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Conjunctival Stromal Tumor: Expansion of Findings in a Newly Described Entity

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Conjunctival myxoma is a rare benign tumor that accounts for < 0,001 % of conjunctival lesions ¹. It is important to recognize this entity since it might be associated with cardiac myxoma which can be life threatening ². Based on a series of 4 cases, Herwig et al. recently described the new entity “conjunctival stromal tumor” (COST), with its name deduced from the well-known gastrointestinal stromal tumor (GIST) showing a partially similar immunomarker profile ². Positive markers for COST include CD34, Vimentin, and partially for CD68; negative markers include S100 and smooth muscle actin. GIST often are CD34 +, sometimes S100 and smooth muscle actin + ³. Myxomas are CD34 – (unpublished data, and the case described herein) ⁴. Below we report 3 further cases of COST with the purpose of adding these to the spectrum of its clinical and histologic appearances.

Case 1 was the only case diagnosed as COST in the Histology lab’s database at the Eye Center in Freiburg. Cases 2 and 3 originated from the L.F. Montgomery Ophthalmic Pathology Laboratory, Emory University, Atlanta, Georgia. The specimens were fixed in 4 and 10% formaldehyde, respectively, and were routinely processed for light microscopy. The slides were stained with hematoxylin eosin, periodic acid-Schiff and alcian blue, immunohistochemically with antibodies against CD34 (marker for vascular endothelial cells, hematopoietic stem cells, some soft tissue tumors, DAKO; 1:50), CD68 (macrophage marker, DAKO; 1:50), S100 (marker for neural crest-derived cells, DAKO; 1:3200), vimentin (mesenchymal cell marker, DAKO; 1:320) and c-kit (proto-oncogene, CD117, Abcam; 1:100) using the Avidin-Biotin method. Institutional review board/ethics committee approval was obtained for this study. The research adhered to the tenets of the Declaration of Helsinki.

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Case 1 was a 46 year-old otherwise healthy male patient presented with a large soft gelatinous reddish conjunctival tumor of the left eye extending from the limbus to the equator (figure 1). It had first been noticed 3 years before and had enlarged within 3 months prior to our surgical removal. Histologically, we found abundant alcian blue positive extracellular substance with cells of various sizes containing one or multiple small spindle shaped nuclei and vacuolated cytoplasm, which also stained positive for alcian blue. Immunohistochemical stains showed that the tumor cells were CD34 +. Smaller cells stained positively with antibodies against CD68. Immunohistochemical stains for c-kit showed cytoplasmic as well as membranous positivity (Fig. 2, available at <http://aaojournal.org>). The tumor cells of a CD34 – corneal myxoma ⁴, nevertheless, showed a similar staining pattern against c-kit.

Case 2 was an 11 year-old boy presented with a tumor at the medial bulbar conjunctiva of his right eye causing exotropia. The rather whitish tumor was removed surgically; it extended to the margins of resection and recurred 3 years later. Histology showed fibrovascular tissue with scattered vascular channels. The intervening stroma contained scattered spindle shaped cells with bland nuclei and spindle shaped cytoplasm, round cells with bland nuclei and abundant intercellular collagen fibrils. Immunohistochemical stains were positive in the spindle-shaped cells for CD34 and vimentin.

Case 3 was a 48 year-old male patient presented with a reddish vascularized lesion of his left bulbar conjunctiva. Histologic examination of the excised lesion showed spindle shaped cells with bland nuclei, larger cells with pseudonuclear inclusions, and positive immunohistochemical stains for CD34 and vimentin. Occasional floret-like cells were present in a myxoid stroma.

Conjunctival myxomas only rarely include multinucleated giant cells. Since our cases contained multinucleated tumor cells, which together with the spindle cells were CD34 +, we categorized them as conjunctival stromal tumors. Another differential diagnosis includes pleomorphic lipoma, which also contains floret-like multinucleated CD34 + cells with pseudonuclear inclusions reminiscent of Lochkern cells. Due to the myxoid character of our cases, we consider a pleomorphic lipoma an unlikely diagnosis. Conjunctival myxoma is CD34 –, including our corneal case described before ⁴. Thus the positive staining for CD34 helps to distinguish conjunctival stromal tumor from conjunctival myxoma; c-kit does not allow for this distinction as one of our myxoma cases ⁴ also showed c-kit positivity. C-kit, as well as CD34, are characteristically expressed by GIST and considered proto-oncogenes ⁵.

The lesion in case 1 measured 13×11×6 mm with extension from the limbus to the equator occupying the upper bulbar circumference. The specimens of the four COST cases published so far had a maximum size of 4×5×4 mm ². The description of case 4 in Herwig et al's initial description ² is quite similar to our case 1 but the size of the lesion and clinical photograph were not available. Another unusual feature of case 1 is the almost completely myxoid stroma, which has not been described, while the cases in Herwig et al's initial description ² were of a mixed myxoid/collagenous type. Interestingly, the histology of our case 2 showed a purely collagenous stroma without myxoid changes and with multiple spindle-shaped cells.

The 4 COST cases published to date² were in patients between 41 and 53 years-old. Our case 2, however, shows that this tumor can also occur in much younger individuals, such as in children. It recurred 3 years following initial excision, a phenomenon not described in the initial case series.² The original tumor in our case 2 had not been removed entirely during surgery, which might then explain the recurrence. Another explanation may just be the young age of the patient.

Case 3 shows another clinical feature of COST as exhibiting prominent vascularization confined to the conjunctiva, which has also been described by Herwig et al. in their second case which additionally involved the cornea².

In summary, in our case series, we add the following features of the recently described COST.²

1. COST can reach a considerable size occupying the bulbar conjunctiva
2. The conjunctival stromal consistency may show a broad spectrum ranging from purely myxoid to purely collagenous
3. COST can occur in children, and might have a tendency to recurrence if incompletely excised.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.
Unilateral large epibulbar tumor occupying the upper ocular circumference from the limbus towards the equator of the left eye (case 1).