Late-onset Peripheral Ulcerative Sclerokeratitis Associated With Alkali Chemical Burn

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• PURPOSE: **To report delayed-onset peripheral ulcerative keratitis (PUK) following alkali injury.**
• DESIGN: **Retrospective case series.**
• METHODS: SETTING: **Single institution (Cornea and External Disease Service, Moorfields Eye Hospital).** PARTICIPANTS: **Six eyes of 5 patients with PUK and associated anterior scleritis that had a history of ocular alkali injury.** OBSERVATION PROCEDURE: **Patients were identified among PUK patients seen at Moorfields Eye Hospital over a 20-year period.** MAIN OUTCOMES MEASURES: **Patients' demographics, clinical features, treatment, and outcomes.**
• RESULTS: **Recurrent PUK with scleritis following alkali burns occurred in 5 male patients/6 eyes (median age: 22 years, range 18–38) several years after the chemical trauma (average: 6.4 years; range 3–12). Management of PUK in these patients was similar to PUK arising from other etiologies.**
• CONCLUSIONS: **In this series of patients there was no evidence of an underlying vasculitic cause for the PUK. A localized autoimmune response may, however, be involved in the pathogenesis of these cases, as seen in an animal model of chemical injury or in late mustard gas keratitis. We hope that this case series will bring this newly described condition to the attention of ophthalmologists and that this may assist in their treatment, which, in this series, required systemic immunosuppressive therapy. (Am J Ophthalmol 2014;158:1305–1309. © 2014 by Elsevier Inc. All rights reserved.)**

PERIPHERAL ULCERATIVE KERATITIS (PUK) IS A destructive inflammatory process leading to corneal ulceration and stromal destruction, which involves primarily the juxtalimbal region. PUK is an uncommon disease, with a reported incidence of 3 cases per million per year.[1] It is commonly present in association with conjunctival, episcleral, or scleral inflammation. The associated anterior scleritis can be diffuse, nodular, or necrotizing.

An underlying systemic condition, usually a vasculitis, is responsible for over half of the cases of PUK.[1,2] The most common vasculitides associated with PUK include rheumatoid arthritis; the ANCA-positive vasculitides, such as granulomatosis with polyangiitis and microscopic polyangiitis; and systemic lupus erythematosus.[2] PUK may also be infectious in etiology. Bacteria, fungi, herpes simplex virus, and Acanthamoeba have all been reported to cause PUK and scleritis by direct invasion or immune mechanisms.[1] Exposure or mechanical trauma to the ocular surface can also cause PUK.[3] Therefore PUK has multiple causes, and the underlying pathobiology may well differ between these.

The pathogenesis of PUK associated with vasculitis, although not thoroughly elucidated, relies on the abnormal activation of T cells with production of a cell-mediated and antibody response against corneal autoantigens.[1,4]

In this retrospective case series, we report 5 cases of idiopathic PUK occurring several years after an alkali chemical burn.

METHODS

THIS IS A DESCRIPTIVE CASE SERIES OF PATIENTS WITH LATE-onset PUK following alkali ocular injury. Institutional review board and ethics committee approval was obtained for this study. Consecutive cases were selected from the PUK patients followed between 1992 and 2012 in Professor John Dart's clinic, Cornea and External Disease Service at Moorfields Eye Hospital, London, United Kingdom. The medical records of 5 patients presenting with signs and symptom of delayed-onset PUK following ocular alkali injury were reviewed. A summary of the patients' characteristics is reported in the Table.

None of the cases had microbiological evidence of infectious PUK or clinical and laboratory evidence of underlying autoimmune diseases, with the exception of 1 patient with a history of Crohn disease. No exposure, dry eye, or impaired corneal sensation was present in any of the eyes included in the study.

Summary of 2 representative cases is reported below. Description and images of Cases 1, 3, and 4 are reported

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TABLE. Peripheral Ulcerative Sclerokeratitis Associated With Alkali Burn: Characteristics of the Patients Included in the Series

Characteristic	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	M	M	M	M	M
Age at trauma	22	22	38	18	29
Ocular comorbidities	None	None	Amblyopia	None	None
Systemic comorbidities	None	None	Crohn disease	Depression	None
Type of chemical injury	Ammonia	Ammonia	Ammonia	Ammonia	Ammonia
Cultures	Neg	Neg	Neg	Neg	Neg
Autoimmunity screening	Neg	Neg	Neg	Neg	Neg
Time from injury (y)	4	3	8	5	12
Involvement	Unilateral	Unilateral	Unilateral	Unilateral	Bilateral
Systemic treatment	Prednisolone, methylprednisolone (IV), cyclosporin, mycophenolate, infliximab	Prednisolone, cyclosporin, mycophenolate	Prednisolone, cyclosporin	Prednisolone	Prednisolone, cyclosporin, mycophenolate
Known episodes of inflammation	3	2	2	N/D	2
Average time between episodes of inflammation (y)	0.4	2	2	N/D	2.5
Surgical procedures	AMG (inlay and overlay)	LK (x3), DLC	Glue, PK, cataract extraction, upper lid skin graft	None	Cataract extraction
Resolution	Yes	Yes	Yes	N/D	Yes
Final CDVA	HM	HM	20/40	HM	20/30 in both eyes

AMG = amniotic membrane graft; CDVA = corrected distance visual acuity; DLC = diode laser cyclophotocoagulation; HM = hand motion; LK = lamellar keratoplasty; N/D = not determined; Neg = negative; PK = penetrating keratoplasty.

as Supplemental Text and Supplemental Figure (available at AJO.com).

• **DESCRIPTION OF REPRESENTATIVE CASES:** *Case 2.* This subject suffered an alkali chemical injury (ammonia) to his right eye in 1986 at the age of 22. He had been originally seen in 1989 elsewhere for a recurrent sclerokeratitis and lipid deposition in the peripheral stroma. When he came to our attention in 1994, he had a large epithelialized descemetocele under a central tarsorrhaphy. As the corneal epithelial phenotype was found to be conjunctival according to the impression cytology cytokeratin profile, we carried out a successful lamellar keratoplasty using full-thickness tissue and including half of the donor limbus in the graft with diathermy of the major trunks of corneal neovascularization.[5]

Unfortunately, the patient developed a recurrence of the sclerokeratitis 1 year later (1996) with lipid keratopathy and extensive stromal thinning, for which he was started on oral flurbiprofen and steroids (Figure, Top left). Ultimately, a repeat lamellar keratoplasty was performed in June 1999, which completely epithelialized in a few weeks. In 2000 the patient began using a cosmetic contact lens, even though his visual acuity in the affected eye was 20/30 with the aid of a rigid gas-permeable contact lens.

In the following years the patient started suffering from persistent corneal epithelial defects, leading to corneal stromal melt and ultimately a necrotizing peripheral sclerokeratitis with a large superotemporal scleral rupture and uveal prolapse in 2007 (Figure, Top center), for which a large tectonic sclerocorneal graft was necessary (January 2007). Control of the postoperative inflammation required the use of oral immunosuppression (prednisolone 50 mg daily, cyclosporin A 150 mg twice daily, and mycophenolate 1 g twice daily), which was tapered slowly over time and discontinued in early 2009. The eye ultimately stabilized with hand motion vision, residual bullous keratopathy, and several areas of scleral thinning (Figure, Top right, detail). Over the years the patient also developed secondary glaucoma that required topical treatment as well as diode laser cyclophotocoagulation in October 2009.

Case 5. This 29-year-old patient suffered a chemical injury to both eyes with ammonia as a result of an assault in 1996. The patient had very few ocular symptoms until late 2008, when he started experiencing increasing