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Corneal Melt Associated with Subcutaneous Allergen Immunotherapy

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Introduction

Subcutaneous allergen immunotherapy (SCIT) is a treatment for moderate-to-severe seasonal allergies. SCIT is not known to cause serious ocular complications beyond transient exacerbations of pre-existing allergic symptoms. We report a unique case of corneal melt associated with SCIT in a patient with severe allergies.

Case Report

A 53-year-old male was referred for recurrent pain and redness of both eyes. He first experienced symptoms after starting twice-weekly injections of SCIT for severe seasonal allergies 4 months prior to presentation. Early on, these injections were temporally associated with the development of sinus congestion, tearing, and photophobia without eye pain or vision changes. These symptoms waxed and waned over several months, with exacerbations occurring in the hours to days following immunotherapy administration. On one occasion he experienced a systemic reaction (nausea, diarrhea, shortness of breath) which resolved within minutes without intervention.

Following a subcutaneous immunotherapy injection 4 months into the treatment course, the patient presented to the emergency department with redness, pain, and photophobia in both eyes. Ophthalmic exam showed evidence of a submillimeter corneal epithelial defect in the right eye, for which he was prescribed topical erythromycin and olopatadine drops. He presented three days later with progressively worsening redness, tearing, and foreign body sensation in both eyes.

Besides seasonal allergies, the patient was otherwise healthy with no other past medical history. His past ocular history included a pterygium excision in the left eye one year prior to presentation. Of note, corneal pachymetry preoperatively had demonstrated normal corneal thickness in both eyes (Figure 1). Following this surgery, he had a prolonged steroid taper over 12 months which was complicated by infectious keratitis of both eyes. These had resolved prior to initiating SCIT. The patient reported no smoking or alcohol use. His medications included daily fexofenadine in addition to the previously mentioned topical erythromycin and olopatadine drops. Review of systems was negative for additional symptoms.

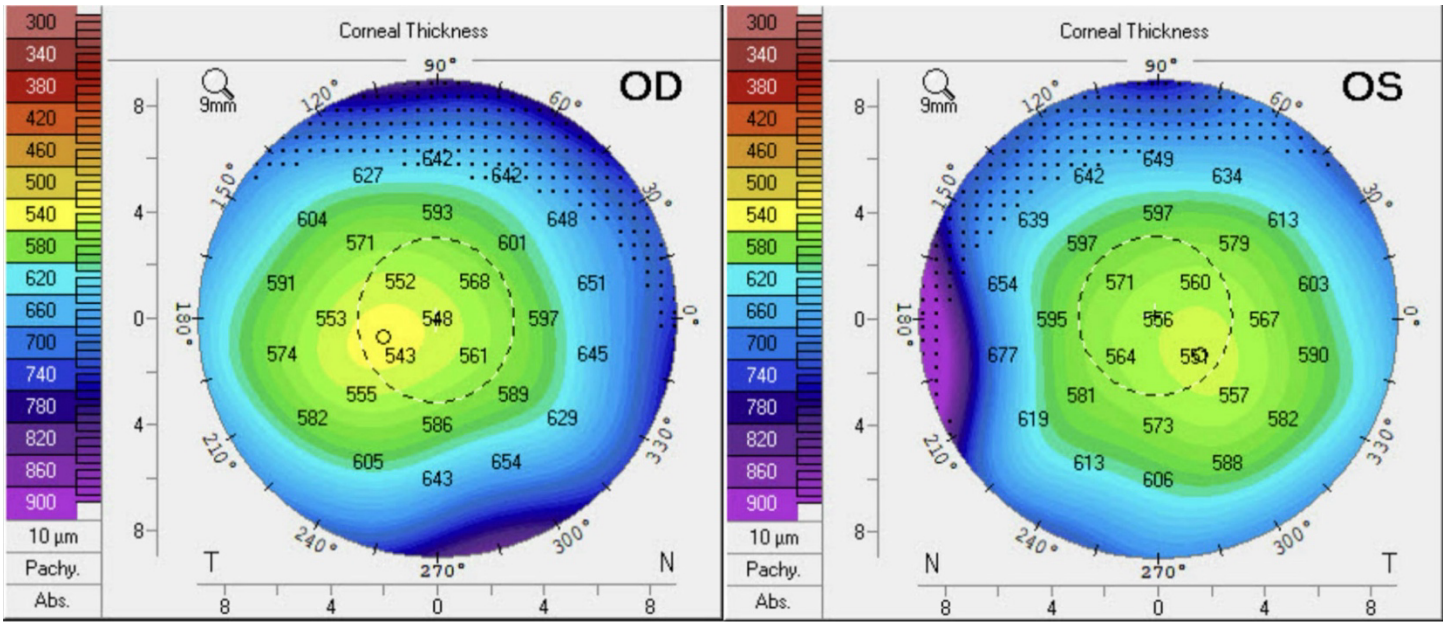

Figure 1. Corneal pachymetry (Pentacam, Oculus) of both eyes 2 years prior to corneal melt, demonstrated normal to greater-than-normal thickness in all regions. Increased thickness in the nasal portion in the left eye was consistent with pterygium that was later excised.

Exam revealed a visual acuity of 20/20 in both eyes and normal intraocular pressure. Slit lamp exam of the right eye demonstrated diffuse conjunctival injection with focal limbitis from 3:00-6:00, a crescentic peripheral epithelial defect with underlying thinning from 3:00-6:00, and white blood cell infiltration. The left eye demonstrated diffuse conjunctival injection with a clear cornea and nasal corneal autograft consistent with prior pterygium surgery. Oral prednisone 50mg daily, topical prednisone 4 times daily, and topical moxifloxacin 4 times daily were initiated. One week later, symptoms only minimally improved, and there was persistent corneal thinning of the right eye with new conjunctival overgrowth. Of note, the patient was still receiving immunotherapy injections.

Two weeks after onset, a corneal melt was observed in the inferonasal portion of the right eye with adjacent conjunctival overgrowth, corneal neovascularization, and limbal injection (Figures 2A-B).

Corneal scrapings for bacterial culture, fungal cultures and multiplex polymerase chain reaction (HealthTrackRx, Denton, TX) were negative. Laboratory studies revealed anti-ribonucleic protein of 8.0 AI,

anti-Scl70 of 1.2 (normal <1 AI), and IgG4 of 121.8 mg/dL (normal 2.4-121 mg/dL). Laboratory studies that were either negative or normal included: anti-nuclear antibody, other nuclear antigen antibodies (dsDNA, chromatin, ribosomal P, SS-A/SS-B, centromere B, SM, Jo-1), anti-myeloperoxidase, anti-proteinase 3, anti-cyclic citrullinated peptide, other IgG subclasses, rheumatoid factor, HIV, hepatitis B/C, syphilis, tuberculosis, erythrocyte sedimentation rate, c-reactive protein, and uric acid. Complete blood count and metabolic panel were notable only for mild elevation in alanine aminotransferase. Urinalysis was normal.

Given the largely negative review of systems and immunologic workup in the clinical context, a diagnosis of peripheral ulcerative keratitis (PUK) associated with severe allergies was made with SCIT acting as an immunologic trigger. SCIT injections were discontinued, and periocular tacrolimus was added to the existing treatment regimen of oral and topical prednisone.

Oral prednisone was then tapered over 2 months. At follow-up 4 months after onset, symptoms had resolved and exam findings showed resolution of the corneal epithelial defect, stable corneal thinning, and no signs of inflammation (Figures 2C-D).

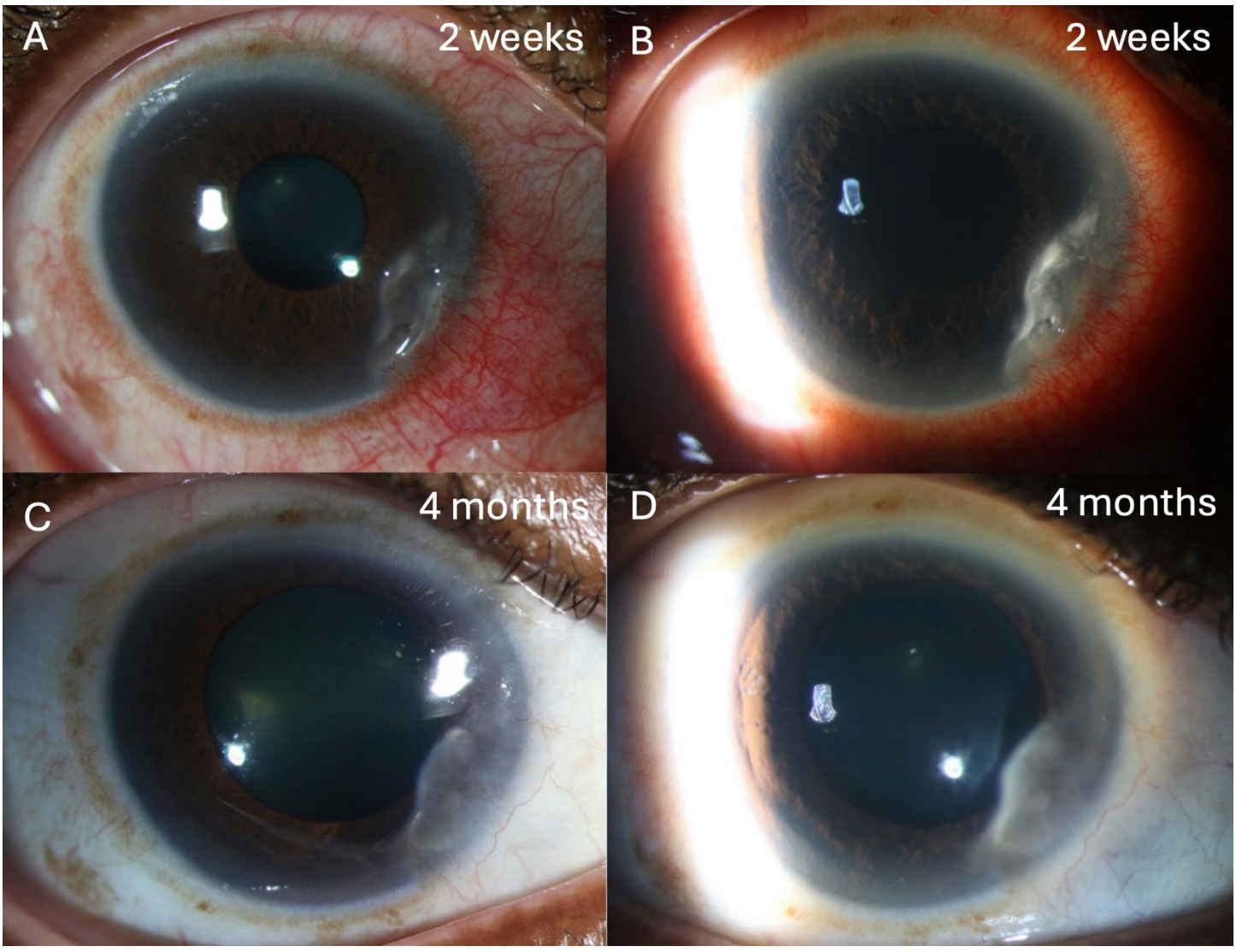

Figure 2. Slit lamp photographs of the right eye taken 2 weeks after onset with A. diffuse illumination and B. sclerotic scatter demonstrating an inferonasal, peripheral corneal melt with corneal neovascularization, conjunctival overgrowth, and limbal injection. C, D. Repeat photographs taken 4 months after onset show a decrease in size of the melt, stable corneal scarring, and improved conjunctival injection.

Discussion

Corneal melt involves rapid degeneration of the corneal stroma that can lead to perforation and blindness. Associated conditions include inflammatory diseases, infections, medications, toxin exposures, and surgeries.[1] Peripheral ulcerative keratitis is a type of corneal melt typically occurring in the peripheral cornea with adjacent conjunctival/limbal inflammation and associated systemic inflammation.[2] In the present case, we strongly suspected SCIT as the primary cause of corneal melt and PUK, specifically acting as an immunologic trigger in the background of severe allergies.

Our differential included atopic keratoconjunctivitis (AKC), a known allergic complication that can cause corneal melt. However, prominent features of AKC including significant eyelid inflammation and mucoid discharge were not present.[3] Furthermore, a case of AKC that was successfully treated with SCIT has been reported.[4]

This patient's workup was largely negative for known etiologies of PUK such as vasculitis, autoimmune disease, and infection.[2,5] Elevated anti-RNP and anti-Scl70, markers of autoimmune connective tissue diseases, likely represented false positives given the low titers and absence of accompanying symptoms. Mildly elevated IgG4 is non-specific and may occur in patients with allergies or undergoing SCIT.[9]

The timing of both onset and resolution of the corneal melt suggested an association with SCIT. Our patient had begun a course of SCIT several months before initial presentation, involving serially increased titers of allergen injections. Resolution of the corneal melt occurred after SCIT was discontinued and standard PUK treatment was initiated.

Although the concept of an external, immunologic trigger for underlying autoimmune disease has been described,[8] the mechanism of SCIT-related corneal melt is unclear. SCIT is associated with shifts in T-cell subpopulations and immunoglobulin subtypes, both of which are implicated in PUK pathogenesis.[9,10] Our patient's prior systemic reaction may have indicated a hyperreactive immune response to SCIT as well. Vasculitis is commonly associated with PUK,[11] and instances of allergen immunotherapy triggering vasculitis have been reported.[12,13] Given that SCIT can increase circulating immune complexes,[14] a vasculitis-like mechanism involving immune complex deposition in limbal blood vessels may explain SCIT-related PUK.[5]

Conclusion

We present a case of corneal melt and PUK associated with SCIT. We theorize that SCIT acted as an immunologic trigger with a background of severe seasonal allergies. When developing a differential for corneal melt, consideration of all potential immunologic disturbance may be helpful. Monitoring patients receiving allergen immunotherapy may facilitate the early detection of associated ocular sequelae.

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Statement of Ethics

This case series adheres to patient confidentiality and ethical principles in accordance with the guidelines of the Declaration of Helsinki and relevant local regulations. Consent was obtained from the patient for the publication of this case report.

Conflict of Interest Statement

Authors declare no conflicts of interest related to this topic.

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