• Letter to the Editor •

Conjunctival cyst with apocrine hidrocystoma-like features: a case report

Takafumi Igarashi[1], *Satoru Kase*[1], *Yuka Suimon*[1], *Emi Takakuwa*[2], *Susumu Ishida*[1]

[1]Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo 0608638, Japan
[2]Department of Surgical Pathology, Hokkaido University Hospital, Sapporo 0608638, Japan
Correspondence to: Satoru Kase. Department of Ophthalmology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, N-15, W-7, Kita-ku, Sapporo 0608638, Japan. kaseron@med.hokudai.ac.jp
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Dear Editor,

I am Takafumi Igarashi from Hokkaido University Hospital, Japan. Apocrine hidrocystoma is a benign cystic tumor arising in the apocrine sweat glands proposed by Mehregan[1] in 1964. It is likely that apocrine hidrocystoma arises in the uvula, ears, chest, and shoulders, as well as the (peri)ocular regions such as the eyelid, and sclera[2-4]. Of the 35 cases with eyelid cystic lesions in the authors' institute, apocrine hidrocystoma was noted in only one case[5]. In fact, apocrine hidrocystoma arising in the conjunctiva is extremely rare, with only four cases reported in the literature[6-8]. The clinical diagnosis of apocrine hidrocystoma of the conjunctiva is based on the identification of the cyst by slit-lamp examination and microscopic findings. In this report, we describe a case of the bulbar conjunctival cyst with apocrine hidrocystoma-like features, and analyze its clinicopathological relationship.

CASE REPORT

An 86-year-old man was referred to our hospital because of a yellowish conjunctival mass in his left eye (Figure 1A). There was no history of ocular surgery or trauma in the past. Anterior segment optical coherence tomography (ASOCT) showed a cystic lesion beneath the conjunctival epithelium. The content of the lesion presented with a diffuse, heterogeneous, hyper-reflective materials with posterior shadowing (Figure 1B). Total excision of the mass including the conjunctival epithelium was performed under local anesthesia. Histopathologically, the lesion was a cyst beneath the conjunctival epithelium with eosinophilic globular materials in the lumen (Figure 1C). At a high magnification, the cyst wall consisted of presumed bilayer epithelial cells with a roundish nucleus and an acidophilic cytoplasm, with scattered findings of decapitation secretion (Figure 1D). There was no cellular atypia in the epithelium. Immunoreactivity for p63 verified bilayer epithelium in the cyst wall (Figure 1E). Immunoreactivity for gloss cystic disease fluid protein-15 (GCDFP-15) was negative (Figure 1F), whilst cytokeratin 7 (CK7) was diffusely positive in the superficial layer of epithelial cells (Figure 1G). After 3mo of follow-up, there was no recurrence of the cyst. Institutional Review Board of Hokkaido University Hospital waived application for clinical study because this is a single case report based on clinicopathological studies for diagnosis. Written informed consent was obtained from this patient to use the clinicopathological data in clinical researches. This study adhered to the Declaration of Helsinki.

DISCUSSION

Comparing the present case with four previously reported cases (Table 1), Kim and Kang[7] reported a yellowish apocrine hidrocystoma located on the temporal conjunctiva, which might share similar clinical features with the present case. Kim and Kang[7] also speculated that the yellowish appearance of the cyst was correlated with the Tyndall phenomenon, which is caused by the presence of colloids in the lumen. However, the present case showed a stronger yellowish tone than the previous reports. Indeed, it is difficult to diagnose the cysts from slit-lamp microscopic findings because the locations of lesion on the conjunctiva and coloration are various according to the previous reports[6-8]. The sex and age of the patients are also inconsistent. However, the pathological findings are all characterized by bilayer epithelial cysts with lumens filled with secretory materials. Therefore, surgical resection and histopathological diagnosis are necessary to make a definitive diagnosis of conjunctival cystic lesions.

In immunohistochemical examinations, it is likely that GCDFP-15 and CK7 are positive in other apocrine hidrocystoma arising from the mammary glands[9-10], and Charles *et al*[8]

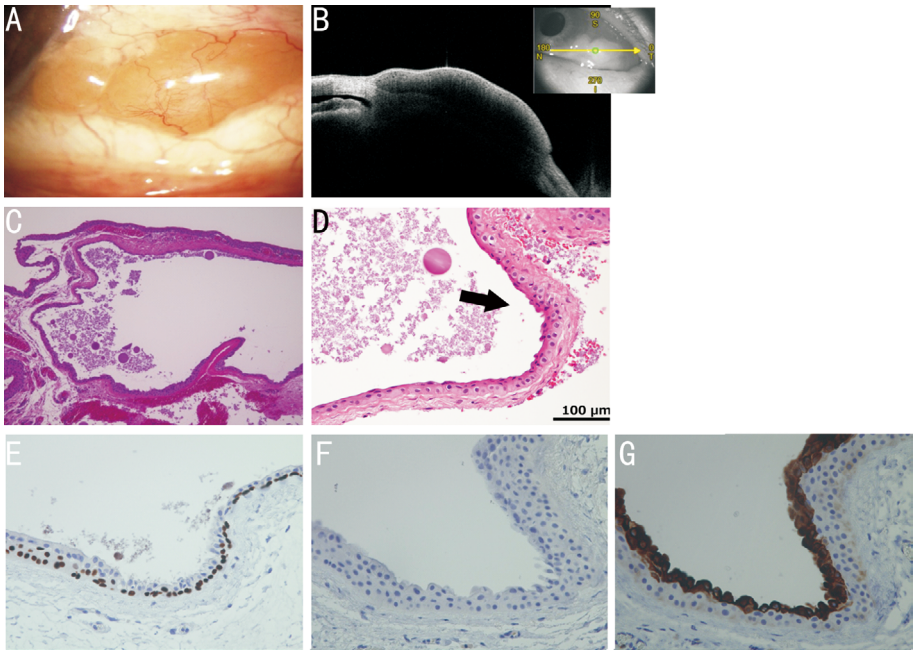

Figure 1 Conjunctival cyst with apocrine hidrocystoma-like features A: Slit-lamp examination revealed a yellow-toned elevated lesion in the bulbar conjunctiva; B: ASOCT depicted a diffuse, heterogeneous hyper-reflective lesion in the subepithelium; C: A cystic structure was seen beneath the conjunctival epithelium, with a lumen containing globular materials (hematoxylin-eosin, ×100); D: Decapitation secretory cells were present on the luminal surface (arrow, hematoxylin-eosin, ×400); E: p63 verified the bilayer epithelium; F: GCDFP-15 was negative in epithelial cells; G: CK7 showed diffuse staining in the superficial layer of the epithelium. ASOCT: Anterior segment optical coherence tomography; GCDFP-15: Gloss cystic disease fluid protein-15; CK7: Cytokeratin 7.

Table 1 Clinicopathological features of conjunctival cysts with apocrine hidrocystoma-like features

Author	Report	Age/sex	Location	Color	Pathological findings	GCDFP-15
Chin *et al*[6]	2003	72/female	Left, nasal conjunctiva	Blue-grey	Cyst covered with a bilayer and filled with amorphous material	n.d
		71/male	Left, nasal conjunctiva	Black	Cyst covered with a bilayer and filled with amorphous material	n.d
Kim and Kang[7]	2012	54/female	Right, temporal conjunctiva	Yellow-grey	Monoblastic solitary cyst, lumen-filling secretions	n.d
Charles *et al*[8]	2021	57/female	Right, temporal conjunctiva	Colorless	Cyst covered with cuboidal epithelial bilayer and acid-Schiff positive secretions in lumen	Positive
Present case	2022	86/male	Left, temporal conjunctiva	Yellow-brown	Monoatrial cyst, bilobed with image of decapitation secretion, eosinophilic globular materials in lumen	Negative

GCDFP-15: Gloss cystic disease fluid protein-15; n.d: Not determined.

reported a case of conjunctival apocrine hidrocystoma made up of GCDFP-15-positive epithelial cells. On the other hand, although the current case shared histological features of apocrine hidrocystoma including bilobed epithelial cells, and eosinophilic globular materials in the lumen with decapitation secretion, GCDFP-15 was not positive in the epithelium. Chin *et al*[6] and Kim and Kang[7] also reported two and one patients with conjunctival apocrine hidrocystoma, respectively; however, immunohistochemistry with anti-GCDFP-15 antibody was not tested. p63 is a marker for squamous epithelium and was bilayer stained in this case. This result is consistent with the apocrine-derived tissue. Taken together, there are two possible mechanisms underlying the pathogenesis of conjunctival apocrine hidrocystoma: 1) the cysts could be originated from metaplasia of GCDFP-15-negative conjunctival cysts, and 2) from *de novo* GCDFP-15-positive ectopic apocrine gland cells. Therefore, this study summarized "conjunctival cysts with apocrine hidrocystoma-like features" regardless of GCDFP-15 immunoreactivity.

ASOCT provides noninvasive, quick, and useful information on the shape and content of anterior ocular tumors. However, ASOCT findings in conjunctival apocrine hidrocystoma remain unreported. This is the first report describing ASOCT findings of the conjunctival cyst with apocrine hidrocystoma-like features. In this case, it showed diffuse, heterogeneous hyper-reflective areas under the conjunctival epithelium with posterior shadows. The histopathologic findings revealed a similarly shaped material deposition in the lumen of the cyst. Therefore, ASOCT findings reflected the pathological features

of the conjunctival cyst with apocrine hidrocystoma-like features.

Comparing the ASOCT findings of other conjunctival masses, ASOCT displays smooth cyst walls and a somewhat heterogeneous, low-luminance lumen in conjunctival epithelial cysts[11], while thickened conjunctival epithelium with diffuse hyperintense findings and rapid transition points are noted in ocular surface squamous neoplasia[12]. Conjunctival lymphoma shows uniform internal hypointense foci under the epithelium[13]. Conjunctival myxoma shows a high intense epithelial layer and uniform hyporeflective areas[14]. We have shown that ASOCT in a patient with molluscum contagiosum revealed a homogeneous hyper-reflective elevated lesion[15], the results of which contributed to clinical diagnosis and the managements. Taken together, all characteristic ASOCT findings in various ocular surface tumors are different from those of the apocrine hidrocystomas on the conjunctiva.

It has been reported that methylthionium staining can distinguish the conjunctiva from the Tenon's capsule, leading to improved visualization of the conjunctiva in conjunctival cysts[16]. Therefore, the intraoperative methylthionium staining might assist isolation of conjunctival apocrine hidrocystoma during the cyst removal.

In conclusion, the optical signs seen on ASOCT of apocrine hidrocystoma were thought to reflect histopathologically confirmed cystic elements, suggesting that ASOCT may contribute to the clinical diagnosis of the cyst with apocrine hidrocystoma-like features arising on the conjunctiva.

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