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# "Mooren's Ulcer" Following Salmonella Gastroenteritis

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Peripheral ulcerative keratitis (PUK) is a potentially sight-threatening condition. The peripheral cornea has a predilection to be ulcerated in association with a variety of inflammatory disorders as a result of its anatomic position and especially the presence of blood vessels and lymphatic channels from the adjacent conjunctiva. PUK can be the result of local and systemic infectious disorders. Noninfectious causes of PUK include trauma, and neurologic, neoplastic, and autoimmune disorders such as rheumatoid arthritis, Wegener's granulomatosis, relapsing polychondritis, systemic lupus erythematosus, and polyarteritis nodosa. PUK may be the presenting manifestation of life-threatening systemic vasculitis and therefore is an indication for immunosuppressive therapy, if such a disorder is present or discovered. Duke-Elder described marginal corneal ulcers in patients with systemic infection including bacillary dysentery in 1965. Since then, however, there have been no reported cases of PUK after bacterial gastroenteritis. We report a patient who developed PUK bilaterally after Salmonella gastroenteritis.

CASE REPORT: In July 1996, a 78 year-old white man developed severe diarrhea; a culture confirmed Salmonella gastroenteritis. Fourteen days of therapy with ciprofloxacin resulted in resolution of the gastroenteritis, but as the latter was resolving, photophobia developed, followed by bilateral ocular pain and redness, and then by decreased vision. The patient's ophthalmologist referred him to Dr. Foster for diagnosis and therapy, one month after the onset of the bilateral PUK that was worsening despite topical ciprofloxacin therapy. On examination of the patient, we found bilateral PUK, with diffuse peripheral corneal stromal edema and extreme (4+) conjunctival inflammation. The right eye was the more severely involved one. The patient's visual acuities with correction were counting fingers at 2 feet OD and 20/100 OS. Slit lamp biomicroscopy revealed bilateral PUK, 360•, OD, extending 3 mm into the cornea, and 270•, OS, extending 2 mm into the cornea; the ulcers, OU, were ~80% corneal depth, with no epithelium over them. Peripheral corneal neovascularization into the bed of ulcers was present. The anterior chamber, irides, and lenses appeared normal, except for the presence of a posterior chamber lens implant, OS, placed in early 1995. The fundi could not be seen because of central striate keratopathy. The intraocular pressures were normal. Conjunctival resection, keratectomy, and cyanoacrylate application with soft contact lens fitting were performed for the right eye because of the extensive progression of the PUK in that eye. An immunologic investigation, including a complete blood count, chest radiograph, sinus radiograph, urinalysis, rheumatoid factor, antinuclear antibody, antineutrophil cytoplasmic antibody, hepatitis B antigen and antibody, hepatitis C (HCV) antibody, circulating immune complexes by C1Q and

Raji cell assays were all negative. Erythrocyte sedimentation rate, C-reactive protein, and interleukin 2 receptor levels were mildly elevated. HLA typing was negative for HLA-B27. Histopathology of the resected conjunctiva revealed perivascular inflammatory cell infiltration and microangiopathy. The patient was treated postoperatively with topical 1% prednisolone acetate hourly while awake, as well as ofloxacin 4 times daily, and cyclopentolate 1% 3 times daily. The patient's ocular inflammation gradually subsided, and the PUK slowly resolved in both eyes, with vision improving to 20/100 OD (primarily secondary to cataract) and 20/25 OS.

DISCUSSION: The unique anatomic position and physiologic characteristics of the peripheral cornea predisposes it to a variety of inflammatory disorders. Compared to the center of the cornea, the peripheral cornea was demonstrated by several authors to possess more antigen-presenting cells, mast cells, eosinophils, as well as immunoglobulins and complement components. Its unique position in juxtaposition to conjunctival and episcleral vessels, as well as the dense packing of the collagen bundles and lamellae may help to account for the accumulation of these immunocompetent cells and immunoreactants in the corneal periphery. PUK represents the final common pathway of proteolytic enzyme release from these inflammatory cells as a result of many inflammatory disorders with various etiologies. Salmonella gastroenteritis was the only significant associated disease in the patient we report here.

Duke-Elder described a type of marginal corneal ulceration without accompanying conjunctivitis occurring in association with systemic infections such as influenza, brucelosis, and bacillary dysentery. Our patient had well-documented, culture-confirmed Salmonella dysentery one week before the onset of the ocular symptoms, and the PUK was accompanied by severe conjunctival inflammation. Mooren type corneal ulceration (progressive PUK without associated scleritis, with a an undermined advancing edge) was reported in association with HCV infection, similar to our case of post-Salmonella gastroenteritis PUK; Wilson and colleagues reported two patients with Mooren type corneal ulcers who had chronic HCV infection. The ulcers markedly improved with systemic interferon a 2b treatment for the HCV infection. The improvement of the ulcers paralleled the normalization of the liver enzyme levels. The corneal ulcers in these cases were unlikely to be a result of direct infection of the corneas by HCV; HCV was not detected in the conjunctival specimen of one of the patients. Similarly in our case, the PUK was not the result of direct Salmonella infection; scrapings and cultures were negative for microbes. One possible pathogenic mechanism could be the deposition of immune complexes in the limbal vessels or in the peripheral cornea, with resultant release of proteolytic enzymes. In the cases of HCV-associated Mooren type ulcer, the improvement of the corneal ulcers with interferon a treatment could result from a decrease in serum antigen and therefore a decrease of HCV-associated immune complex deposition. We found no elevated circulating immune complexes by C1Q of Raji cell assays in our patient. Another possible mechanism for the PUK is an autoimmune phenomenon as a result of molecular mimicry between the infectious agents and self-antigens. For example, molecular mimicry between HLA-B27 and subspecies

of Salmonella, Shigella, Klebsiella, and Yersinia was demonstrated. Specifically, a cationic outer membrane protein of Salmonella typhimurium shares homology with five amino acids of HLA-B27 in a nonlinear fashion. This molecular mimicry could explain the fact that individuals with HLA-B27 account for 40-80% of those with post-Salmonella reactive arthritis. Despite the fact that our patient is HLA-B27 negative, it is possible that the subspecies of Salmonella causing our patient's gastroenteritis shared common epitopes with corneal stromal antigens, triggering an immune response after the Salmonella infection, creating antibodies or antigen-antibody complexes that targeted corneal cells. This report adds post-infectious gastroenteritis ulcerative keratitis to the long list of possible causes of PUK.