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CASE REPORT

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Subconjunctival mucosa-associated lymphoid tissue (MALT) lymphoma arising in Tenon's capsule

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Abstract *Purpose:* We report the first case of subconjunctival mucosa-associated lymphoid tissue (MALT) lymphoma arising in Tenon's capsule (fascia bulbi). *Methods:* A 75-year-old woman presented with painless swelling of the superior bulbar conjunctiva in her left eye. During the biopsy of the bulbar lymphoid lesion, it was noticed that the conjunctiva was movable and that the lesion was located in the subconjunctiva. The tissues were studied by conventional light microscopy, immunohistochemistry, flow cytometry, and gene rearrangement analysis. *Results:* Histopathological examination revealed that a diffuse lymphoid infiltrate consisting of small-sized lymphoid cells was present in Tenon's capsule but not in the substantia propria of the conjunctiva. Immunohistochemical and flow cytometric studies documented tumor cells of B-lymphocyte lineage. Molecular analysis demonstrated positive immunoglobulin heavy chain gene rearrangement. The final diagnosis was subconjunctival MALT lymphoma arising in Tenon's capsule. *Conclusion:* Ophthalmologists and pathologists need to distinguish the subconjunctival lymphoma that arises in Tenon's capsule from the conjunctival lymphoma in the substantia propria during diagnosis of epibulbar lymphoid tumors.

Keywords MALT lymphoma · Conjunctiva · Tenon's capsule · Histopathology

Introduction

Conjunctival lymphoid tumors, including reactive lymphoid hyperplasia and malignant lymphoma, have been recognized to arise in the substantia propria of the conjunctiva [6, 9]. Our experience with microscopic examinations of conjunctival lymphoid tumors also supports this description; however, in the present case the lymphoid lesion was unusually restricted to the Tenon's capsule (fascia bulbi). We report the first case of subconjunctival mucosa-associated lymphoid tissue (MALT) lymphoma arising in Tenon's capsule.

Case report

A 75-year-old Japanese woman had uneventful cataract surgery with a self-sealing sclerocorneal tunnel incision (3.5 mm from the 12 o'clock position) in both eyes at a private clinic in February 2002. A painless swelling of the superior bulbar conjunctiva was noted in the left eye in November 2002, and the patient was referred for further evaluation to the Department of Ophthalmology, Jichi Medical School. The lesion occupied almost the entire superior bulbar conjunctiva of the left eye and was a diffuse, slightly elevated, fleshy-pink mass (Fig. 1a). Conjunctival lymphoid tumor was diagnosed clinically. The

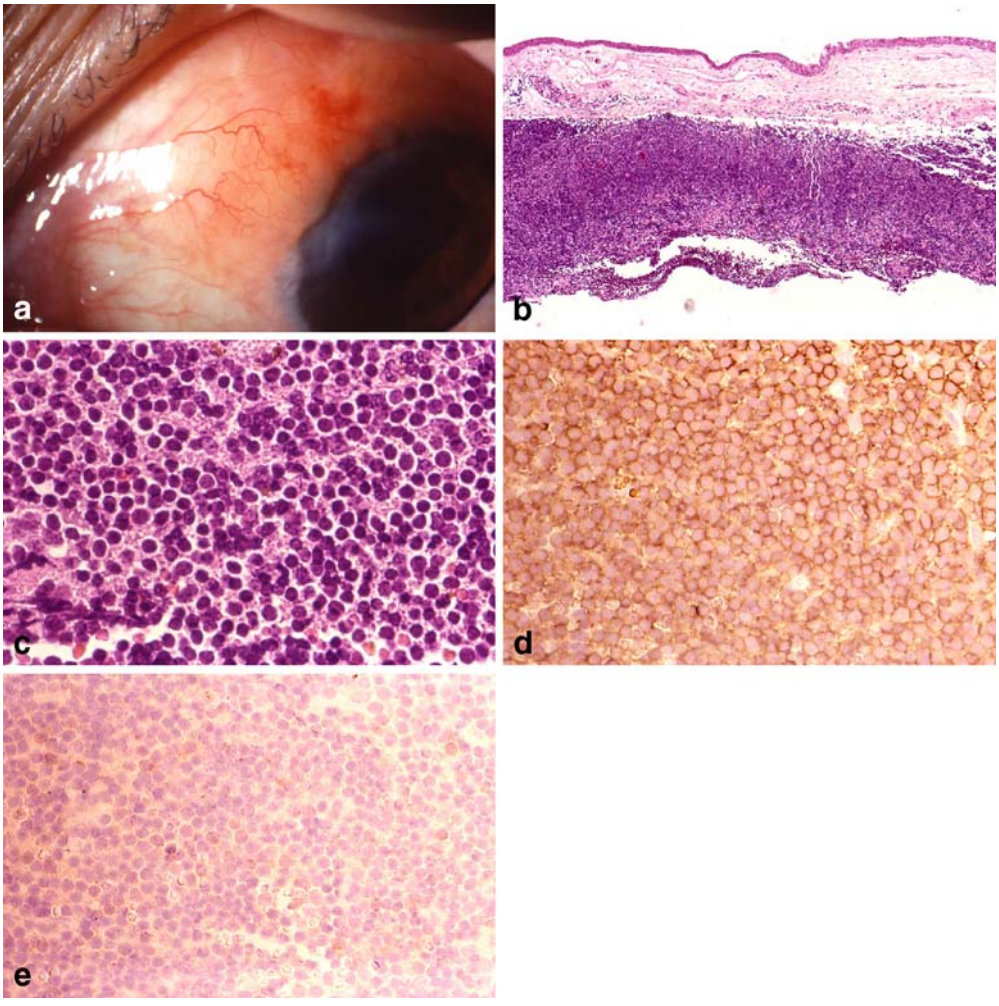

Fig. 1 **a** A diffuse, slightly elevated, fleshy-pink mass occupied the entire superior bulbar conjunctiva of the left eye. A focal corneal opacity due to an unknown cause of keratitis is seen. **b**, **c** Histopathologic findings. **b** A diffuse infiltration of small lymphoid cells is present in Tenon's capsule. Note that the substantia propria of the conjunctiva is free of lymphoid cells. **c** The dense infiltrating small lymphocytes generally show mild atypia (hematoxylin–eosin, original magnification ×17.5 [**b**], ×200 [**c**]). **d**, **e** Immunohistochemical staining for the B-cell marker, CD20, is positive (**d**), and the T-cell marker, CD3, is negative (**e**). (Original magnification ×150)

patient's past medical history included bilateral keratitis of an unknown cause in the 1960s. Best-corrected visual acuity was 20/20 in each eye. The results of the ocular examinations were otherwise normal.

Excisional biopsy of the lesion was performed in December 2002. During the biopsy, it was noticed that the conjunctiva was movable and appeared normal and that the lesion, which was adherent to the episclera, was located in the subconjunctiva. The episcleral area after the removal of the lesion appeared normal. The tissues excised with the conjunctiva from the sclera were processed for routine histopathologic studies that included immunohistochemical staining, flow cytometric analysis, and immunoglobulin (Ig) gene rearrangement analysis. Microscopic examination revealed a diffuse infiltration of centrocyte-like cells and the presence of small lymphoid cells in the Tenon's capsule but not in the substantia propria of the conjunctiva (Fig. 1b,c). Immunohistochemical staining for the B-cell marker, CD20, was positive, and the T-cell marker, CD3, was negative, suggestive of a lymphoid tumor of B-cell origin (Fig. 1d,e). Cyclin D1, for which mantle cell lymphomas are positive, was negative. The infiltrating lymphocytes generally showed mild atypia, but the findings listed above were consistent with the neoplastic lymphoid proliferation's being monoclonal and were characteristic of extranodal low-grade B-cell lymphoma of MALT type. Flow cytometric analysis showed a monotypic B-cell population expressing CD19, CD20, and lambda light chains. The cells were negative for CD5 and CD10. Southern blot analysis showed positive Ig heavy chain (IgH) gene rearrangement, confirming the diagnosis of B-cell lymphoma.

After clinical staging that included systemic computed tomography scans, fiberoptic gastroscopy, and bone marrow biopsy, no other foci of this lymphoma were found. Radiation therapy with a total dosage of 30 Gy was given,

and the tumor resolved completely. No recurrence or complications of radiotherapy have been observed so far. The patient currently remains free of lymphoma 18 months after diagnosis.

Discussion

The Tenon's capsule or fascia bulbi is a thin fibrous sheath that envelops the globe from the margin of the cornea to the optic nerve [3]. The conjunctiva has an epithelial covering of stratified columnar cells resting on a substantia propria of loose connective tissue. The bulbar conjunctiva is in contact with the Tenon's capsule. The episclera consists of a few loose vascularized surface layers of scleral collagen beneath the Tenon's capsule. Taken together, the wall of the anterior part of the eyeball is composed of conjunctival epithelium, substantia propria, Tenon's capsule, episclera, and sclera, in that order (Fig. 2).

Only a few cases of diseases of Tenon's capsule have been described in the literature [5, 7]. One involved nodular fasciitis [5], while the other involved fibroma [7]. In the current case, it was noted that the lesion was present beneath the conjunctiva during the biopsy, and histopathologic examination revealed diffuse infiltration of lymphoma cells at the level of the Tenon's capsule, which was distinct from the conjunctival epithelium. The lymphoma cells may arise from the episclera and affect the Tenon's capsule. Moreover, the Tenon's capsule tumors at the limbus mostly affect the underlying episclera since both structures are very close at this site. For instance, Auw-Haedrich et al. reported a case of episcleral plasmacytoma mimicking episcleritis [2]. However, based on the clinical and histopathologic findings, we finally diagnosed the present case as subconjunctival MALT lymphoma possibly arising from the Tenon's capsule.

MALT lymphoma is a low-grade non-Hodgkin's lymphoma and is recognized as a distinct entity within the marginal zone cell lymphomas listed in the revised European–American lymphoma (REAL) classification. The majority of ocular adnexal lymphomas are MALT lymphomas [1, 6].

MALT lymphoma develops against a background of chronic inflammation [8]. Chronic inflammation or autoimmune disease, such as *Helicobacter pylori* gastritis, Hashimoto's thyroiditis, and Sjögren's syndrome, apparently provide the environment necessary for the emergence of the lymphoma [8]. Recently, it was hypothesized that persistent *Chlamydia psittaci* infection may contribute to the development of ocular adnexal lymphomas [4]. Yeung et al. [10] reported a case of conjunctival MALT lymphoma associated with chronic follicular conjunctivitis. They performed a chlamydial antigen assay, and the results were positive. These studies suggest that conjunctival MALT lymphoma develops within a background of chronic conjunctivitis. In the current case, it was assumed that an inflammation after the cataract surgery or an unknown cause of keratitis might have been involved in the pathogenesis of the MALT lymphoma. It may very well be that subconjunctival lymphoma has a different pathogenesis from conjunctival lymphoma. Therefore, it is crucial to distinguish between the two lymphomas.

To the best of our knowledge, the current case is the first report of subconjunctival lymphoma. When observing epibulbar lymphoid tumors, we, as ophthalmologists, need to carefully examine the findings during biopsies to determine whether a lesion is located in the conjunctiva or the subconjunctiva.

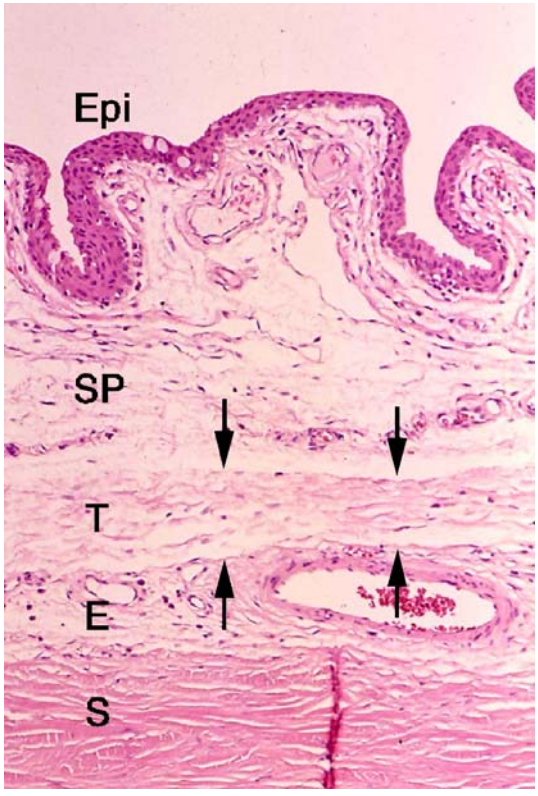

Fig. 2 Normal anatomy of the epibulbar area of the human eye. Note the precise anatomic locations of conjunctival epithelium (*Epi*), substantia propria (*SP*), Tenon's capsule (*T*: between *arrows*), episclera (*E*), and sclera (*S*). Conjunctival lymphoid tumors usually arise in the substantia propria. (Hematoxylin–eosin, original magnification ×40)

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