Idiopathic Limbal Squamous Metaplasia

Squamous metaplasia is an abnormal epithelial differentiation represented on the ocular surface by a spectrum of skin-like changes of conjunctival and corneal epithelium.1-3 This pathologic condition can be observed in a variety of ocular surface disorders, including systemic vitamin A deficiency and cicatricial keratoconjunctivitis.4 We recently encountered a patient with a progressively enlarging limbal epithelial ovoid lesion, who was given a histologic diagnosis of corneal and conjunctival squamous metaplasia of unknown cause. Herein we report this rare case and our successful surgical management of the lesion.

Report of a Case. An otherwise healthy 30-year-old man visited an eye clinic because of mild irritation and discomfort in his left eye. A slitlamp examination revealed a flat temporal ovoid lesion (approximately 4 mm x 6 mm) spanning the cornea and conjunctiva. The patient was treated with a short course of steroid and antibiotic eyedrops without improvement. A conjunctival biopsy was performed. Pathologic testing showed only squamous metaplasia, without evident dysplasia or carcinoma. After the biopsy, the lesion rapidly recurred and enlarged. The patient was referred to us for further evaluation 4 months later. He had worked at a gas station for several years. He did not wear contact lenses. A slitlamp examination revealed the large ovoid lesion (approximately 5 x 8 mm) with positive fluorescein staining (Figure 1A and B). The surface of the lesion was irregular, and a slightly raised epithelial ridge was noted. His corrected visual acuity was 20/16 OU. Intraocular pressure was 13 mm Hg OD and 12 mm Hg OS. Results of a Schirmer test without anesthesia were 11 mm OD and 10 mm OS. The remainder of the ocular examination findings were unremarkable. There was no evident maculopathy or retinal pigment epithelium changes in the fundus. The patient’s medical hist-

Figure 1. Slitlamp photographs. A, Left eye at the initial visit (4 months after a biopsy was performed elsewhere). An ovoid demarcated lesion was observed on the peripheral cornea and limbus. B, Fluorescein staining of the left eye shows the lesion extending from the peripheral cornea to the temporal bulbar conjunctiva. C, Left eye at 3 months after surgical excision. The cornea and conjunctiva were completely epithelialized, and no recurrence or neovascularization has been noted. D, Fluorescein staining of the left eye 3 months postoperatively. No fluorescein staining was observed on the cornea or conjunctiva.
tory was unremarkable. There was no history of nocturnal lagophthalmos.

Under the suspicion of possible xerophthalmia or zinc deficiency, laboratory work-ups were performed. The serum vitamin A level was 47.4 µg/dL (reference range, 28-80 µg/dL), serum retinal palmitate level was 2.8 µg/dL (reference range, <5 µg/dL), serum retinal binding protein level was 3.3 mg/dL (reference range, 2.4-7.0 mg/dL), and serum β-carotene level was 20.5 µg/dL (0.38 µmol/L) (reference range, <55.0 µg/dL [<1.02 µmol/L]). The serum level of zinc was 61 µg/dL (3.3 µmol/L) (reference range, 65-110 µg/dL [3.9-16.8 µmol/L]). The remainder of the laboratory test results were all negative.

A specimen for impression cytologic testing was obtained from the left temporal limbus and processed according to a published method.1 Cytologic analysis revealed that the unaffected superior bulbar conjunctiva was entirely normal (Figure 2A); however, the specimen imprinted from the lesion showed diffuse keratinization, squamous metaplasia, and total loss of goblet cells, graded as stage 4 (Figure 2B and C).1 No cellular dysplasia or malignancy was observed.

After informed consent was obtained, surgical debridement of the corneal lesion (leaving the stroma intact) and resection of the conjunctival lesion, including a ring of presumably normal conjunctiva (1 × 1 cm), were performed. Histologic examination of the excised conjunctival specimen showed mild keratinization with moderate inflammatory infiltrates in the affected conjunctival epithelia (Figure 2D). No dysplasia or malignancy was observed.

Postoperatively, 0.3% ofloxacin and 0.1% betamethasone were applied 4 times daily for 1 month. As a result, the lesion was epithelialized successfully within 1 week, and the patient’s irritation and discomfort disappeared. Zinc supplements were prescribed to ameliorate his mild zinc deficiency. Normal conjunctival and corneal phenotypes of the healed lesion were confirmed by impression cytologic analysis. No recurrence was observed after 1 year of follow-up (Figure 1C and D).

Comment. We described an enlarging limbal epithelial lesion in a healthy man. Initially, a conjunctival intraepithelial neoplasm was suspected; however, repeated examination of the excised specimen and impression cytologic analysis of the lesion showed neither malignancy nor dysplasia, but only focal squamous metaplasia.

Squamous metaplasia of the ocular surface occurs in the pres-
ence of chronic inflammation and irritation, often in association with dry eyes, cicatrizing diseases, and inflammation. In this patient, cicatricial keratoconjunctivitis, ie, ocular pemphigoid, drug-induced pseudopemphigoid, Stevens-Johnson syndrome, or chemical burns, was not observed. Moreover, the signs and symptoms did not suggest evidence of other types of chronic keratoconjunctivitis, such as superior limbic keratitis, graft-vs-host disease, or atopic keratoconjunctivitis. Systemic vitamin A deficiency is also known to cause squamous metaplasia of the ocular surface, characterized by a Bitot spot: a superficial, foamy, gray triangular area on the bulbar conjunctiva that appears in the palpebral aperture. This spot consists of keratinized epithelium, inflammatory cells, debris, and Corynebacterium xerosis. Results of conjunctival histologic and impression cytologic analysis suggested that the lesion was a Bitot spot; however, systemic vitamin A deficiency was ruled out by the laboratory examination. We also suspected that this patient might have local squamous metaplasia at the limbus or nocturnal lagophthalmos with chronic exposure. However, none of this could be proven.

Systemic zinc deficiency can lead to xerosis of the skin. On laboratory examination, it was revealed that this patient had mild zinc deficiency. He was treated with oral zinc supplementation. Zinc is necessary in trace amounts in the body, and hence, in the diet. It forms an essential part of many enzymes and plays an important role in protein synthesis and cell division. Zinc deficiency is associated with growth retardation, alopecia, impaired spermatogenesis, impaired wound healing, and hyperkeratosis of the skin. Although the association of zinc with squamous metaplasia of the ocular surface has not been reported yet, zinc deficiency might be a contributory cause of the lesion in this patient.

We performed surgical excision of the lesion. The patient responded well to the excision and zinc supplementation, and there has been no recurrence to date. The precise cause of the limbal squamous metaplasia in this patient remains unclear.

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The authors have no relevant financial interest in this article.

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Unilateral Tuberculous Conjunctivitis With Tarsal Necrosis

Conjunctival tuberculosis, although a well-established clinical entity in the literature, could masquerade as other forms of conjunctivitis. A diagnostic biopsy, confirmed by a molecular method of diagnosis, may be warranted. We report 2 cases of chronic granulomatous conjunctivitis of tuberculous origin, confirmed by histopathologic and molecular diagnostic techniques. The associated tarsal necrosis in these 2 patients was presumably a sequel of supratarsal depot corticosteroid injections, administered for papillary conjunctivitis of suspected allergic origin. These 2 cases highlight the need for a systematic approach for determining the cause and instituting appropriate treatment.

Report of Cases. Case 1. A 15-year-old girl had a 6-month history of a mass in her left eye. Elsewhere, she was diagnosed and treated for phlyctenular conjunctivitis, nodular episceratitis, and vernal keratoconjunctivitis, with no significant improvement. She had received a supratarsal injection of triamcinolone acetonide in the left upper eyelid a month earlier for presumed vernal keratoconjunctivitis. There was no history suggestive of infectious disease or allergies. Preauricular and cervical lymph nodes were not palpable. Laboratory work-up for collagen vascular disorders and erythrocyte sedimentation rate, chest radiographs, Mantoux test, and immunoglobulin G and immunoglobulin M titers for tuberculosis revealed no abnormality. The best-corrected visual acuity was 20/20 OD and 20/60 OS. The results of an examination of the right eye were unremarkable. The left upper tarsal conjunctiva had giant papillae with necrosis laterally. An ulcerated conjunctival mass (6-mm diameter) was noted at the superior limbus contiguous with an ulcer extending 3 mm on the cornea (Figure 1A and B). Fine keratic precipitates and 1+ cells and flare were seen. Results of a fundus examination of this eye were normal.

A clinical diagnosis of keratoconjunctivitis, tarsal necrosis, and nongranulomatous anterior uveitis was made. Scrapings from the cornea and upper tarsus subjected to Gram stain, Giemsa stain, and potassium hydroxide with calcofluor white stains showed no organisms. There was no improvement after 2 days of hourly fortified cefazoline (50 mg/mL) and gentamicin (14 mg/mL) eye drops. The cultures for bacteria and fungi were sterile. After obtaining informed consent, a diagnostic biopsy of the conjunctival lesion was performed under peribulbar anesthesia. The raw bulbar surface was covered with preserved human amniotic membrane. The underlying sclera was healthy, and no areas of necrosis were noted. The peripheral thinned cornea was covered with cya-

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