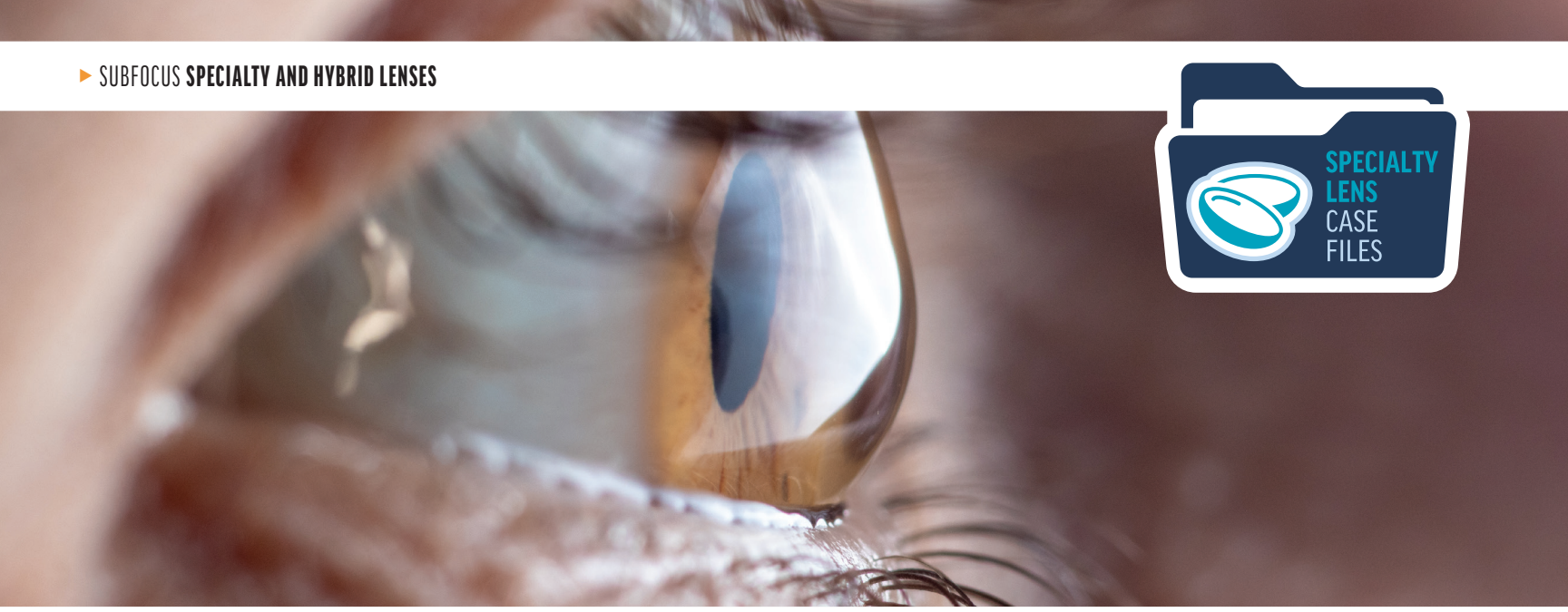

SPECIALTY LENS CASE FILES

DUPILUMAB-ASSOCIATED KERATOCONJUNCTIVITIS

Find out how this biologic affected a patient's scleral lens fit for pre-existing keratoconus and how his case was managed.

BY STEVEN SORKIN, OD, FSLS, AND PETER CHUDOLIJ, OD

As health care providers, we know that most medications have side effects or involve some degree of risk with use—especially those administered systemically. The first biologic to be approved for the treatment of moderate to severe atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyposis was dupilumab injection (Dupixent, Sanofi and Regeneron Pharmaceuticals). Dupilumab is a monoclonal antibody administered via a prefilled syringe or pen for subcutaneous injection in patients 6 years of age or older in either a 100 mg, 200 mg, or 300 mg dose, typically given every 2 weeks. It has a known association with ocular surface disruption and conjunctivitis, although most cases are self-limiting and can be treated conservatively with artificial tears.

Clinical trials have reported an increase in ocular side effects in 5% to 37% of those receiving dupilumab.[1]

AT A GLANCE

- Dupilumab has a known association with ocular surface disruption and conjunctivitis, although most cases are self-limiting and can be treated conservatively with artificial tears.
- The main treatment for dupilumab-related keratoconjunctivitis is topical steroids.
- Patients should be followed closely upon starting dupilumab and treated aggressively to prevent more severe sequelae such as conjunctival cicatrization, punctal stenosis, and periocular skin changes.

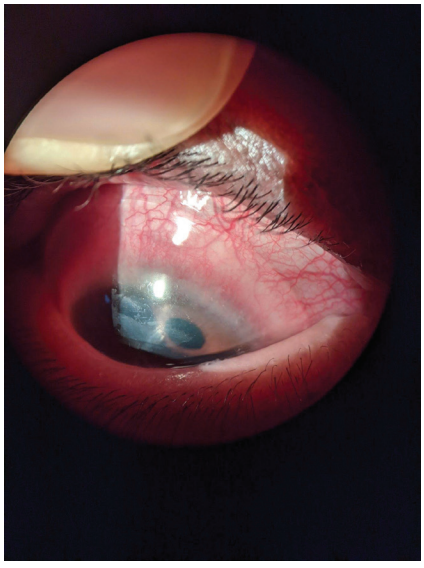

Figure 1. After 1 month of taking dupilumab, this patient presented with red, dry, irritated eyes.

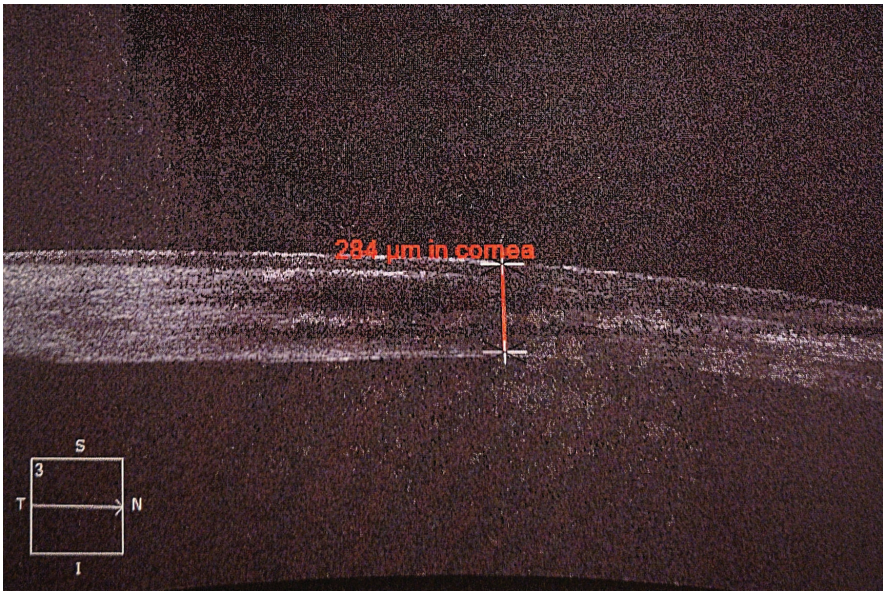

Figure 2. Anterior segment OCT of the patient in Figure 1 shows severe thinning and scarring due to keratoconus and hydrops.

These side effects are more prevalent in patients with atopic dermatitis and less prevalent in those with asthma. The patient case example below discusses the management of someone with concurrent keratoconus and eczema who presented with keratoconjunctivitis after beginning treatment with dupilumab.

CASE EXAMPLE

A male patient had been diagnosed with keratoconus at 16 years of age. He also had severe eczema and asthma, which had been treated with various dermatologic topical medications and antihistamines. He underwent corneal collagen crosslinking in both eyes at 17 years of age and was subsequently fit with scleral lenses. He is now 24 years of age, his keratoconus has progressed, and he developed corneal hydrops bilaterally at the age of 20 in his right eye and at the age of 22 in his left eye. He has been successfully wearing scleral lenses in both eyes since the episode of hydrops with BCVA of 20/50 OU.

The patient presented to my office with complaints of redness, dryness, and irritation in both eyes 1 month after starting dupilumab. His eyelids were also red, and he noted decreased tolerance to wearing his scleral lenses, but he maintained that his vision was unaffected. He was also using an albuterol inhaler and a fluticasone nasal spray.

The patient's entering VAs with his habitual scleral lenses were 20/40-1 OD and 20/60 OS. Slit-lamp examination revealed 2+ bulbar injection with trace chemosis, grade 1 papillae, superior palpebral conjunctiva OU, central corneal scarring OU with severe bowing/thinning, (Figures 1 and 2) mild pannus inferior OU, and scattered superficial punctate keratopathy OU. His lenses were clear and his IOPs measured with Goldmann applanation tonometry were 10 mm Hg OD and 12 mm Hg OS.

The Treatment Plan

I prescribed the following treatment regimen for this patient:

- Preservative-free artificial tears every 2 hours
- Fluorometholone OU four times daily

> BEFORE STARTING DUPILUMAB IT IS RECOMMENDED THAT PATIENTS CONSULT WITH THEIR EYE CARE PROVIDER FOR A BASELINE EVALUATION AND TO DETERMINE IF THEY HAVE ANY OSD OR PRE-EXISTING ATOPIC EYE DISEASE.

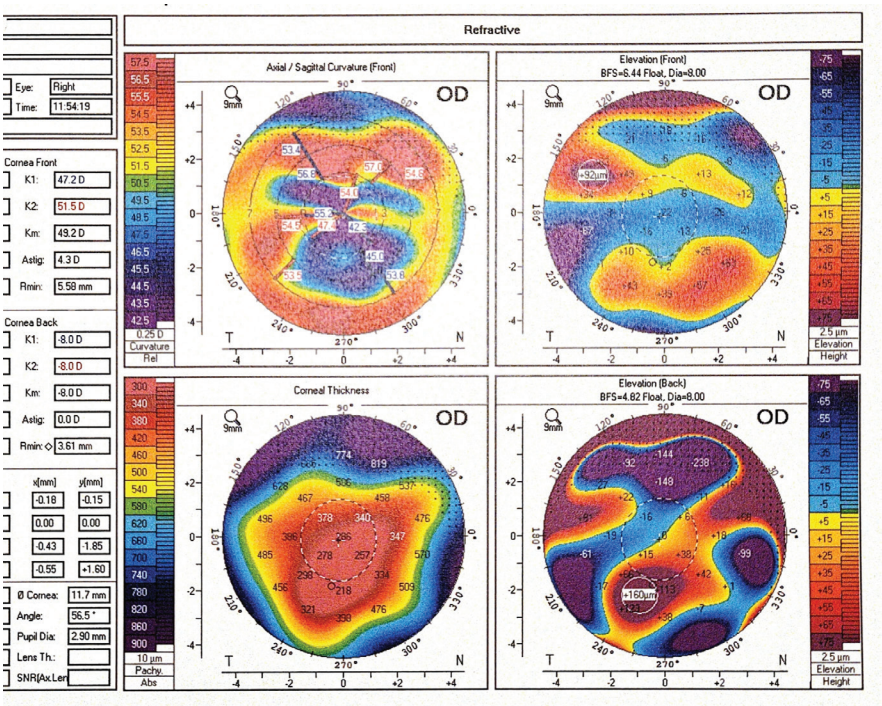

Figure 3. Corneal topography of the right eye taken with the Pentacam (Oculus).

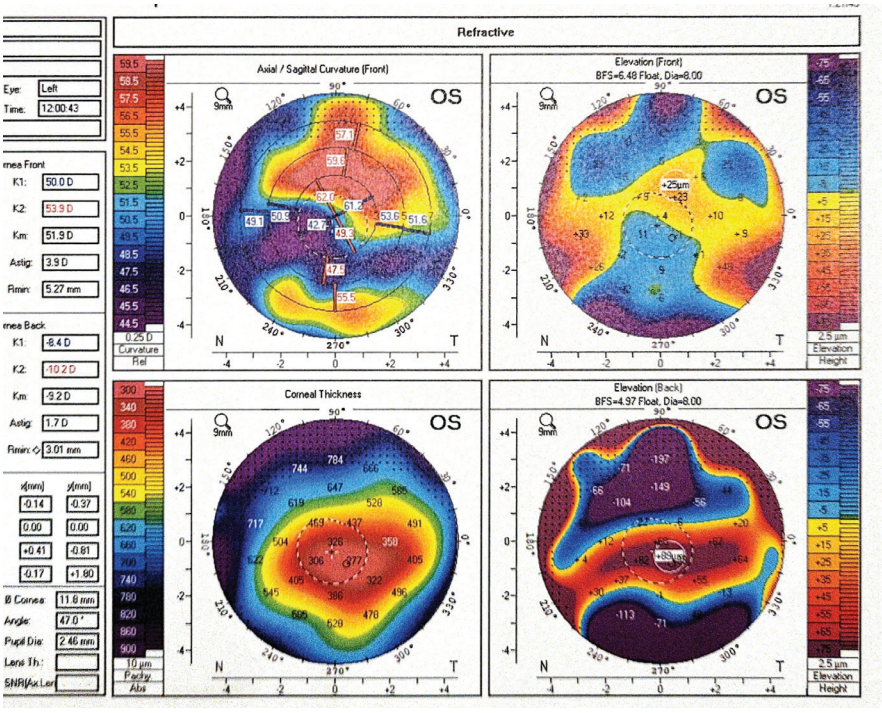

Figure 4. Corneal topography of the left eye taken with the Pentacam.

- Compounded cyclosporine 1% OU every 4 hours
- Lid scrubs twice daily OU
- Optase Hylo Night eye ointment (Scope Ophthalmics) at bedtime

The Check-In

The patient presented 1 month later with a reduction in symptoms. He had modified his contact lens wearing schedule by reducing his contact lens wearing time and removing his lenses throughout the day during treatment to allow for the instillation of his ocular medications.

Clinical examination revealed a reduction in hyperemia and corneal staining OU. The fluorometholone was tapered to three times daily OU. All other medications remained the same.

Follow-Up Visits

Subsequent follow-up visits over the next 3 months showed continued improvement in clinical findings and symptoms (Figures 3-5). The patient was tapered off of the topical steroids and is using cyclosporine 0.09% (Cequa, Sun Ophthalmics) twice daily OU and the ointment. He is back to wearing his scleral lenses 10 to 12 hours a day OU, and his VA is stable at 20/40 OD and 20/60 OS.

DISCUSSION

Atopic dermatitis, commonly known as eczema, is a chronic inflammatory skin disorder caused by an IgE–mediated type-1 hypersensitivity reaction commonly resulting in skin erythema with edema, vesicles, and thickening of the skin. Atopic dermatitis can also present with allergic conjunctivitis, blepharitis, and ocular surface disease (OSD), which are typically also associated with keratoconus. Dupilumab targets the interleukin (IL)-4/IL-13 receptor and inhibits the signaling of IL-4 and IL-13, two key mediators of inflammation that are associated with improvement of clinical signs and symptoms of atopic dermatitis.[2] In one study, the mean time to develop self-reported eye symptoms after the start of dupilumab therapy was 6 ± 5.5 weeks.[3] Other possible findings, in addition to blepharoconjunctivitis, include severe follicular conjunctivitis, limbal nodules, cicatricial ectropion, keratitis, and dry eye.[4]

The etiology of dupilumab–associated conjunctivitis is not fully understood, but it is similar to that of atopic blepharitis and allergic conjunctivitis

in that all of these conditions exhibit an increase in OX40 ligand activity, eosinophilia, and a decrease in goblet cell density.[5]

One study found that 80% of patients in the clinical trials for dupilumab had resolution of conjunctivitis, but 20% had ongoing ocular surface inflammation while on the drug.[6] Another study showed that 67% of patients needed ongoing treatment of OSD.[3] The study also reported that 60% of OSD cases were mild enough to require only topical lubricants, but the remaining 40% had conjunctivitis severe enough to require topical steroid treatment.[3]

The main treatment for dupilumab–related keratoconjunctivitis is topical steroids. In one study, topical steroids alone were sufficient in reducing signs and symptoms of acute conjunctivitis in 89% of patients.[7] Close monitoring for well-known complications of concurrent steroid use, including increased IOP and cataract, should be put in place. Topical medications such as lifitegrast ophthalmic solution 5% (Xiidra, Novartis) can maximize the ocular surface.

Topical cyclosporine is another treatment option for OSD. Cyclosporine is a calcineurin inhibitor that can increase goblet cell density and inhibit T cell–mediated immune responses. As previously mentioned, dupilumab targets IL-13 and can deplete goblet cells and mucin production.[8] Either commercially available preparations or compounded versions of cyclosporine can be prescribed to treat dupilumab–associated OSD and conjunctivitis. Alternatively, tacrolimus 0.03% ophthalmic ointment (various) twice daily or pimecrolimus cream 1% (Elidel, various) can be used to treat this condition. Note that the black box warning for tacrolimus states that rare cases of malignancy (skin cancer and lymphoma) have been reported with the use of immunosuppressive drugs.

With dupilumab–related keratoconjunctivitis, concurrent treatment of the eyelids is also important. Lid hygiene, supplementation with omega 3 fish oil, meibomian gland expression, and thermal treatments such as the LipiFlow Thermal Pulsation System (Johnson & Johnson Vision Care) and the TearCare System (Sight Sciences) can be used as well. A recent case report demonstrated that intense pulsed light therapy is effective in treating chronic dupilumab–induced OSD as an adjunctive therapy, along with topical steroids and lifitegrast.[9]

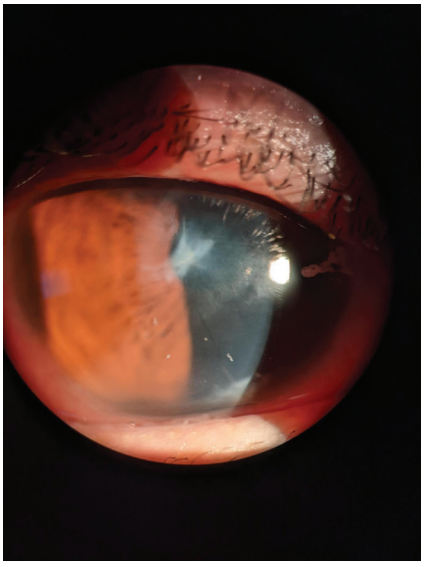

Figure 5. Slit-lamp photo of the patient's cornea post hydrops.

PROCEED MINDFULLY

Before starting dupilumab it is recommended that patients consult with their eye care provider for a baseline evaluation and to determine if they have any OSD or pre-existing atopic eye disease. It is important to carefully identify these patients and to start ocular surface therapy before initiating treatment with dupilumab. Patients should be followed closely upon starting this medication and treated aggressively to prevent more severe sequelae such as conjunctival cicatrization, punctal stenosis, and periocular skin changes. A number of patients require long-term treatment to manage ongoing ocular surface inflammation. Concurrent conditions such as keratoconus can make this condition more challenging, as many patients rely on gas permeable or scleral lenses to function in daily life.

One final note: Many patients with keratoconus are likely to be eye rubbers, which can exacerbate both their conjunctivitis and keratoconus. Be sure to communicate with the patient's prescribing doctor to alert them of any clinical findings. It is rare for a patient to be required to discontinue dupilumab due to ocular reasons. In many cases, dupilumab is life-changing for patients. When given the option of discontinuing dupilumab, the patient in this case refused to stop taking the medication. ■

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