American Academy of Ophthalmology
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Dendritiform Keratopathy Associated with Exposure to Polyquarternium-1, a Common Ophthalmic Preservative

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Purpose: To describe dendritiform keratopathy associated with exposure to polyquaternium-1, a common preservative found in contact lens solutions and tear replacement products.

Design: Case series.

Participants: Sixteen patients who demonstrated dendritiform keratopathy during topical ophthalmic exposure to polyquaternium-1.

Methods: Records were reviewed of all patients diagnosed with dendritiform keratopathy between 1999 and 2014 who had documented exposure to contact lens care disinfecting solutions or artificial tear solutions containing polyquaternium-1. Patients were excluded who had coexisting potential causes for dendritiform keratopathy, such as prior herpes simplex keratitis, varicella-zoster viral keratitis, the linear form of Thygeson's superficial keratitis, epithelial regeneration line, *Acanthamoeba* keratitis, mucus plaque keratopathy, medication-related keratopathy, or limbal stem cell deficiency characterized by conjunctivalization of the corneal epithelium.

Main Outcome Measures: Effect of discontinuation of exposure to polyquaternium-1 on the dendritiform keratopathy.

Results: Sixteen patients demonstrated dendritiform keratopathy after exposure to the preservative polyquaternium-1. Thirteen patients had a history of recent exposure to contact lens disinfecting solutions (Opti-Free, Equate) containing polyquaternium-1. Three patients used a tear replacement product (Systane) containing a polyquaternium-1 preservative. Four patients were treated with antiviral medications for presumed herpes simplex keratitis; 4 patients underwent diagnostic testing for *Acanthamoeba* keratitis. Two additional patients were diagnosed sequentially with herpes simplex keratitis, then *Acanthamoeba* keratitis before referral. All dendritiform lesions resolved within 2 to 6 weeks after elimination of exposure to polyquaternium-1.

Conclusions: Ophthalmic products containing polyquaternium-1 may cause dendritiform keratopathy that may be confused with infections of the superficial cornea, such as herpes simplex virus keratitis or *Acanthamoeba* keratitis. *Ophthalmology 2015;■:1–6 © 2015 by the American Academy of Ophthalmology.*

Polyquaternium-1 (Polyquad) is a polycationic preservative that was introduced in the United States first in 1985 as a disinfecting agent for soft contact lenses.[1] Polyquad was marketed first in Opti-Soft and subsequently reformulated into Opti-Free (Opti-Free Express and Opti-Free Puremoist) contact lens care products at a concentration of 0.001%. The same concentration of polyquaternium-1 also is used in the artificial tear product Systane (Systane and Systane Balance). In the past, it was also found in Equate, the Walmart contact lens care solution; however, the current formulation for Equate no longer contains polyquaternium-1. During a 15-year observation period, we identified 16 patients in whom dendritiform keratopathy developed in association with the use of Opti-Free or Equate contact lens care products or Systane tear replacement products. To our knowledge, this is the first report of the association of dendritiform keratopathy with the preservative polyquaternium-1.

Methods

Records were reviewed of all patients diagnosed with dendritiform keratopathy between 1999 and 2014 who had documented exposure to contact lens care disinfecting solutions or artificial tear solutions containing polyquaternium-1. Patients were excluded who had coexisting potential causes for dendritiform keratopathy, such as prior herpes simplex keratitis, varicella zoster viral keratitis, the linear form of Thygeson's superficial keratitis, epithelial regeneration line, *Acanthamoeba* keratitis, mucus plaque keratopathy, or medication-related keratopathy. For contact lens-related polyquaternium-1 keratopathy, patients with clinical limbal stem cell deficiency (LSCD), characterized by conjunctivalization of the cornea, were excluded. Institutional review board or ethics committee approval was obtained.

Results

During a 15-year period, 16 patients were identified with dendritiform keratopathy in association with the use of Opti-Free or

http://dx.doi.org/10.1016/j.ophtha.2015.10.063
ISSN 0161-6420/15

Table 1. Patient Characteristics

Patient No.	Age (yrs)	Gender	Unilateral or Bilateral Disease	Solution	Daily or Extended Wearing Schedule	Duration of Exposure	Misdiagnosis of Herpes Simplex Virus or *Acanthamoeba* Keratitis	Time to Resolution (wks)
1	60	F	Bilateral	Opti-Free, Systane	Daily	6 mos		2
2	17	F	Bilateral	Opti-Free	Daily	Unknown	*Acanthamoeba* keratitis	3
3	20	F	Bilateral	Opti-Free	Daily	4 mos		6
4	35	F	Bilateral	Opti-Free	Daily	4 mos	Both	6
5	76	M	Unilateral	Systane	—	3 mos		2
6	27	F	Unilateral	Opti-Free	Daily	2 mos		3
7	28	F	Bilateral	Opti-Free	Daily	Unknown		3
8	16	F	Bilateral	Opti-Free	Extended	Unknown	*Acanthamoeba* keratitis	3
9	37	F	Bilateral	Opti-Free	Daily	Unknown		5
10	22	F	Bilateral	Opti-Free	Daily	3 yrs	Herpes simplex virus	3
11	48	F	Unilateral	Equate	Daily	Unknown	Herpes simplex virus	4
12	24	F	Bilateral	Opti-Free	Daily	6 mos	*Acanthamoeba* keratitis	2
13	57	F	Bilateral	Opti-Free	Daily	Unknown	Both	4
14	61	F	Unilateral	Opti-Free, Systane	Extended	2 yrs	Herpes simplex virus	2
15	85	F	Unilateral	Systane	—	Unknown		4
16	65	M	Unilateral	Systane	—	Unknown		4

F = female; M = male.

Equate contact lens care products or with Systane tear replacement products (Table 1). Six cases were unilateral and 10 were bilateral. Eight patients with contact lens-related keratopathy had begun using lens care products containing polyquaternium-1 from 2 to 36 months before the onset of symptoms. In 8 patients, the exposure duration was unknown. All 3 with Systane-associated keratopathy had pre-existing ocular surface disease: 2 patients had tear deficiency, and 1 patient had completed topical mitomycin therapy for corneal intraepithelial neoplasia 1 month before the diagnosis of dendritiform keratopathy. One of the patients also used topical betaxolol 0.25% (preserved with benzalkonium chloride 0.001%). Rarely, the use of a topical β-blocker has been associated with dendritiform keratopathy.[2] However in this case, the keratopathy resolved after discontinuation of only the Systane product while continuing betaxolol. The dendritiform keratopathy had 3 main forms: (1) branching, coarse epitheliopathy with tiny nodular components scattered along the linear formation (Figs 1, 2, and 8); (2) a primarily linear keratopathy with minor branching (Figs 3, 4, and 9); and (3) whorl-like keratopathy (Figs 5, 7, and 10).

Case Reports

Patient 1. A 60-year-old woman was referred with a 1-month history of irritation of the right eye. She had been wearing daily wear soft contact lenses (DWSCLs) and used an Opti-Free brand contact lens solution for 6 months. The patient had been treated with prednisolone acetate 1% and Systane 4 times daily for 1 week without improvement. Contact lens wear had been discontinued for 2 weeks, but she continued to use Systane 4 times daily. Despite increase in the prednisolone regimen to 1 drop every hour for 1 week, she had persistent irritation. On examination, the conjunctiva was noninflamed. The superior cornea had a dendritiform lesion composed of thickened, gray epithelium located just superior to the visual axis. The limbus was normal. The stroma had minimal haze. The lesion persisted despite

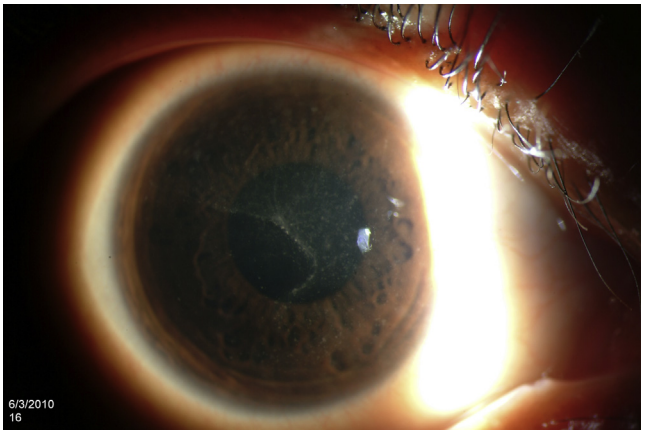

Figure 1. Slit-lamp photograph showing bilateral dendritiform keratopathy in patient 2 associated with daily wear soft contact lens wear and Opti-Free contact lens solution.

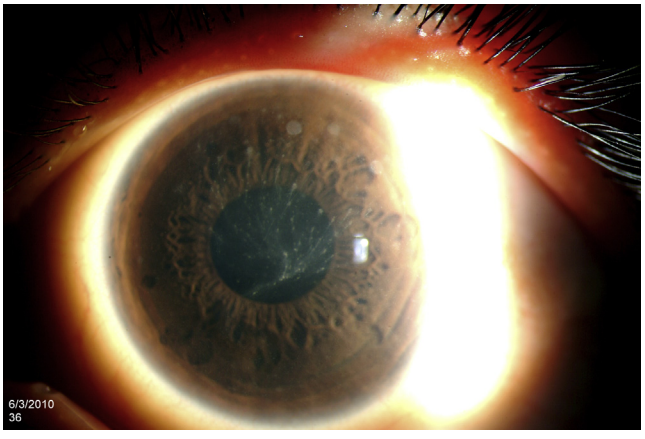

Figure 2. Slit-lamp photograph showing bilateral dendritiform keratopathy in patient 2 associated with daily wear soft contact lens wear and Opti-Free contact lens solution.