Idiopathic CD4^+ Lymphocytopenia and Sjogren Syndrome

Idiopathic CD4^+ lymphocytopenia (ICL) is a rare syndrome that is marked by a CD4^+ count that is less than 300 cells/mm^3 without human immunodeficiency virus infection. Its course differs from that of AIDS in that although patients with this disorder may develop opportunistic infections, the majority of them remain stable. No transmissible agent has been implicated in the pathogenesis of ICL. The ocular manifestations of ICL have only rarely been described, and there are no reports of ICL in ophthalmology literature. We report the case of a patient with ICL and Sjogren syndrome.

Report of a Case. A 52-year-old woman was referred to the ophthalmology department because of a several-year history of burning and stinging in both eyes. Her medical history was significant for ICL, with 5 CD4^+ counts during 6 years ranging from 93 to 253, despite 3 negative human immunodeficiency virus infection test results. Additionally, assays for Epstein-Barr virus, cytomegalovirus, and human herpesviruses 6 and 8 were all negative. At the time, her visual acuity was 20/20 OD and 20/25 OS. The patient had marked superficial punctate keratitis and abundant mucus production in both eyes, and as a result, she began a course of applying artificial tears to both eyes every 2 hours with only minimal relief.

During the ensuing months, a bandage contact lens was placed over the patient’s left eye, but it failed to relieve her symptoms. Schirmer testing with topical anesthesia showed 6 mm of tearing in the right eye and 5.5 mm in the left. Subsequent bilateral inferior punctal plug placement provided some relief, but her symptoms and superficial punctate keratitis persisted. In addition to the aggressive use of artificial tears, other modalities (corticosteroid eye drops and systemic doxycycline administration) were employed, but the patient’s condition did not improve.

A diagnosis of Sjogren syndrome was confirmed after testing showed a Sjogren syndrome antigen antibody level of 13.1 (range, 0-4.9 U/mL). The patient then began a course of celestone hydrochloride (30 mg by mouth 3 times a day), and her symptoms improved considerably. Furthermore, her superficial punctate keratitis diminished appreciably. She remains stable and comfortable on this regimen with the use of artificial tears 4 times per day.

Comment. Idiopathic CD4^+ lymphocytopenia is a rare disorder of CD4^+ lymphocytopenia without human immunodeficiency virus infection. The ophthalmic sequelae of this syndrome have not yet been elucidated. In this report, we describe the characteristics and clinical courses of a patient with ICL and Sjogren syndrome.

The underlying pathophysiology of ICL results from apoptosis of CD4^+ cells, with subsequent limitations on the repertoire of the T-cell population. Autoimmune processes such as Sjogren syndrome may result from restriction of T-cell diversity, which may lead to a subsequent decrease in immune surveillance. This scenario would allow autoantibodies that may otherwise be cleared from systemic circulation to flourish. Kirtava et al^3 found an increased prevalence of ICL among patients with Sjogren syndrome.

In summary, both ophthalmologists and internists should be aware of the connection between Sjogren syndrome and patients with ICL. Further evaluation is necessary to determine other ocular manifestations of ICL.

Edward J. Wladis, MD
Rajendra Kapila, MD
David S. Chu, MD

Financial Disclosure: None.
Correspondence: Dr Chu, Doctor's Office Center, Sixth Floor, 90 Bergen St, Newark, NJ 07103 (chuda @umdnj.edu).

Advanced Keratomalacia With Descemetocoele in an Infant With Cystic Fibrosis

Xerophthalmia refers to the spectrum of ocular manifestations of vitamin A deficiency. It represents the leading cause of childhood blindness worldwide but is uncommon in industrialized countries, where xerophthalmia is more often the result of malabsorption than malnutrition due to poverty. Cystic fibrosis (CF) is an autosomal recessive disease with hyperviscosity of mucus secretions causing chronic pulmonary changes and pancreatic insufficiency. Anderson^7 was the first to note the association between xerophthalmia and CF, now thought to be due to fat malabsorption resulting in fat-soluble vitamin deficiency. Advanced xerophthalmia has been reported as an initial sign of CF. A recent review article summarized the ocular findings of CF to include xerophthalmia, tear film abnormalities, papilledema, and nystagmus. To our knowledge, this is the first clinicopathologic report of keratomalacia with a descemetocoele requiring keratoplasty as the initial manifestation of CF.

Report of a Case. A 5-month-old girl from Juarez, Mexico, was admitted to a hospital in Las Cruces, NM, with...
corneal opacities, vomiting, pneumonia, and failure to thrive, with almost no weight gain since birth. The diagnosis of bilateral ulcerative keratitis was made. Corneal cultures were obtained and treatment was started with hourly fortified cefazolin sodium (50 mg/mL) and tobramycin (14 mg/mL) eyedrops. Cultures yielded light growth of *Staphylococcus aureus*. Five days later, the infant was transferred to the University of New Mexico Health Sciences Center, Albuquerque, because of impending perforation of the left cornea.

Examination of her eyes showed roving eye movements and marked xerosis (Figure 1). The right cornea had a large paracentral corneal opacity with ulceration. The left cornea had more advanced ulceration and a 4-mm descemetocoele. The infant weighed 3.8 kg and was 55 cm long (less than the fifth percentile for weight and height). The diagnosis of keratomalacia was made, and xerophthalmia was suspected. She was immediately given an intramuscular dose of 50 000 IU of water-miscible vitamin A palmitate after serum vitamin A levels were drawn. The following day, the patient underwent an ocular examination under anesthesia in which corneal scrapings were performed for microbiology. Cyanoacrylate tissue adhesive with a bandage contact lens was applied to the left cornea. Fortified topical antibiotics were tapered.

A serum vitamin A level of 0.02 mg/L confirmed vitamin A deficiency (reference range, 0.2-0.5 mg/L). Figure 2 demonstrates the marked improvement in the xerosis 3 days after vitamin A repletion. The patient underwent an extensive pediatric evaluation because of failure to thrive.

On hospital day 4, neurosurgeons performed a ventriculoperitoneal shunt because of hydrocephalus with bradycardia, lethargy, and a bulging fontanel. Microscopic evaluation of the patient’s stool showed 60 to 80 fatty acid droplets (reference range, <60 droplets), prompting a workup for fat malabsorption. She was also deficient in vitamins D, E, and K. The result of a stool *Giardia* enzyme immunoassay test was positive, and a course of metronidazole was initiated.

The patient underwent penetrating keratoplasty in the left eye on hospital day 8. Gross examination of the specimen showed a hazy 8-mm corneal button with central thinning and uveal tissue adherent to the endothelial surface. Figure 3 demonstrates the histopathologic appearance of the specimen. Tissue Gram stain and silver stain failed to demonstrate any organisms. By post-

---

**Figure 1.** Corneal opacities with ulceration in a 5-month-old girl. A, Xerotic (dry) conjunctiva of the right eye. There is a large paracentral corneal opacity with ulceration and approximately 30% stromal loss. B, More advanced ulceration in the left eye, with evidence of a 4-mm descemetocoele. Well-demarcated, inferonasal, cylindrical ulcers are typical of stromal loss in xerophthalmic keratomalacia.

**Figure 2.** Conjunctivas and corneas 3 days after vitamin A dosing, showing increasing luster and less xerosis. A, The ulceration in the right eye is beginning to heal. B, Cyanoacrylate tissue adhesive with bandage contact lens is in place over the descemetocoele of the left eye.
operative day 5, the graft still had a 90% epithelial defect. A bandage contact lens was placed and the corneal graft slowly reepithelialized during the following 2 weeks. Figure 4 shows the appearance of the eyes 17 days after keratoplasty.

Despite nasogastric feeding, the infant gained only several ounces during the first 2 months of hospitalization. Although giardiasis was initially suspected as the cause of malabsorption, it was not sufficient to explain her failure to thrive. The malabsorption workup confirmed CF. Results of successive sweat chloride tests were elevated both times at 89 mEq/L and 96 mEq/L (reference range, 0-40 mEq/L). The patient’s DNA was tested for the 87 known CF mutations, and one copy of the ΔF508 mutation was identified. After initiation of a CF regimen (supplemental pancreatic enzymes, albuterol nebulizer treatments, and chest physical therapy) and placement of a percutaneous endoscopic gastrostomy tube for dysphagia, the patient began to thrive and grow.

She underwent weekly examinations under anesthesia to monitor the graft and remove loose sutures. All sutures were removed by 6 weeks postoperatively. Eight weeks postoperatively, the patient had a corneal graft rejection episode that was aggressively treated with a single pulse of methylprednisolone intravenously, a sub-Tenon injection of triamcinolone acetonide, and hourly 1% prednisolone acetate eyedrops, with significant improvement in the corneal decompensation. Four weeks after vitamin repletion, 0.1% fluorometholone once daily in the right eye was initiated for 6 months. Part-time patching of the right eye and spectacle correction were initiated. The patient’s near-target fixation remained central, steady, and maintained in both eyes 1½ years after keratoplasty. Figure 5 shows her eyes 1 year after initial examination.

Comment. Xerophthalmia is a leading cause of blindness worldwide, affecting 5 million children.1 Risk factors include low socioeconomic status, poor nutrition, preschool age, and pregnancy. Other precipitating factors in western countries include alcoholism, CF, other malabsorption states (sprue, intestinal nematodes, and giardiasis), and food faddism. The spectrum of ocular manifestations has been described and staged by the World Health Organization as follows: nightblindness, XN; conjunctival xerosis, X1A; Bitot spots, X1B; corneal xerosis, X2; keratomalacia.
X3; corneal scar, XS; and xerophthalmic fundus, XF. (Xerophthalmic fundus is largely a clinical oddity and does not necessarily correlate to severity of disease.1)

Xerophthalmia is treated with 2 oral doses of oil-miscible vitamin A, 200,000 IU. Intramuscular administration of 100,000 IU of water-miscible vitamin A retinol palmitate may replace the first dose if parenteral replacement is required. Considered equally effective, the oral dose is generally preferred in developing countries because of lower cost and higher safety (no needles). Infants younger than 12 months require only half the dose.

Children with undiagnosed CF may show signs of xerophthalmia and failure to thrive. Bulging fontanelles have been described in association with both vitamin A deficiency and CF.6 Early reports of CF reported a high incidence of corneal ulceration without pancreatic enzyme and vitamin A supplementation.4 Our patient’s other medical problems may have contributed to the marked xerophthalmia.

Immediate vitamin A replacement is important for the restoration of the ocular surface. This case illustrates the importance of giving vitamin A several days before keratoplasty. Although the keratoplasty was performed 8 days after vitamin A repletion, reepithelialization of the graft took longer than 2 weeks. Although the xerosis may improve within days of vitamin A repletion, the delay in reepithelialization in our case suggests that weeks may be required for the epithelial dysfunction and ocular surface to recover. Serial photographs of our patient’s right eye document the remarkable degree of remodeling and scar reduction that may occur in the infant cornea after vitamin A supplementation. Vajpayee et al7 reported poor outcome after penetrating keratoplasty performed for keratomalacia in preschool children, with clear grafts seen in only 57% of cases at a mean follow-up of 6.4 months. Immediate corneal grafting may not be indicated except in the setting of descemetocele or perforation given the challenges of pediatric keratoplasty.

Histopathologic specimens of isolated xerophthalmic keratomalacia are rare; Sommer1 reported 1 well-studied case with sharply demarcated edges, a paucity of inflammatory cells, intact but keratinized epithelium, and an absence of bacteria. Our case, however, demonstrated an acute and chronic inflammatory response localized to the area of ulceration and iridocorneal adhesion. The pathophysiology of xe-
rophthalmic keratomalacia is poorly understood and requires further investigation.

Sonja Wamsley, MD, MPH
Sarit M. Patel, MD
Mark G. Wood, MD
Robert Villalobos, MD
Daniel M. Albert, MD, MS
V. Vinod Mootha, MD

Correspondence: Dr Mootha, Department of Ophthalmology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-9057 (vinod.mootha@utsouthwestern.edu).

Funding/Support: This study was supported by an unrestricted grant from Research to Prevent Blindness, New York, NY.


Notice to the Authors of Reports From Clinical Trials

The Journal of the American Medical Association (JAMA) and the Archives of Ophthalmology function as an editorial consortium.

With one submission and one set of reviews, your clinical trial manuscript will be considered for publication in both JAMA and the Archives of Ophthalmology.

Submit your paper to the journal of your choice according to the appropriate “Instructions for Authors” and the following guidelines will apply:
1. If your manuscript is accepted by JAMA, it will be considered for an editorial or commentary in JAMA. Your abstract will also be published in the Archives of Ophthalmology with a commentary or editorial.
2. If your manuscript is accepted by the Archives of Ophthalmology, it will be considered for an editorial or commentary in the Archives of Ophthalmology. Your abstract will also be considered for publication in JAMA.