JAMA Ophthalmology Clinical Challenge

A Man With a Cloudy Cornea

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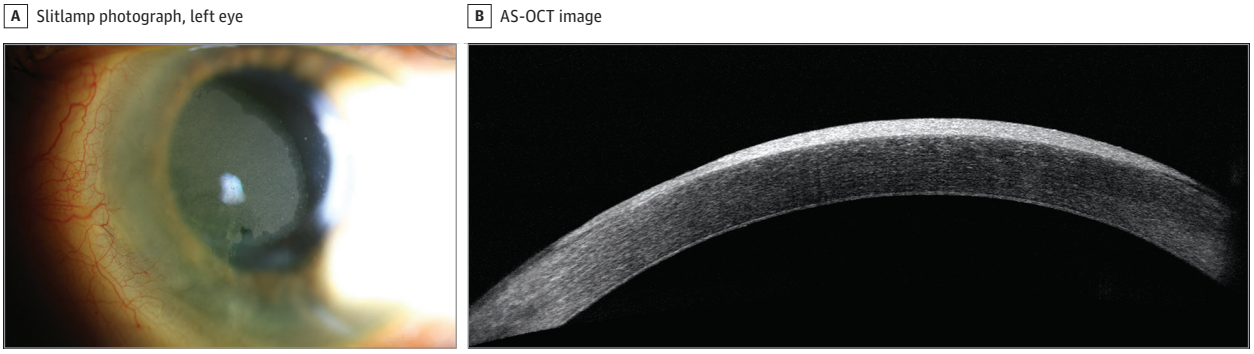

Figure 1. Examination findings at presentation. A, Slitlamp photograph of the left cornea revealing a translucent gray, lusterless lesion that extends into the visual axis. B, Anterior segment optical coherence tomography (AS-OCT) showing hyperreflective thickened epithelium.

A 77-year-old man was referred to the cornea service for painless, progressive blurring of vision in his left eye. His best-corrected visual acuity was 20/40 OS, and the patient reported that his vision had waxed and waned over several months. His ocular history included cataract surgery in the left eye, followed by yttrium-aluminum-garnet capsulotomy 2 months before his referral. Of note, he had recently undergone Mohs surgery and subsequent reconstruction for squamous cell carcinoma in situ of the lateral canthus in the fellow eye; he also had a medical history of multiple skin malignant neoplasms.

Slitlamp examination findings were notable for a grayish cornea opacity that appeared to be lusterless, abutting the nasal limbus and extending into the visual axis (**Figure 1**A). There was no apparent conjunctival erythema or appreciable feeder vessels at the limbus. The rest of the examination findings, including the fundus, were unremarkable. Anterior segment optical coherence tomography (AS-OCT) indicated that the hyperreflective corneal lesion did not involve the cornea stroma (Figure 1B).

WHAT WOULD YOU DO NEXT?

- **A.** Discuss superficial keratectomy to confirm the diagnosis by histopathologic examination
- **B.** Discuss calcium chelation with EDTA therapy
- **C.** Discuss penetrating keratoplasty
- **D.** Observation with follow-up for changes over the next 6 to 12 months

Quiz at jamacmelookup.com

Diagnosis

Corneal intraepithelial neoplasia

What to Do Next

A. Discuss superficial keratectomy to confirm the diagnosis by histopathologic examination

Discussion

Calcium chelation with EDTA therapy (choice B) is not recommended because the appearance and location of the lesion are atypical for band keratopathy. Performing a penetrating keratoplasty (choice C) would not be indicated because the lesion is superficial and does not affect the deeper cornea stromal layers. Finally, observation (choice D) would not be preferred because the patient is experiencing visual issues due to the lesion, and other conditions, such as a malignant neoplasm, should be excluded.

Corneal intraepithelial neoplasia (CIN), also known as corneal epithelial dysplasia, is usually grouped with conjunctival intraepithelial neoplasia under the broader classification of ocular surface squamous neoplasia (OSSN). Ocular surface squamous neoplasia is one of the most common ocular tumors in the US and is generally found in males of advanced age.[1] Risk factors include prolonged exposure to UV light, infection with human papillomavirus or human immunodeficiency virus, smoking, and immunosuppression.[2] Patients customarily present with nonspecific progressive symptoms of painless vision loss, which may be associated with ocular foreign body sensation or redness.[3] Corneal intraepithelial neoplasia onset is typically in the limbal area, with a gradual extension toward the

central visual axis. Lesions may or may not be accompanied by neovascularization.

Given its translucent, lusterless, sheetlike appearance, CIN may be misdiagnosed as a corneal dystrophy, corneal pannus, pterygium, or viral keratitis.[3] Although rare, Lisch epithelial dystrophy may present asymmetrically, and look similar to CIN on clinical examination.[4] Histopathologic examination can be valuable for confirming the diagnosis. Histologically, dysplastic cells stain for vimentin and keratin 14.[3]

Impression cytology, high-definition AS-OCT, and in vivo confocal microscopy (IVCM), have all been described in establishing the diagnosis of CIN/OSSN.[1,3,5,6] Impression cytology requires an expert ocular pathologist and cannot differentiate between dysplasia and invasive squamous cell carcinoma of the deeper layers.[3] More recent publications on AS-OCT and IVCM have reported on the use of these noninvasive techniques to provide "optical biopsies" in establishing the diagnosis as well as for early detection of recurrent or residual disease.[1,3,6] In CIN, AS-OCT demonstrates hyperreflectivity and thickening of the epithelium.[1,6] In vivo confocal microscopy has been reported to correlate well with histologic findings in CIN.[3] The major limitation of IVCM, however, is its inability to provide either cross-sectional views or an entire scan of the whole ocular surface, making it difficult to correlate scans in follow-up imaging (**Figure 2**).

Traditionally, treatment for OSSN was surgical excision with or without adjunctive cryotherapy.[6,7] However, this method has a recurrence rate ranging between 33% and 56%.[6] The translucency of the lesion can make it challenging to determine, by clinical examination alone, the extent of conjunctival involvement as the subclinical microscopic disease can be missed.[1] The most popular gold standard is to combine surgical excision with the addition of chemotherapeutic drops, such as interferon alfa-2b, fluorouracil, or mitomycin C.[1] Interferon alfa-2b is often the preferred option because of its efficacy and limited side effects, but it can be more expensive.[1,6,8]

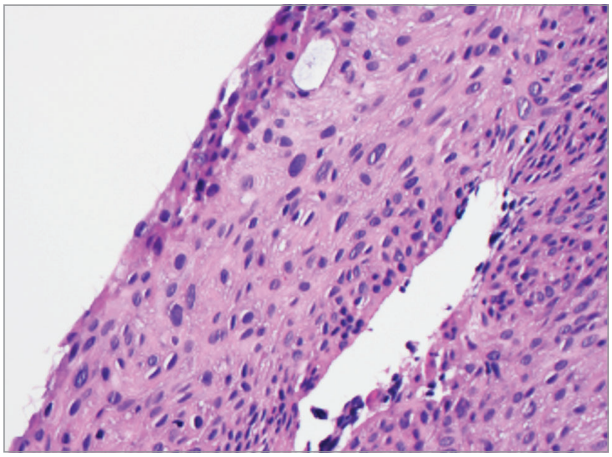

Figure 2. Pathology specimen. Photomicrograph of a cross-section of corneal squamous epithelium with dysplasia of the basal layers characterized by disorganization, lack of maturation, and nuclear atypia (hematoxylin-eosin; original magnification ×400).

Patient Outcome

The patient's histopathology confirmed the diagnosis of corneal intraepithelial neoplasia, and he underwent interferon alpha-2b topical treatment. He did not have any signs of recurrence at his last follow-up visit.

ARTICLE INFORMATION

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