfunction of Meibomian glands leads to evaporative dry eye disease and other injury to the corneal surface. Ectropion of the eyelid and corneal exposure can lead to keratinization of the conjunctival and corneal epithelium (1).

Treatment for eye manifestations in lamellar ichthyosis includes the use of emollients and keratolytics. The goal of management is maintenance of an intact corneal surface by use of lubricants. A moisture chamber eye patch can ease night-time lagophthalmos, and massaging the eyelids with emollients reduces the layers of keratin scales (1,6). In a study of five children with LI, tazarotene, a topical retinoid cream, was applied to the eyelids and resulted in improvement in the degree of ectropion present, with two patients showing complete resolution of the ectropion. There were no adverse reactions reported in these patients (9). Oral retinoids are used in the more severe cases (5). Acitretin can be given at doses up to 1 mg/kg/day. Singh *et al.* described the case of an infant who had complete resolution of ectropion following use of systemic acitretin (10). We have also observed the beneficial effects of acitretin on reduction of ectropion and scales on the eyelids and on resolution of epithelial defects. Plastic surgery to correct the ectropion can be done using autologous or engineered skin (11). Autologous buccal mucosa can be used when performing the surgery (12). Another option is to use inverting sutures in conjunction ectropion surgery (13).

We performed a search of the PubMed database using the search terms "corneal perforation" and "ichthyosis" and found four publications on corneal perforation in the setting of ichthyosis. The first report was by Eltutar *et al.* on patients with congenital ichthyosiform erythroderma in 1988 (14). The other three reports were on patients with LI and all had risk factors for perforation including cicatricial ectropion, lagophthalmos, and dry eye disease (15-17).

Chaudhary *et al.* reported a case of bilateral spontaneous corneal perforations in a patient with LI, cicatricial ectropion, and dry eye disease. Visual acuity was limited to light perception in each eye. The patient underwent bilateral penetrating keratoplasty, cataract extraction, and ectropion repair of the right eye. Three months later, the patient's visual acuity was 4/60 in the right eye, whereas he could count fingers with the left eye (15).

Cinar *et al.* published a case of an 8-month-old woman with LI and bilateral spontaneous corneal perforation in the setting of cicatricial ectropion and dry eye disease. The patient had bilateral corneal transplantation using amniotic membrane and reconstructive surgery on her eyelids. Five months postoperatively, the patient developed a corneal leucoma in the inferior part of the cornea (16).

Consistent with our experience, infection of the cornea can rapidly progress to corneal melting and

inflammatory reaction in the anterior chamber in patients with severe cicatricial ectropion, narrowing of the palpebral fissure, and lagophthalmos. In our case, lubricants containing hyaluronic acid and topical eye ointment containing vitamin A and perfluorohexyl octane effectively provided symptomatic relief. The corneal graft was stabilized with the use of chronic topical steroids and cyclosporine eye drops. The use of systemic retinoids correlated with improvement in ocular symptoms and the patient's overall condition. A final recommendation is surgical correction of the ectropion using autologous skin transplant.

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