Bilateral interstitial keratitis as the presenting manifestation of systemic lupus erythematosus in a child

Interstitial keratitis (IK) is defined as a nonsuppurative inflammation of the corneal stroma with associated cellular infiltration and vascularization commonly caused by infections or rheumatologic conditions. Although extremely rare, IK may be seen with systemic lupus erythematous (SLE). We present the first case of a child without known history or symptomatology of rheumatologic or infectious disease presenting with bilateral IK that ultimately led to a diagnosis of SLE.

A 9-year-old African American girl with a medical history of asthma and no known rheumatologic or infectious disorders was referred for management of extensive bilateral corneal scarring and vascularization, mild eye pain, and photophobia. Her condition had been examined by multiple ophthalmologists since age 7 years when her mother noted that her eyes were becoming "blue and cloudy." She was inconsistently taking prednisolone acetate 1% 2 to 3 times per day in both eyes (OU). Review of symptoms was negative for fevers, rashes, skin lesions, arthralgias, myalgias, intestinal symptoms, oral or nasal ulcerations, foreign travel, and animal or insect bites.

Uncorrected visual acuity was 20/25 right eye (OD) and 20/50 (pinhole 20/30) left eye (OS). Pupils were equal and symmetric without a relative afferent pupillary defect. Extraocular movements were full, and her intraocular pressures were 14 mm Hg OU. External examination was unremarkable. On slit-lamp examination, the conjunctiva was white and quiet without evidence of follicles, papillae, or granulomas. There was significant bilateral superficial and deep peripheral corneal stromal opacification with large vascular loops deep within the corneal stroma. The opacification extended from the peripheral cornea centrally for virtually 360 degrees, with involvement of the superior visual axis. No corneal epithelial or endothelial disease was noted. Anterior chambers were deep and quiet OU. The lenses appeared clear. Dilated examination was within normal limits.

Her basic metabolic panel, liver function tests, sedimentation rate, thyroid studies, Lyme titer, tuberculin test, rapid plasma reagin, fluorescent treponemal antibody absorption, lipid panel, angiotensin converting enzyme, rheumatoid factor, anti-neutrophil cytoplasmic antibody (p and c-ANCA), hepatitis A and C antibodies, myeloperoxidase antibody, and proteinase 3 antibody were all within normal limits. Hepatitis B surface antibody was positive (patient was immunized), with the rest of the hepatitis B panel negative. Epstein–Barr virus Immunoglobulin G (IgG) and herpes simplex virus IgG antibodies were positive, but IgM titres were negative for both. Antinuclear antibody was positive at 1:160, with a speckled appearance. Positive autoantibodies were detected against Ro/SSA antigens but were negative against La/SSB antigens.

Chest x-ray showed mild coarsening of the peribronchial markings in the right lower hilum. Computerized tomography of the chest indicated several small pulmonary nodules consistent with inflammatory disease. These findings prompted referral to pediatric rheumatology, where she was ultimately diagnosed with Ro+ lupus and started on systemic methotrexate (MTX).

Improvement of the stromal inflammatory changes and vascularization was noted 3 months after initiation of MTX. Although extensive peripheral corneal scarring remained, there was regression of the corneal vascular loops with no evidence of active stromal inflammation after MTX was started (Fig. 1A–C). Topical steroid drops were gradually discontinued over 6 months. Over a 12-year course, she did eventually manifest arthralgia and myalgia, which were well controlled on MTX. At the 12-year follow-up, her best-corrected visual acuity was 20/30 OD and 20/25 OS without recurrence of the corneal inflammation.

SLE is an autoimmune connective tissue disorder with multisystem involvement that primarily affects women of childbearing age and has a higher incidence in African American females. It is characterized by the production of autoantibodies that form immune complexes leading to end-organ damage, including in ocular structures.[1] Several ocular manifestations have been reported, including optic neuritis, episcleritis/scleritis, and retinopathy.[1] Corneal

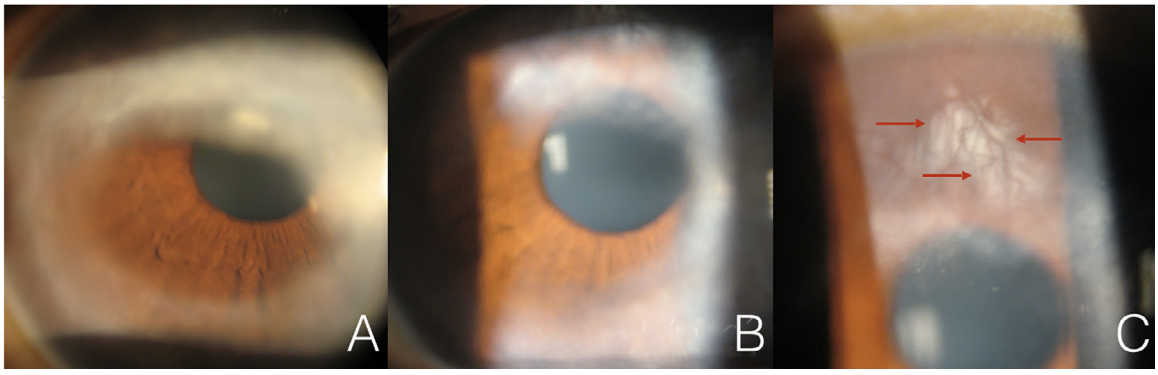

Fig. 1—Slit-lamp photographs showing extensive corneal stromal scarring extending into visual axis. (A) Low magnification, right eye. (B) Low magnification, left eye. (C) High magnification, left eye, showing superior stromal scarring and ghost vessels (arrows).

manifestations of SLE include keratoconjunctivitis sicca and rarely keratoendothelitis, corneal infiltrates, and peripheral ulcerative keratitis.[1] In 1964, Halmay and Ludwig first reported a case of band-shaped keratitis in a patient with SLE.[2] Since then, IK has been reported rarely.[3,4]

The previous case reports all involved adult patients who had either pre-existing SLE or presented with characteristic associated systemic complaints (e.g., skin rash, arthritis, or myalgias). They also had focal corneal involvement, either band shaped or localized to a quadrant. Most presented with significant ocular pain and photophobia. In contrast, our pediatric patient had not been previously diagnosed with SLE, nor did she have any of the classic systemic or ocular complaints. Her pulmonary symptoms were felt to be consistent with asthma, and she was treated accordingly for years. Her corneal pathology also featured more circumferential inflammation with deep stromal neovascularization.

Although other etiologies such as viral may be theoretically implicated, her IgM titres were negative. Over her 12-year follow-up, she did not develop any other ocular manifestations consistent with viral corneal disease. It has been also previously reported that herpes simplex virus and Epstein–Barr virus are exceedingly rare in active bilateral IK, with a prevalence of 2% and 1%, respectively.[5] In addition, the improvement of her corneal disease and stability of her ocular examination on MTX for several years also provides stronger evidence for lupus as the underlying etiology of her stromal inflammation and vascularization.

The dramatic corneal findings and relative lack of symptoms may be unique to the presentation of lupus IK in a child. The lack of symptoms, or ability for the child to identify them, may have delayed medical attention, allowing the inflammatory process to progress to a more advanced state. Additional cases are needed to further detail potential differences of this rare disease between adults and children. We present the first report of a child with lupus IK. Even though it is extremely rare, SLE should be considered in the differential diagnosis of a child with IK. Prompt recognition and treatment with topical steroids and systemic immunosuppression can prevent permanent corneal scarring and vision loss.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

Simple limbal epithelial transplantation (SLET) in conjunction with keratoplasty for severe congenital corneal opacities

Congenital corneal opacities (CCO) are rare, with an incidence of 1 in 26,000 to 37,000 live births.[1,2] There is a wide spectrum of CCO disease severity from mild and small opacities to fully opaque cornea with severe lens involvement and vascularization or conjunctivalization of the cornea. The severe form of CCO is usually associated with large corneal opacity and the presence of extensive superficial corneal vascularization. Such eyes may have conjunctival epithelial ingrowth, which can increase the risk of allograft rejection.[3]

Limbal epithelial stem cells reside at the limbus and act as a barrier against the invasion of conjunctival epithelium onto the corneal surface.[3,4] The limbal stem cells are also essential for the epithelialization of the cornea.[3,4] Limbal stem cell deficiency (LSCD) can lead to a wide range of clinical problems, including recurrent or persisting epithelial defects, conjunctivalization of the cornea, scarring, localized neovascularization, chronic inflammation, and corneal perforation.[3,4] Limbal stem cells can fail in primary ocular diseases such as congenital aniridia[5] or become damaged in acquired disease as seen in chemical injuries and Stevens-Johnson syndrome.[4] There is very little in the literature on LSCD in CCOs and the mechanism is not well understood.