Lacrimal Gland Hamartoma (Formerly Termed Dacryoadenoma)

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• PURPOSE: Since the original description of "dacryadenoma" by Jakobiec and associates, the data on this unusual epibulbar lacrimal gland lesion remain sparse. The aim of this study was to characterize clinically, morphologically, and immunohistochemically this isolated epibulbar lacrimal gland lesion.
• DESIGN: Retrospective observational case series.
• METHODS: Institutional pathology records between 2000 and 2019 were searched for all cases of isolated epibulbar lacrimal gland lesions. Tissue from 3 normal lacrimal glands and 1 complex choristoma were included for comparative analysis. Clinical, histopathologic, and immunohistochemical findings were recorded.
• RESULTS: Four patients with isolated epibulbar lacrimal gland lesions, 2 male and 2 female, with a median age of 18 years (range, 12-57) were identified. All patients presented with recent onset of unilateral pink-to-orange, well-circumscribed subepithelial juxtaforniceal (3/4, 75%), or nasal (1/4, 25%) bulbar conjunctival nodules, which were asymptomatic (3/4, 75%) or associated with foreign body sensation (1/4, 25%). When compared with the normal lacrimal gland and complex choristoma, all isolated epibulbar lacrimal gland lesions were composed predominantly of variably dilated, branching tubular structures with pseudo-apocrine snouts, and either totally absent (2/2, 50%) or rare (2/2, 50%) ducts and rare acinar zymogen granules (3/4, 75%).
• CONCLUSION: Our study confirms that a subset of isolated epibulbar lacrimal gland lesions differs morphologically and immunohistochemically from normal lacrimal gland tissue and the lacrimal gland in a complex choristoma. These differences range from subtle to overt, suggesting that isolated epibulbar lacrimal gland lesions may have originated from precursor cellular elements indigenous to the conjunctiva (hamartia) and grew into disorganized lacrimal gland tissue. (Am J Ophthalmol 2020;217:189–197. © 2020 Elsevier Inc. All rights reserved.)

INTRODUCTION

SINCE THE ORIGINAL DESCRIPTION OF A SINGLE PATIENT with conjunctival dacryadenoma by Jakobiec and associates in 1989, the data on the clinical and pathologic features of this lesion have been sparse and generally limited to article reviews and textbook chapters citing the original publication.[1–4] In pathology practice, the distinction between this intriguing, presumably neoplastic lesion, and the congenital, heterotopic epibulbar lacrimal gland tissue, also known as lacrimal gland choristoma, is made infrequently. In this study we describe the clinical, morphologic, and immunohistochemical features of 4 epibulbar lacrimal gland lesions and compare these lesions to the normal main lacrimal gland tissue and to the congenital ectopic lacrimal gland tissue in a complex choristoma.

MATERIALS AND METHODS

THE WILLS EYE HOSPITAL INSTITUTIONAL REVIEW BOARD approved this retrospective observational case series and deemed that the informed consent was not required for this study. The study was performed in compliance with HIPAA guidelines and with the tenets of Declaration of Helsinki.

• PATIENT AND TISSUE SELECTION: Wills Eye Hospital Pathology records were searched for all cases of epibulbar ectopic lacrimal gland/lacrimal gland choristoma/dacryoadenoma between December 1, 2005, and December 1, 2019. Morphologically normal main lacrimal gland tissue from 3 patients (3 main lacrimal glands and 1 accessory lacrimal gland) and congenital ectopic lacrimal gland tissue from 1 patient with complex choristoma were selected for comparative analysis. Medical records of identified patients were reviewed. Data collected included patient's

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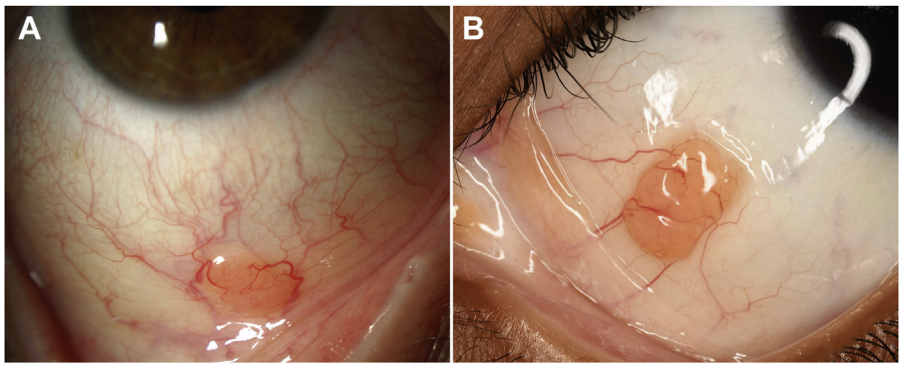

FIGURE 1. Clinical characteristics of isolated epibulbar lacrimal gland lesions. A. Patient 4. Well-circumscribed pink-orange, vaguely lobulated, subepithelial mass with feeder vessels involves the right inferior bulbar conjunctiva close to the fornix. B. Patient 2. Well-circumscribed, pink-orange, lobulated, subepithelial mass with feeder vessels involves the inferonasal bulbar conjunctiva, close to the plica semilunaris and the fornix.

age, sex, presenting symptoms and their duration, clinical findings at presentation, management, and follow-up information.

• **HISTOPATHOLOGY:** Routine sections stained with hematoxylin-eosin (2-5 sections per tissue), periodic acid-Schiff postdiastase (PAS/D), Masson-trichrome, and Alcian blue were prepared from paraffin-embedded, formalin-fixed tissues. Morphologic parameters assessed included the contiguity of the conjunctival lesions with the surface epithelium, morphology of the ductular and acinar elements, and cellular constituents of the intervening stroma.

• **IMMUNOHISTOCHEMISTRY:** Immunostaining was performed with the following primary antibodies: SOX10 (prediluted; Biocare, Yorba Linda, CA, USA), S100 (prediluted; DAKO, Carpinteria, CA, USA), smooth muscle actin (SMA) (1:600; DAKO), calponin (1:300; DAKO), p63 (prediluted; Biocare), cytokeratin (CK) 5/6 – antigen CK5, major partner of CK14 (prediluted; DAKO), and mammaglobin (prediluted; DAKO). Peroxidase activity was visualized by applying diaminobenzidine solution containing 0.05% H_2O_2. Sections were counterstained with modified Mayer's hematoxylin, dehydrated, cleared, and mounted. Appropriate positive and negative controls were run with each batch. All immunohistochemical stains were prepared on Leica autostainer BOND III in accordance with the manufacturer's instructions.

Immunohistochemical stains were scored semiquantitatively based on the strength of cytoplasmic (S100, SMA, calponin, CK5/6, and mammaglobin) and nuclear (SOX10, S100, and p63) expression as (–) no staining, (+) weak staining, (++) moderate staining, and (+++) strong staining. The tissue distribution of the reaction product also was recorded.

RESULTS

• **CLINICAL CHARACTERISTICS:** Review of pathology medical records identified 4 patients with isolated epibulbar lacrimal gland lesions, 2 male and 2 female, with a median age of 18 years (average, 26; range, 12-57). All patients presented with unilateral pink-to-orange, well-circumscribed subepithelial inferior juxtaforniceal (2/4, 50%), superior juxtaforniceal (1/4, 25%), or nasal juxtaplica semilunaris (1/4, 25%) bulbar conjunctival nodules (Figure 1), which were asymptomatic in 3/4 (75%) patients and associated with foreign body sensation in 1 patient (25%). Duration of symptoms ranged from several months to 1 year. The leading clinical diagnoses were lymphoproliferative lesions (2/4, 50%), fibrous histiocytoma (1/4, 25%), and cyst (1/4, 25%). Lacrimal gland choristoma and dacryoadenoma were not considered in the differential diagnoses of any of these lesions. All lesions were excised with no recurrence (average follow-up 4 months; range 1-12 months). Two lesions (2/4, 50%) bore the pathologic diagnosis of "dacryoadenoma" and 2 lesions (2/4, 50%) were diagnosed as "ectopic lacrimal gland/lacrimal gland choristoma." One of these cases was received in consultation. The clinical characteristics of the patients with isolated epibulbar lacrimal gland lesions, three normal lacrimal gland biopsies, and one complex choristoma are summarized in Supplemental Table 1.

• **HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY:** The synopsis of morphologic and immunohistopathologic differences between "dacryadenoma" and normal lacrimal gland biopsies is provided in the Table.

The 3 normal lacrimal gland tissues and the ectopic lacrimal gland in a complex choristoma demonstrated morphologically well-defined intralobular and interlobular ducts, composed for the most part of a cuboidal ductal bilayer with outer basal cells and inner luminal cells. The

TABLE. Lacrimal Gland Hamartoma (Dacryoadenoma) Versus Normal Lacrimal Gland: Synopsis of Morphologic and Immunohistochemical Differences

Pathologic Feature	Normal Lacrimal Gland	Lacrimal Gland Hamartoma (Dacryadenoma)
Morphology		
Overall architecture within a lobule	Orderly arrangement of acinar units draining into intralobular ducts, which drain into interlobular ducts	Haphazard arrangement of tubular and acinar units
Ducts	• Intralobular and interlobular ducts composed of low cuboidal epithelial-basal cell bilayer • Short segment of intralobular duct directly adjacent to acinus composed of low cuboidal epithelial-myoepithelial bilayer	• Mostly composed of irregular tubular units lined by cuboidal-to-columnar epithelium with pseudo-apocrine snouts and outer myoepithelial layer • Absent to rare ducts composed of low cuboidal epithelial-basal cell bilayer
Acini	Prominent pink and purple zymogen granules in many acinar cells	Mostly pink subtle zymogen granules in rare acinar cells
Immunohistochemistry		
CK5/6	• Strong staining of myoepithelial cells in acini and in ducts immediately adjacent to acini • Strong staining of basal and luminal cells in larger ducts • Absent to very weak staining of acinar cells	• Weak to moderate staining of entire lesion without apparent differences between ducts and acini
S100	• Focal nuclear and cytoplasmic staining of luminal cells in intralobular and interlobular ducts • Focal staining of myoepithelial cells	• Absent staining
P63	• Staining of scattered myoepithelial cells in acini • Stains cohesive basal layer in intralobular and interlobular ducts	• Staining of scattered myoepithelial cells
Smooth muscle actin/calponin	• Staining of myoepithelial cells limited to the acini and to ducts immediately adjacent to acini	• Staining of myoepithelial cells throughout the entire lesion
Mammaglobin	• Strong staining in many acinar cells	• Strong staining in rare acinar cells

proximal intralobular ducts at the junction with the acini were rimmed by myoepithelial cells. The acini were composed of tall columnar-to-pyramidal cells with prominent dark and light zymogen granules, highlighted with Masson-trichrome and PAS/D stains. Occasional acinar and ductal cells featured goblet cell-like morphology with intracytoplasmic mucin, highlighted with Alcian blue and PAS/D stains. The intervening stroma contained a lymphoplasmacytic infiltrate (Figures 2 and 3A, and Supplemental Figures 1 and 2A-C). Immunohistochemically, the intralobular and interlobular ducts expressed SOX10 and S100 in the luminal cells, p63 in the basal cells, and CK5/6 (antigen CK5, major partner of CK14) in both luminal and basal cells. The acinar cells expressed SOX10 and mammaglobin (strong, granular expression in scattered cells). The myoepithelial cells in the acini and in the intralobular ducts immediately adjacent to the acini expressed SMA, calponin, p63 (focal), and S100 (weak-to-moderate, focal) (Figure 3B-F, and Supplemental Figures 2D-H and 3).

The 4 isolated epibulbar lacrimal gland lesions were composed of 1 or 2 well-circumscribed stromal based lobules, containing a central dilated and irregular duct-like tubular structure, which branched into progressively smaller, irregular tubular structures and terminated in acinar-like units. The tubular structures were lined by tall, cuboidal to columnar epithelium with focal pseudo-apocrine snouts and an outer myoepithelial layer, reminiscent of apocrine epithelium. In the 2 lesions from teenage patients, no morphologically normal ducts or acini were identified. The acinar structures in the two lesions from the teenage patients contained focal small pink zymogen granules, highlighted with PAS/D and Masson-trichrome stains. In the lesions from 2 adult patients, rare morphologically normal ducts and acini were present. Prominent apical mucin was highlighted in the tubular structures with Alcian blue and PAS/D stains. Connection with the surface conjunctival epithelium via a dominant poral opening was noted in two lesions, in which the

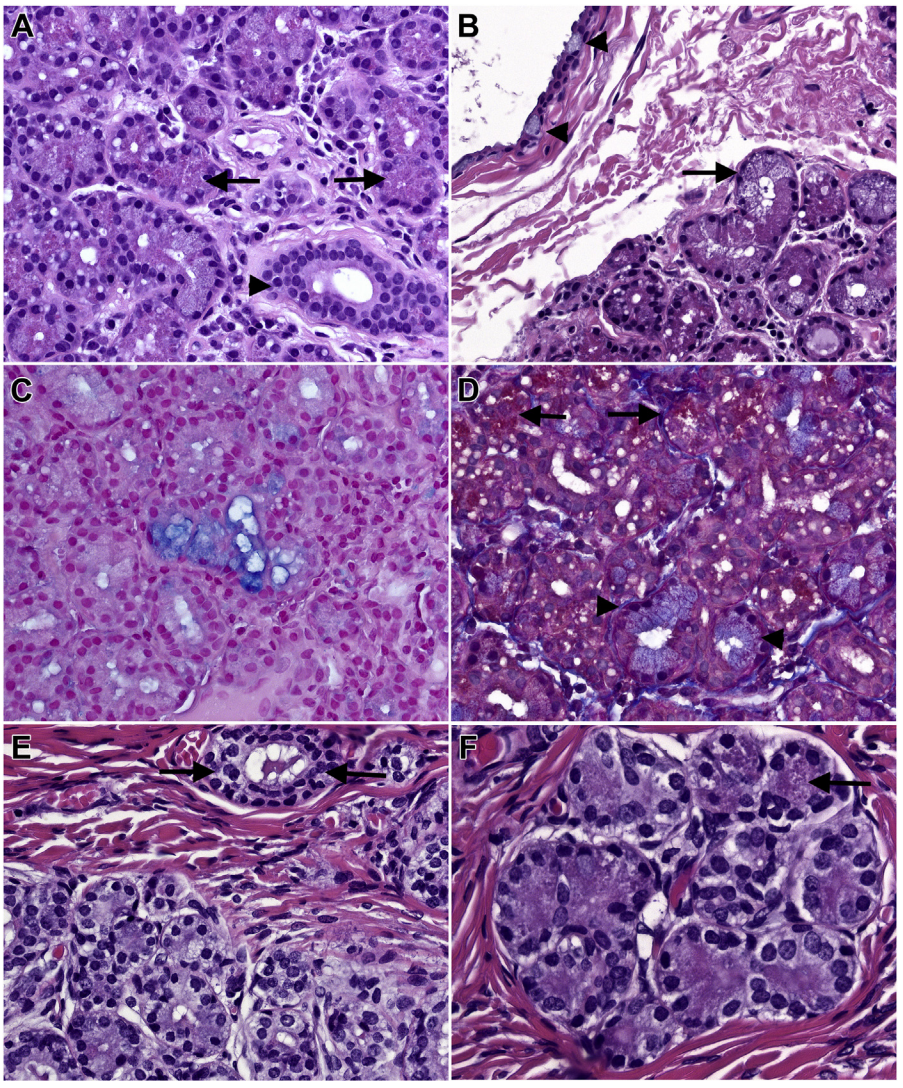

FIGURE 2. Morphologic findings in normal lacrimal gland tissue and ectopic lacrimal gland of complex choristoma. A. Normal lacrimal gland (case 7). Lacrimal gland lobule is composed of acini with prominent pink and purple zymogen granules in pyramidal cells (arrows) and intralobular ducts lined by a cuboidal bilayer (arrowhead). Scattered lymphocytes and plasma cells are present in the stroma [stain, hematoxylin-eosin; original magnification ×100]. B. Normal lacrimal gland (case 7). Occasional acinar cells are depleted of zymogen granules and filled with gray material reminiscent of goblet cell mucin (arrow). Interlobular duct in the adjacent stroma features a cuboidal epithelial bilayer with occasional inter-dispersed goblet cells (arrowheads) (stain, hematoxylin-eosin; original magnification ×100). C. Normal lacrimal gland (case 7). The focal intracytoplasmic mucin in the acinar cells is highlighted with Alcian blue stain (stain, Alcian blue; original magnification ×100). D. Normal lacrimal gland (case 7). Masson-trichrome highlights the bright red zymogen granules (arrows) and focal gray-blue intracytoplasmic mucin (arrowheads) in acinar cells (stain, Masson-trichrome; original magnification ×1000. E. Complex choristoma (case 5). Ectopic lacrimal gland tissue in a complex choristoma features an aggregate of acini and an adjacent duct (arrows), morphologically similar to the normal lacrimal gland tissue [stain, hematoxylin-eosin; original magnification ×100]. F. Complex choristoma (case 5). The acini contain prominent pink-purple zymogen granules (stain, hematoxylin-eosin; original magnification ×150).

duct-like tubular epithelium extended onto the ocular surface and was continuous with the conjunctival epithelium, with an abrupt transition between the 2 epithelia. The stroma in all lesions contained a variably dense lymphoplasmacytic infiltrate (Figure 4, and Supplemental Figures 4 and 5). Immunohistochemical studies performed on the lesions from 2 teenage patients showed an immunophenotype intermediate between that of the acini and ducts of the normal lacrimal gland and the ectopic lacrimal gland of a complex choristoma. The entire lesion expressed SOX10 in the luminal cells, and p63, SMA, and calponin in the myoepithelial cells.

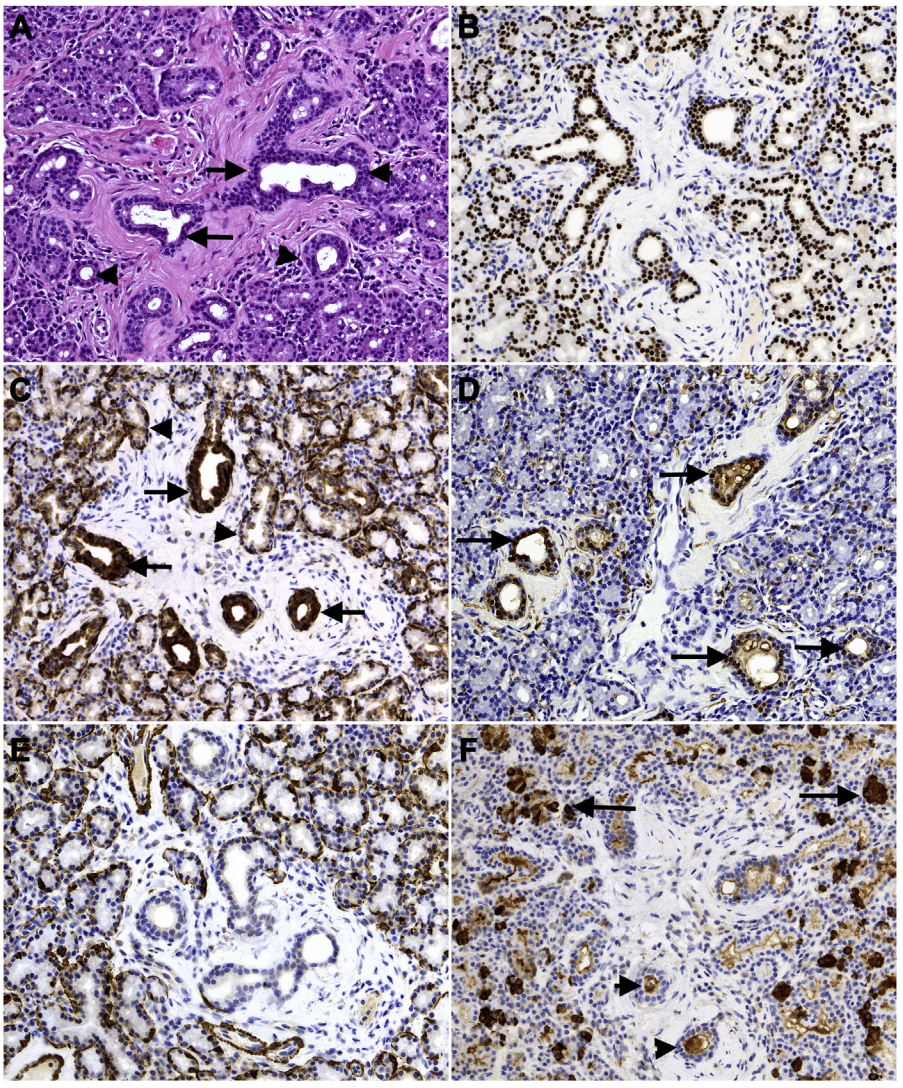

FIGURE 3. Normal lacrimal gland (case 7): Morphologic and immunohistochemical features. A. Lacrimal gland lobules with acini and intralobular ducts (arrowheads), which are continuous with interlobular ducts (arrows) (stain, hematoxylin-eosin; original magnification ×50). B. SOX10 immunostain diffusely labels the nuclei of the acinar cells and the luminal intralobular and interlobular ductal cells (stain, SOX10; original magnification ×50). C. CK5/6 strongly stains the myoepithelial cells in the periphery of the acini (arrowheads) and the basal and luminal cells of the ducts (arrows) (stain, CK5/6; original magnification ×50). D. Moderate nuclear staining for S100 in the nuclei and cytoplasm of the intrerlobular and intralobular ducts (arrows). The myoepithelial cells in the periphery of the acinar cells stain weakly and focally (stain, S100; original magnification ×50). E. Calponin strongly labels the myoepithelial cells surrounding the acinar cells and the adjacent proximal intraloblar ductules (stain, calpoinin; original magnification ×50). F. Mammaglobin strongly labels scattered acinar cells (arrows). The staining in the ducts is mainly limited to the secretory luminal material (arrowheads) (stain, mammaglobin; original magnification ×50).

CK5/6 expression was weak to moderate throughout the lesion. The rare acinar-like cells strongly expressed mammaglobin. S100 was negative in the entire lesion (Figure 5, and Supplemental Figure 6).

The histopathologic and immunohistochemical features of isolated epibulbar lacrimal gland lesions, 3 normal lacrimal gland biopsies, and 1 complex choristoma are summarized in Supplemental Table 2.

DISCUSSION

THE TERM "DACRYOADENOMA" WAS COINED BY JAKOBIEC and associates in 1989, who described a 48-year-old woman with a 15-year history of a pink, translucent inferior epibulbar, juxtaforniceal mass, which originated from the surface conjunctival epithelium, lacked true ducts, and contained goblet cells, zymogen granules, and myoepithelial cells.[1]

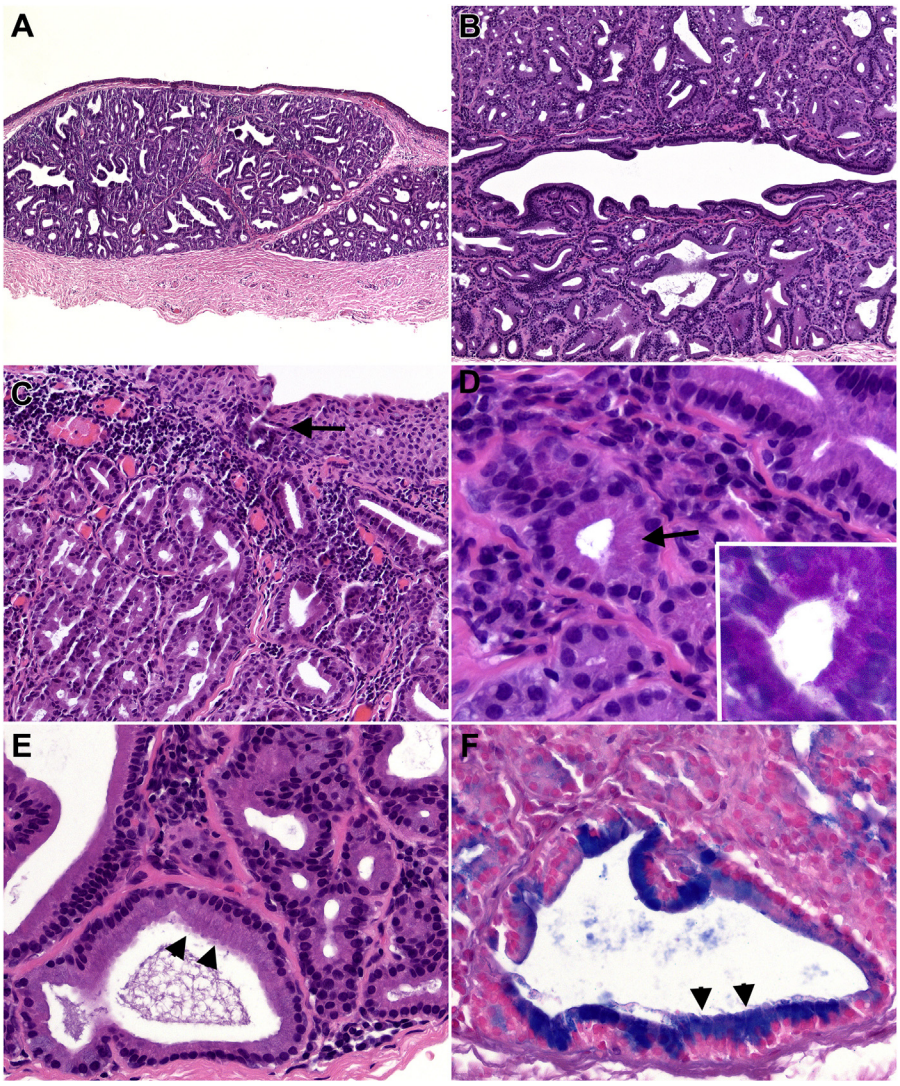

FIGURE 4. Morphologic features of the isolated epibulbar lacrimal gland lesion of patient 2. A. Well-circumscribed bilobed stromal-based mass (stain, hematoxylin-eosin; original magnification ×10). B. The lesion is composed of a central irregular dilated duct-like structure, which branches into progressively smaller irregular tubular units (stain, hematoxylin-eosin; original magnification ×20). C. Focal communication with the surface epithelium is present (arrow) (stain, hematoxylin-eosin; original magnification ×50). D. Focally, subtle pink zymogen granules are present in the acini (arrow) highlighted with PAS postdiastase stain (inset). Lymphoplasmacytic infiltrate is present in the surrounding stroma (stains, hematoxylin-eosin (main figure), PAS/D (inset); original magnification ×150 (main figure); ×175 (inset)). E. The lesion is predominantly composed of the irregular, variably dilated tubular structures, lined by the tall cuboidal to columnar epithelium with focal pseudo-apocrine snouts. (stain, hematoxylin-eosin; original magnification ×100). F. Alcian blue stain highlights the foci of apical mucin in the tubules (stain, Alcian blue; original magnification ×100).

The combined morphologic and ultrastructural electron microscopic findings led the authors to conclude that the lesion likely originated from modified conjunctival surface epithelium and was a true neoplasm composed of a benign proliferation of lacrimal secretory-type cells, rather than a heterotopia of lacrimal gland tissue.[1] Although the term "dacryoadenoma" has been repeatedly used in various book chapters and reviews, most of these publications cite the original microscopic and ultrastructural findings of the lesion described by Jakobiec and associates.[2–4] As a result, clinical and pathologic data on this unusual conjunctival tumor are sparse. In contrast, the epibulbar lacrimal gland choristoma, also known as ectopic lacrimal gland, has been much more frequently described in the literature and diagnosed in clinical practice, either as an isolated entity or as a heterotopic component of a complex choristoma.[5–7] This knowledge together with observation that 2 cases in our series originally were diagnosed as ectopic lacrimal gland/complex choristoma indicate that dacryoadenoma may have been largely

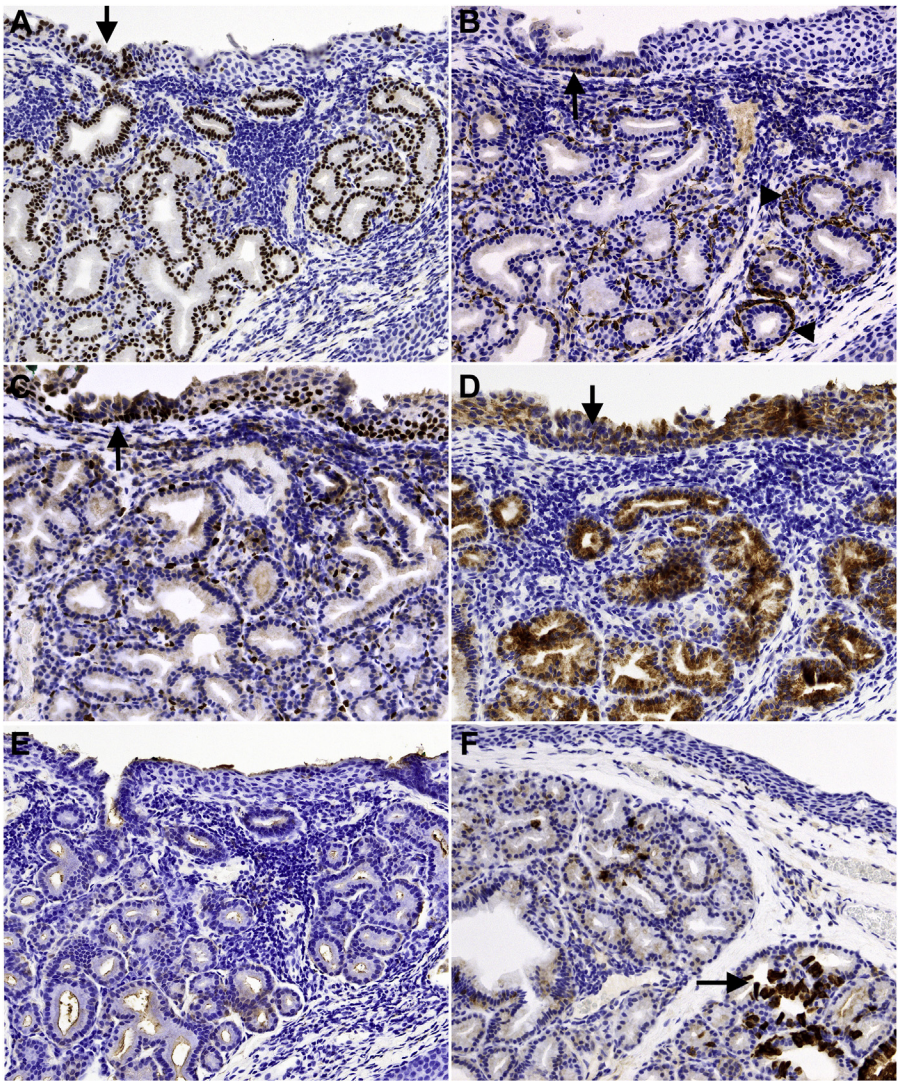

FIGURE 5. Immunohistochemical features of the isolated epibulbar lacrimal gland lesion of patient 2. A. SOX10 immunostain diffusely labels the nuclei of the luminal cells throughout the lesion and highlights a small segment of lesional epithelium (arrow) sharply demarcated from the adjacent conjunctival epithelium (stain, SOX10; original magnification ×50). B. Smooth muscle actin (SMA) highlights the peripheral flattened myoepithelial cells surrounding the tubular and acinar structures in the lesion (arrohwhead) and in the lesional epithelium on the ocular surface (arrow) (stain, SMA; original magnification ×50). C. P63 is expressed in the peripheral myoepithelial/basal cells of the stromal and surface epithelial (arrow) components of the lesion, and in the basal cells of the conjunctival epithelium (stain, p63; original magnification ×50). D. CK5/6 diffusely weakly-to-moderately stains the luminal and myoepithelial cells in the stromal and surface epithelial (arrow) components of the lesions, and the adjacent conjunctival epithelium (stain, CK5/6; original magnification ×50). E. No staining is noted with S100 (stain, S100; original magnification ×50). F. Mammaglobin strongly labels rare scattered acinar cells (arrows) (stain, mammaglobin; original magnification ×50).

interpreted in pathology practice as a lacrimal gland choristoma.

Observation of lacrimal gland tissue outside of its typical location raises etiologic considerations of (1) a congenital stationary lesion; (2) a congenital lesion with progressive evolution; and (3) an acquired lesion. Clinically, all lesions in our study and the lesion described by Jakobiec and associates had a predilection for the juxtaforniceal and juxtaplica semilunaris bulbar conjunctiva and were not apparent at birth. This contrasts with the congenital nature and predilection for the temporal bulbar conjunctiva of a typical lacrimal gland choristoma, supporting its hypothetical origin from the palpebral lobe of the lacrimal gland.[5,8] While these contrasting clinical observations may support the acquired nature of "dacryoadenoma," the possibility of an occult congenital lesion with progressive growth or a stationary, previously undetected lesion located in nonexposed forniceal conjunctiva is favored in light of several

reports documenting progressive growth of congenital epibulbar choristomatous lesions, including an isolated lacrimal gland choristoma.[7–9]

The atypical location with predilection for juxtafornicial and juxtaplica semilunaris region and translucent pink-orange coloration has accounted for a clinical impression of a lymphoproliferative lesion in two of four cases in this study and in the initial report.[1] This clinical consideration is not unexpected. Although lymphoproliferative conjunctival lesions tend to have a more diffuse configuration and are centered in the conjunctival fornix, reactive lymphoid hyperplasia and pediatric-type follicular lymphoma may also manifest as well-circumscribed salmon-colored nodules adjacent to plica semilunaris and in the bulbar conjunctiva.[10,11]

In their original description of dacryoadenoma, the authors commented on 4 morphologic features that serve to distinguish that lesion from normal and ectopic or aberrant lacrimal gland tissue including (1) the absence of a separate ductal component; (2) a discontinuous myoepithelial layer; (3) the presence of scattered mucin-rich goblet-type cells; and (4) the absence of interstitial lymphocytes and plasma cells.[1] Histopathologically, the lesions in our study bore a striking similarity to dacryoadenoma, as originally described, featuring a central dilated and irregular, branching duct-like structure and acini, without well-defined intralobular and interlobular ducts or prominent zymogen granules in the acini. These observations were supported by immunohistochemical studies, which documented an aberrant dual ductal-acinar immunophenotype, contrasting with the expected immunophenotype of normal and heterotopic lacrimal gland tissue, identical to that described in the salivary gland.[12] Although we did not evaluate the myoepithelial cell layer ultrastructurally, we did note a difference in the distribution and immunoreactivity for CK5/6 and p63 between the myoepithelial cells of the lesions in our study and the myoepithelial cells of normal and heterotopic lacrimal gland tissue. Similar to Jakobiec and associates we observed goblet-like cells in the lesions we studied. However, the latter feature no longer serves to distinguish dacryadenoma from lacrimal gland heterotopia, since goblet-type cells recently have been documented in the normal lacrimal gland and were evidenced in the normal and ectopic lacrimal gland tissue in this study.[13] Additionally, while 2 lesions in our study lacked an appreciable lymphoplasmacytic stromal component, the other 2 lesions featured a brisk lymphoplasmacytic stromal infiltrate, further accentuating the morphologic overlap with normal and ectopic lacrimal gland tissue.

Our study confirms the clinical and morphologic differences between a subset of epibulbar lacrimal gland tumors and the typical lacrimal gland choristoma and normal lacrimal gland tissue. In light of the foregoing findings and in the context of 4 new cases in this study that supplement the data in the initial report by Jakobiec and associates, it seems appropriate to address the question whether the term "dacryoadenoma" is the best one to apply to the current lesion.[1] This term was suggested to Dr. Jakobiec by the late Dr. Lorenz Zimmerman when he was consulted on their case (personal communication). An adenoma, however, is a de novo, acquired benign neoplasm with glandular features. It typically is architecturally relatively simple, examples in the lacrimal gland would be pleomorphic adenoma (a mixture of ductular and myoepithelial cells) and so-called rare monomorphic adenomas and myoepitheliomas, whereas "dacryoadenoma" is more complex and essentially a travesty of normal lacrimal gland structure. An alternative hypothesis is that the lesions in our study and the lesion in Jakobiec and associates' report constitute heterotopic normal lacrimal gland tissue (ectopic lacrimal glands of Krause and Popoff) at different stages of embryologic development, with some lesions demonstrating incomplete maturation of the ducts and acinar units and other lesions more closely resembling normal lacrimal gland tissue.[14,15] However, this hypothesis of developmental arrest of an otherwise normal lacrimal gland tissue is not supported by the overall haphazard architecture of the tubular and acinar elements in these lesions that is not in keeping with the established sequence of embryologic events in normal lacrimal gland development, in which maturation of ducts precedes maturation of the acini.[14,15]

For help in naming our lesion, we drew on an estimable paper by Ferry and Font on the phakomatoses.[16] The authors distinguish between hamartia/hamartoma and chorista/chroristoma. Hamartia and chorista signify a small congenital rest of germ cells (primordia or anlagen). These germ cell rests are either precursor cellular elements for later differentiation that are indigenous to the tissue in which they arise (hamartia) or alien to such tissue (chorista). When these precursor cells progressively grow to create a clinically detectable mass they become hamartomas or choristomas.[16] In a corneal lacrimal gland choristoma evaluated in our study morphologically and immunohistochemically, and in a prior study by Pokorny and associates with electron microscopy, the lesion demonstrated virtually normal cytoarchitechures and immunophenotype.[8] These considerations lead us to believe that the malformed lacrimal gland epibulbar lesions could have been derived from pluripotential conjunctival cell rests either during fetal development or postnatally, influenced by the regional and individualized epithelial-mesenchymal interactions that drive the development of glandular tissue.[15] We have concluded that present lesions arose from hamartia and grew into disorganized cellular elements that partially recapitulated an organ or adnexal structure (lacrimal tissue) in its mature, fully differentiated state.

Embryologically the conjunctiva is the source of outgrowths of its many normal lacrimal glands: the major lacrimal gland and the accessory glands of the fornices (Krause), poles of the tarsi (Wolfring), and the caruncle

(Popoff).[17] Our construction is that a focus of conjunctiva with lacrimal differentiation potentiality (a hamartia) can reside anywhere in the conjunctival sac and spawn the current lesions, which are small in an infant or child and fully bloom as one ages. Hence, all of these lesions were detected in individuals 12-57 years of age and not at birth. Since the lacrimal tissue in the present case was malformed we believe the use of the term hamartoma is appropriate. Further, considering that malformation of lacrimal gland tissue ranged from subtle to pronounced, we speculate that an isolated "ectopic lacrimal gland" or "lacrimal gland choristoma" is, in fact, a hamartoma. If any form of ectopic lacrimal tissue should be found in the eyelid skin or cornea (where it can be a component of a complex malformation of tissue also featuring cartilage or smooth muscle) it should be called a choristoma.[8] We therefore recommend a new diagnostic designation in place of "dacryoadenoma" for malformed ectopic lacrimal tissue lesions in the conjunctival sac, like the rare ones reported herein, namely *lacrimal gland hamartoma*. This term comports well with the observations of the origin of the lesion directly from the surface epithelium, the absence of intralesional true ducts, the spotty presence of myoepithelial cells, a variable prominence of goblet cells, variable development of acinar zymogen granules, and usually an overall bilobed structure.

Understanding the spectrum of morphologic variation of dacryoadenoma from normal lacrimal gland tissue is important for accurate pathologic diagnosis. Furthermore, awareness of this benign lacrimal gland lesion by clinicians is important in light of its clinical overlap with lymphoproliferative disorders.

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