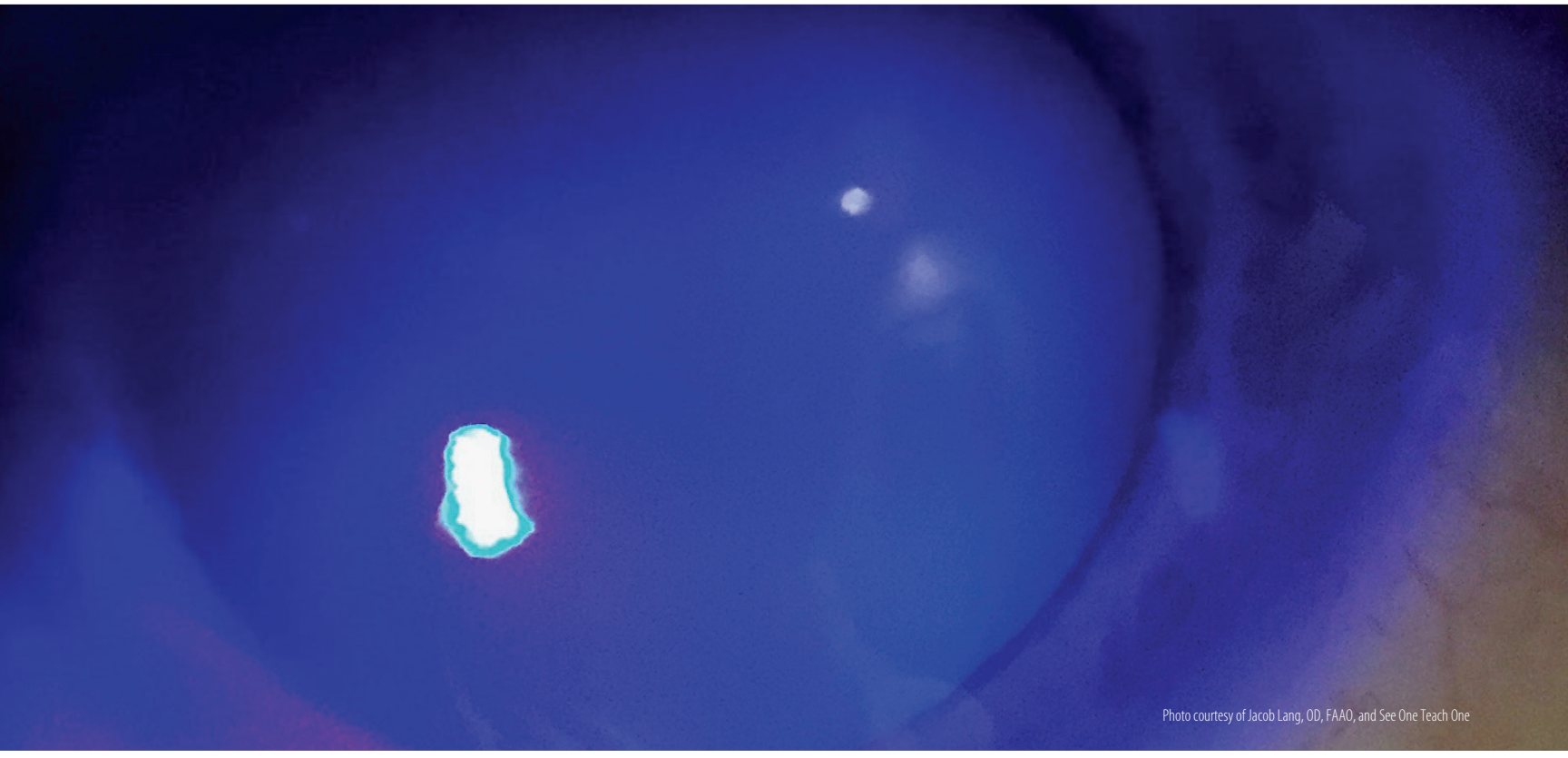
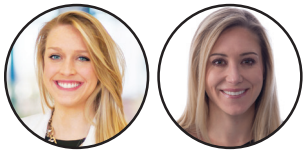


Photo courtesy of Jacob Lang, OD, FAAO, and See One Teach One

RECOGNIZING AND MANAGING LIMBAL STEM CELL DEFICIENCY



Long-term soft contact lens use is a common cause.

BY JADE COATS, OD; AND MICAELA CROWLEY, OD

Seeing clearly on any given day involves a complex process that requires a transparent corneal epithelium with a stable tear film, a clear stroma with homogeneous collagen fibrils, and a well-functioning endothelium. *Limbal stem cell deficiency* (LSCD) is a complex, multifactorial disease that is associated with the compromise of limbal stem cells that play a crucial role in maintaining the vital transparency and stability of the cornea.[1]

The corneal epithelium is constantly undergoing cell renewal and regeneration thanks to the proliferation of limbal stem cells; however, with LSCD, there is a partial or complete loss of this corneal regenerative ability. When the limbal zone is affected or destroyed, *conjunctivalization* occurs, resulting in the invasion of conjunctival epithelium on the corneal epithelial surface. This leads to development of a thickened, irregular, unstable epithelium, often associated with secondary neovascularization and inflammation.[2]

Symptoms of decreased vision, photophobia, redness, epiphora, and ocular pain are common in LSCD, along with recurrent episodes of epithelial defects that can lead to corneal ulceration, scarring, and loss of vision.[2] This make the diagnosis of LSCD especially crucial because patients with this abnormality are generally poor candidates for conventional corneal transplants.

CASE PRESENTATION

Initial Appointment

A 30-year-old White woman presented with the complaint of blurred vision worsened within a half-hour of waking, asymmetrical injection, and foreign body sensation, in addition to moderate pain. She was seen at an urgent care facility 2 weeks earlier, where she was prescribed the fluoroquinolone antibiotic ciprofloxacin. She reported no improvement since that time.

She was an established contact lens wearer, having worn a biweekly disposable lens for approximately 12 hours a day since age 14 years. Her BCVA on initial presentation was 20/40-2 OD and 20/30 OS. Slit-lamp examination revealed moderate conjunctival injection, corneal neovascularization, and punctate staining, worse superiorly in each eye.

A diagnosis of keratoconjunctivitis sicca and dry eye syndrome was discussed, with a differential diagnosis of contact lens hypersensitivity, contact lens over-wear, and an ill-fitting contact lens. We advised immediate discontinuation of contact lenses and recommended use of copious preservative-free artificial tears four to six times daily, along with loteprednol etabonate ophthalmic ointment 0.5% (Lotemax, Bausch + Lomb) nightly.

Follow-Up

After 2 weeks of treatment, the patient was compliant with the management plan and reported improvement of symptoms but did not exhibit complete resolution of corneal punctate staining.

The patient mentioned an interest in refractive surgery because her contact lenses were "becoming a hassle." She was sent for a LASIK consultation and told that she is not a candidate. Instead, she was diagnosed with early bilateral LSCD based on 2+ diffuse punctate keratitis with a whorl-like appearance and superior neovascularization. BCVA had worsened to 20/50 OD and 20/70 OS by that point.

She was advised to remain out of contact lenses and referred to an optometrist for refractive management and scleral contact lens fitting. She was also advised to discontinue soft contact lens wear indefinitely and started on cyclosporine ophthalmic emulsion 0.05% (Restasis, Allergan) four times a day.

Scleral Lens Consultation

At 1-month follow-up, the patient's BCVA was 20/25 OD and 20/25 OS, and slit-lamp examination confirmed clearer corneas with receding neovascularization in each eye. She reported improvement in vision and comfort in each eye and felt that her vision was completely "back to normal."

AT A GLANCE

- Limbal stem cell deficiency (LSCD) is a multifactorial disease associated with the compromise of limbal stem cells, which help to maintain the transparency and stability of the cornea.
- LSCD can be challenging to diagnose in early stages, as it has the potential to mimic other ocular surface diseases such as dry eye syndrome.
- Nearly 15% of cases are associated with soft contact lens wear on a daily basis for multiple hours a day.

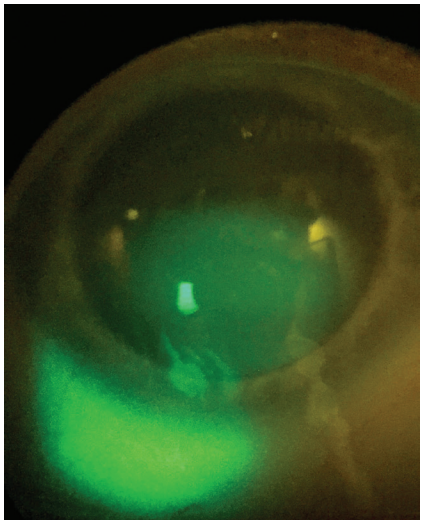


Photo courtesy of Jacob Lang, OD, FAAO, and See One Teach One

Figure. Punctate keratitis in a whorl-like pattern.

She was advised to continue using cyclosporine 0.05% four times a day for 1 more month, then taper to twice daily indefinitely. Scleral contact lenses were dispensed and approved to wear for 10 to 12 hours a day.

DIAGNOSIS

LSCD can be challenging to diagnose in its early stages, as it has the potential to mimic other ocular surface diseases such as dry eye syndrome.

Although there are numerous etiologies for LSCD, nearly 15% of cases are due to soft contact lenses worn on a daily basis for multiple hours a day. LSCD has been reported in patients who have worn contact lenses for as short a period as 6 to 12 months, but it is more common after 14 to 17 years of use. Average daily wear time is 12 to 16 hours per day. The disease is often bilateral and asymmetric between the two eyes.[3]

Early signs of LSCD in contact lens wearers are most often seen in the superior limbus, followed by the inferior limbus. Classically, the punctate staining follows a whorl-like pattern (Figure), and there is an opaque appearance, given the differences between conjunctival and corneal epithelium.[3]

MANAGEMENT

A formal treatment guideline has not been established for LSCD, but choice

of treatment may depend heavily on the severity of the condition. LSCD can be reversed if diagnosed and treated in its early stages. If misdiagnosed or not addressed, it can lead to total limbal deficiency requiring surgical intervention.[4]

Conservative treatment options include discontinuation of soft contact lens wear and copious use of preservative-free lubrication. Medications such as topical steroids, immunomodulators, and autologous serum tears can also be used to reduce inflammation and restore epithelial health.

Surgical management may be considered when conservative therapies fail. Techniques include mechanical debridement, amniotic membrane application, autologous or allograft limbal stem cell transplantation, phototherapeutic keratectomy, and penetrating keratoplasty.[3]

PATHOPHYSIOLOGY

The corneal epithelium comprises five to six layers of nonkeratinized, stratified squamous epithelial cells. At the corneoscleral limbus there is a gradual transition to nonkeratinized, stratified columnar epithelium, containing mucin-secreting goblet cells of the conjunctiva, that is seven to 10 cell layers thick.[1]

Corneal and conjunctival epithelial regeneration is supplied by stem cells likely located in the basal layer of the limbal palisades of Vogt.[1] This area of limbal stem cells serves as a proliferative barrier between the corneal and conjunctival epithelia.

In the absence of healthy corneal epithelium, the conjunctival epithelium proliferates over the cornea, resulting in goblet cell migration and conjunctivalization. Histologically, LSCD can be confirmed by the detection of conjunctival epithelium containing goblet cells on the corneal surface, where it should not be located.[1]

CAUSES

LSCD can be primarily related to an insufficient corneal microenvironment unable to support stem cell function, such as in congenital aniridia and erythrokeratodermia, neurotrophic keratopathy, and keratitis associated with several endocrine deficiencies.[1] Secondary depletion and loss of stem cells, although more frequently associated with chemical and thermal injuries, can also be associated with contact lens wear, toxicity of preservatives, Stevens-Johnson syndrome, chronic trachoma, ocular cicatricial pemphigoid, and aging.[2] Breakdown of the ocular surface, caused by a persistent epithelial defect after ptyergyium repair or limbal tumor removal, can also increase the risk of sectoral or diffuse stem cell deficiency.[1]

MAKE THE RIGHT CALL

A constant equilibrium is necessary to maintain corneal transparency and function. A disturbance of the balance due to LSCD can lead to permanent corneal epithelial defects, visual loss, and ocular pain from conjunctivalization. Thus, it is important to establish a definitive diagnosis of LSCD because failure to do so may ultimately result in the patient undergoing a corneal transplant, which has a poor outcome in this disease. ■

LSCD BY THE NUMBERS

37 M — Estimated number of contact lens wearers in the United States[1]

2.4 TO 5 — Estimated percentage of contact lens wearers who will develop signs of LSCD[2,3]

15 — Percentage of LSCD cases attributed to contact lens use[4]

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