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Cystoid corneoscleral squamous cell carcinoma

Ocular surface squamous neoplasia (OSSN) is a term that incorporates dysplastic lesions originating within the epithelium of the conjunctiva or cornea, including conjunctival intraepithelial neoplasia (CIN) and invasive squamous cell carcinoma. When occurring at the limbus—the most common location—a gelatinous, papillary, or leukoplakic appearance is displayed.[1] Corneal extension usually displays a thin, translucent, grey "frosted" zone. We describe herein an unusual case of limbal conjunctival squamous cell carcinoma that extended as a substantial mass onto the cornea and contained multiple clinically-apparent microcysts. Some "cysts" were lined by atypical epithelial cells that stained positively—along with adjacent malignant epithelium—for cytokeratin 19 (CK19), a conjunctival marker. The lumens contained necrotic cellular remnants and keratinaceous debris. These cystoid foci most likely represented pockets of necrosis that were unavailable for clearing by macrophages. Other cysts appeared to be lined by benign epithelium and probably stemmed from entrapped pseudoepitheliomatous hyperplasia within the malignancy. To our knowledge this is the second report of cystoid conjunctival carcinoma in the literature.[2]

Case Report

A 59-year-old man complained of redness, irritation, and blurred vision of the right eye 3 years previously after "pollen got into the eye." Punctate keratopathy was observed at another institution and was treated with artificial tears and fluorometholone eye drops. The patient also tried home remedies, including tap water, salt water, and eucalyptus oil with minimal relief. An elevated mass gradually formed at the limbus. There was no history of immunosuppression or infection by human immunodeficiency or human papilloma viruses. He was a nonsmoker.

On presentation, visual acuity was 20/25 OD and 20/20 OS. A thick, dome-shaped gelatinous lesion at the inferonasal limbus extended over 3 clock hours and overlay the cornea. A leukoplakic area was present along with prominent feeder vessels. Numerous small white spots were present within the lesion (Fig. 1A). The remainder of the eye examination was unremarkable. A partial-lamellar excision of conjunctiva, sclera, and cornea was performed, including double freeze-thaw cryotherapy and alcohol ablation of epithelium. The ocular surface was reconstructed with an amniotic membrane graft. Subsequently, topical alfa-interferon 2b was administered, and visual acuity remained 20/25 at 3 months.

Pathologic examination showed an invasive epithelial tumour exhibiting marked cytologic atypia (squamous cell carcinoma) (Fig. 1C and D). The tumour surface displayed hyperkeratosis and parakeratosis corresponding to the clinical leukoplakia. Within the carcinoma were multiple variably sized minute cystic spaces, some as large as 0.8 mm, that were lined by atypical conjunctival epithelium and filled either with a proteinaceous material or cellular debris (Fig. 2A and B). The microcysts' malignant

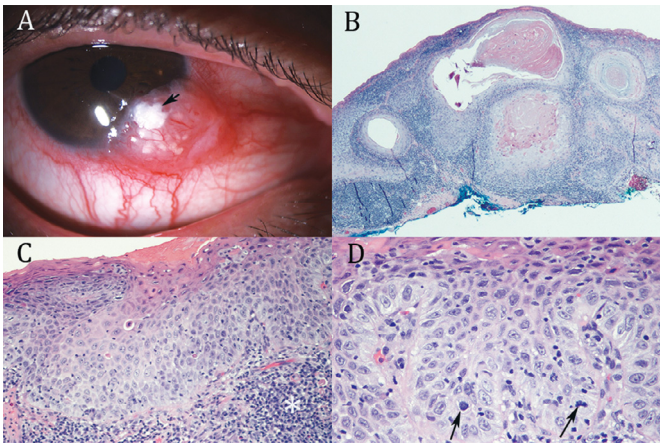

Fig. 1—A, Limbal lesion extending onto cornea with superficial focus of leukoplakia (arrow) and multiple microcysts. B, Low power view of lesion with 4 microcysts. C, Parakeratotic, hyperkeratotic proliferation of atypical keratinocytes with underlying inflammation (asterisk). D, High power view of pleomorphic cells with mitotic figures (arrows). (B–D, hematoxylin and eosin, 20 ×, 200 ×, 400 ×.)

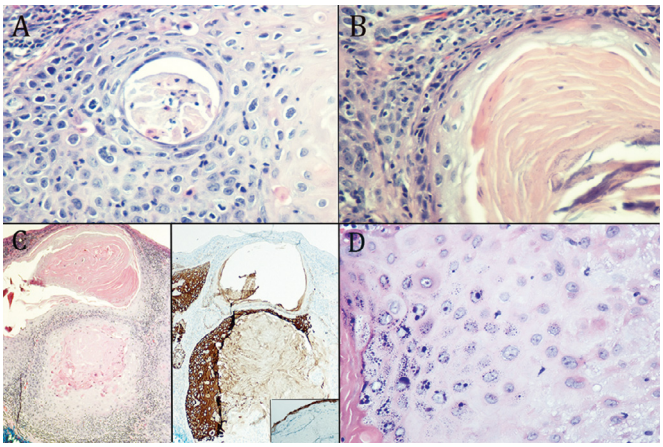

Fig. 2—A, Pseudocyst lined with malignant epithelium and filled with degenerating cells. Note the enlarged, elongated nuclei in the lining cells. B, A larger cyst lined by normal-appearing epithelium contains acellular lamellar debris. C, Left panel shows 2 cystoid foci that are partially lined (right panel) by cytokeratin 19-positive cells, a marker for conjunctival epithelium. The insert shows benign conjunctival epithelium at the periphery of the specimen that is cystokeratin 19-positive (an "internal control"). D, Pseudoepitheliomatous hyperplasia is present in the superficial keratinizing portion of the lesion. (A–D, hematoxylin and eosin, 250 ×, 250 ×, left panel 20 ×, 400 ×. C right panel immunoperoxidase reaction, diaminobenzidine chromogen 20 ×, inset 40 ×.)

"linings" and contiguous squamous cell carcinoma stained positively with CK19, along with bordering normal conjunctiva (Fig. 2C). Ki67 showed a 30% proliferation rate within the malignant epithelial cells, and p53 highlighted the full thickness of zones of cellular atypia. Additional cysts were lined by a more benign-appearing epithelium. A dense subepithelial lymphoid infiltrate contained approximately equal portions of CD3-positive T cells and CD20-positive B cells, denoting an inflammatory, nonneoplastic nature. Bcl2 demonstrated no germinal centers. HMB-45 showed no melanocytes, ruling out a cystic naevus component. Alcian blue stain disclosed no goblet cells within the microcysts and no mucinous pools within the tumour, militating against the diagnosis of mucoepidermoid carcinoma.

Discussion

The pathogenesis of the cystic foci in this lesion remains elusive. It is plausible, however, that some of these foci derived from pockets of necrosis that were unavailable for macrophagic clearance within an unusually thick malignant epithelial lesion. (A true cyst, in contrast, is a cavity lined by benign epithelium or endothelium that is usually surrounded by stroma.) The single previous report describing 2 cases of microcysts within CIN illustrates microscopically minute spaces that were much smaller than those of the current case but probably share a parallel pathogenesis. An electronic microscopic analysis suggested that they originated from disintegrating cells that were enveloped by adjacent cells without being phagocytosed.[2] Cystoid change is well recognized in squamous cell carcinoma elsewhere in

the body, notably in metastatic lymph nodes of head and neck carcinomas.[3]

Additional cysts with the malignant tumour appeared to be lined by a bland, benign- appearing epithelium. It is conceivable that the latter cysts originated in entrapped zones of pseudoepitheliomatous hyperplasia within the carcinoma. Pseudoepitheliomatous (pseudocarcinomatous) hyperplasia is a well-known, benign, reactive process to both chronic inflammation and true neoplasia. Considering the history, it is possible that a pre-existing benign proliferative stage was operative in this case.

The fortuitous presence of a cystic naevus in the current case was eliminated by the absence of nevocytes and the negativity of HMB-45 and S-100 immunostains. True epithelial-lined microcysts within conjunctival nevi are assumed to involve "dragging down" of surface epithelium by nevocytes during maturation.[4] Their presence in conjunctival cystic benign melanosis involves no such dragging and remains etiologically obscure.[5] The microcysts of conjunctival nevi are usually much smaller than in the current case but occasionally reach a large size.[6] Corneal, but not conjunctival, microcysts have been described as a toxic complication of topical alfa-interferon 2b therapy;[7] however, their pretreatment presence eliminates that possibility in this case.

The epithelium of conjunctival and corneal epithelium may be differentiated using highly specific cytokeratin immunostains.[8] The CK19 immunostain, a specific marker for conjunctiva, was employed in our case to further delineate the nature of the malignancy.

The robust inflammatory reaction in this case is much greater than that usually associated with OSSN. Whether the inflammation resulted from the patient's unusual self-treatment and whether that treatment was causative in the development of malignancy remains speculative.

Cystoid OSSN represents an unusual variant of conjunctival malignancy. It should be distinguished from the other entities—usually benign—on the spectrum of conjunctival cystic disorders.

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Corneal atypical fibroxanthoma in xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a rare autosomal recessive disease caused by a mutation in DNA repair genes, particularly those involved in nucleotide-excision repair. This mutation leads to increased sensitivity to ultraviolet (UV) light. Therefore, patients with XP have a high risk of developing cancerous skin lesions at a young age when exposed to sunlight.[1] Cutaneous malignancies commonly seen in XP patients include squamous cell carcinomas, basal cell carcinomas, and malignant melanomas.[2] Ocular and neural abnormalities have also been reported.[3]

Atypical fibroxanthoma (AFX) is a mesenchymal tumour that primarily affects the head and neck; it most commonly occurs in elderly patients and is related to UV sun damage. AFX is a diagnosis of exclusion that must always be distinguished from pleomorphic spindle cell melanoma, sarcomatoid (spindle cell) squamous cell carcinoma, leiomyosarcoma, dermatofibrosarcoma protuberance, epithelioid angiosarcoma, and pleomorphic dermal sarcoma, which is the current designation for a superficial malignant fibrous histiocytoma. Although AFX mimics malignant fibrous histiocytoma histologically, it behaves in a benign manner. The tumour is locally aggressive and rarely metastasizes, with a recurrence rate of less than 5%.[4] AFX has rarely been reported in the eyelid[5] or conjunctiva.[6]

Herein, we describe a 17-year-old female with known XP, who presented with AFX arising from the lamina propria of the cornea. To the best of our knowledge, this is the first instance of AFX in a patient with XP.

A 17-year-old female with known XP presented to the eye clinic with a corneal lesion in her right eye (Fig. 1A). Her visual acuity was 20/40 and 20/50 at presentation. On