ence of chronic inflammation and irritation, often in association with dry eyes, cicatrizing diseases, and inflammation.\(^5\)\(^6\) In this patient, cicatrical 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 limbal keratitis, graft-vs-host disease, or atopic keratoconjunctivitis. Systemic vitamin A deficiency is also known to cause squamous metaplasia of the ocular surface,\(^5\) 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.\(^6\) 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.\(^6\) 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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Unilateral Tuberculous Conjunctivitis With Tarsal Necrosis

Conjunctival tuberculosis, although a well-established clinical entity in the literature,\(^1\) could masquerade as other forms of conjunctivitis. A diagnostic biopsy, confirmed by a molecular method of diagnosis, may be warranted.\(^2\)\(^3\) 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 episcleritis, 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-
noacrylate tissue adhesive. An aqueous tap was done and submitted for polymerase chain reaction.

Case 2. A 31-year-old woman had a 6-month history of multiple conjunctival nodules with central ulceration in the right eye and exacerbation of inflammation despite a course of topical and systemic steroids. Supratarsal depot triamcinolone acetonide and cryoexy of the lesions were ineffective. On examination, her best-corrected visual acuity was 20/20 OU. The left eye was unremarkable. In the right eye, she had an elevated mass with necrosis of the overlying conjunctiva in the superior fornix, extending up to the limbus. The upper tarsal conjunctiva had diffuse papillary hyperplasia with necrosis laterally (Figure 1C and D). The remaining anterior and posterior segments were normal. On suspicion of conjunctival tuberculosis, a diagnostic biopsy of the superior bulbar and tarsal conjunctiva was performed under peribulbar anesthesia. Preserved human amniotic membrane was used to reconstruct the ocular surface.

Histopathologic examination of the bulbar conjunctiva from both cases revealed epithelioid granulomas with giant cells (Figure 2). In addition, sections from the upper tarsus of case 2 revealed epithelioid granulomas with multinucleated giant cells, central caseous necrosis, and acid-fast bacilli in Ziehl-Neelsen-stained sections (Figure 3). Polymerase chain reaction performed on the formalin-fixed, paraffin-embedded tissue sections of bulbar conjunctiva from case 1 (Figure 4) and bulbar and tarsal conjunctiva of case 2 (data not shown) were positive for Mycobacterium tuberculosis DNA. The aqueous tap was negative for Mycobacterium tuberculosis and herpes simplex virus DNA.

After we confirmed the diagnosis of tuberculosis in both cases, the patients started receiving the recommended antituberculosis regimen1 for a year, along with tapering doses of topical prednisolone acetate (1%) and ciprofloxacin hydrochloride (0.3%) for 6 weeks. One year later, the best-corrected visual acuity in case 1 was 20/20, and the conjunctival and eyelid lesions had healed completely (Figure 5A), with resolution of anterior uveitis. In case 2, all lesions, with the exception of one, had healed at 3

Figure 1. A, Left eye, case 1. Bulbar conjunctival mass contiguous with a peripheral corneal ulcer with 80% stromal thinning. B, Everted upper eyelid shows diffuse papillary reaction with tarsal necrosis laterally. C, Right eye, case 2. Down-gaze shows ulcerated bulbar conjunctiva. D, Everted upper eyelid shows diffuse velvety appearance, with cheesy white areas of necrosis involving the upper tarsal border.

Figure 2. Case 1. Section from the bulbar conjunctiva shows an intact epithelium with discrete epithelioid cell granuloma in the deeper stroma, rimmed by lymphocytes (hematoxylin-eosin; original magnification ×250).

Figure 3. Case 1. Section from the bulbar conjunctiva shows an intact epithelium with discrete epithelioid cell granulomas in the deeper stroma, rimmed by lymphocytes (hematoxylin-eosin; original magnification ×1100).
She has been advised to continue the antitubercular medication.

Comment. Conjunctival tuberculosis is a well-established clinical entity, and may appear as an ulcerative lesion, miliary tubercle, hypertrophic granulation, lupus, or pedunculated mass. Although sys-
Etiologic tuberculosis is common in India, ocular tuberculosis is rare. A long-standing, undiagnosed, and untreated unilateral limbal lesion may lead to secondary tarsal inflammation as seen here, raising the suspicion of an allergic origin. An intraleisional depot corticosteroid could lead to tarsal necrosis, as demonstrated in these 2 cases.

In both cases, the presence of epithelioid granulomas with central caseation necrosis, Langhan giant cells, and the demonstration of acid-fast bacilli by Ziehl-Neelsen stain confirmed the diagnosis of tuberculous conjunctivitis. This was corroborated by nested polymerase chain reaction, using primers specific for the DNA of M. tuberculosis.

Papillary conjunctivitis is a nonspecific sign associated with acute or chronic inflammation. In these 2 cases, the associated papillary conjunctivitis could be an additional sign of conjunctival tuberculosis or a reactive process resulting from chronic irritation and friction caused by the long-standing mass in the upper bulbar conjunctiva. We speculate that the treating ophthalmologists mistook the papillae for the giant papillae seen in vernal keratoconjunctivitis, and administered the supratarsal depot corticosteroid. This probably resulted in a flare-up of the underlying undiagnosed conjunctival tuberculosis, resulting in tarsal necrosis. While a biopsy of the tarsus was not performed in the first case, owing to extensive necrosis, caseating granulomas with acid-fast bacilli were demonstrated in the second case. The lack of response to anti-inflammatory medication, tarsal necrosis, and demonstration of acid-fast bacilli in the second case pointed to primary involvement of the tarsal conjunctiva in the disease process rather than a secondary nonspecific inflammation. These 2 cases highlight the fact that the tarsal necrosis could mimic a secondary nonspecific inflammation suggestive of an allergic cause, leading to an alternate mode of management that may have adverse effects. Following systemic evaluation for tuberculosis and human immunodeficiency virus by an internist, both patients were prescribed antitubercular drugs per the recommended regimen. Amniotic membrane transplantation aided in ocular surface reconstruction.

The causes of granulomatous inflammations of the conjunctiva include sarcoidosis, tuberculosis, Parinaud ocular glandular syndrome, syphilis, leprosy, coccidiodomycosis, tularemia, parasites, and foreign bodies. In patients with chronic unilateral conjunctivitis refractory to routine therapy, a diagnosis of neoplasia and floppy eyelid syndrome needs to be considered. Thorough clinical evaluation and histologic features of the excised tissue (granulomatous lesion, presence or absence of necrosis, associated inflammatory cell response) and identification of the possible infectious agents by special stains and molecular methods help differentiate these lesions.

Conjunctival scrapings and biopsy specimens may have a low sensitivity for the detection of acid-fast organisms, requiring approximately 1000 to 100,000 organisms per milliliter of sample for morphologic detection and 100 to 1000 viable organisms per milliliter for a positive culture. This could explain the absence of organisms in the initial conjunctival and corneal scrapings. Polymerase chain reaction, based on the principle of DNA amplification, is highly sensitive and can detect as few as 10 microorganisms. This is a useful modality when special stains do not reveal organisms in the presence of caseating granulomas.

In summary, patients with chronic unilateral conjunctivitis need a detailed evaluation, including a conjunctival biopsy, and if possible, molecular diagnostic techniques for rapid diagnosis and institution of appropriate treatment. A high index of suspicion for tuberculosis is warranted before administering intralesional depot corticosteroid injections, as this may result in a flare-up of the underlying infection and lead to tarsal necrosis.

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