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A conjunctival myxoid stromal tumor (COMST) mimicking phlyctenulosis: A case report and brief review of the literature

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ABSTRACT

Purpose: This is a case report of a patient with a conjunctival myxoid stromal tumor (COMST), mimicking a phlyctenulosis. Tumors of the conjunctiva and cornea occupy a large spectrum ranging from benign lesions of myxoma to aggressive, life-threatening malignancies. Phlyctenulosis and phlyctenular keratoconjunctivitis are hypersensitivity reactions to a foreign antigen.

Observations: A 64-year-old male presented with six-month history of non-painful lump in the conjunctiva of the left eye. It was a mobile, non-tender, non-ulcerated, non-hemorrhagic, non-pigmented lesion and was non-adherent to the sclera. The differential diagnosis of phlyctenulosis or a soft tissue tumor was considered. The lesion was completely excised. The microscopy showed an ill-defined hypocellular myxoid lesion composed of stellate and spindle-shaped cells with eosinophilic cytoplasm, containing round-ovoid and spindle-shaped nuclei with a vesicular chromatic pattern. The tumor cells were diffusely and strongly positive for vimentin and CD 34 and were negative for S100. The immunomorphological features were compatible with a conjunctival myxoid stromal tumor. Complete systemic evaluation excluded the possible association with systemic myxomas.

Conclusions and importance: Myxoid tumors of the conjunctiva are benign tumors, however, they can mimic other benign conditions like phlyctenulosis or more sinister lesions like malignant tumors. Therefore, it is important to do an excisional biopsy to ascertain the definitive pathology of an indeterminate conjunctival lesion. COMST may be the index presentation for the detection of previously undiagnosed myxoma syndromes. One such association is with cardiac myxomas, which can result in vascular embolic events. Therefore, it is important to do cardiac screening in all patients diagnosed with a COMST.

1. Introduction

Tumors of the conjunctiva and cornea occupy a large spectrum ranging from benign lesions of myxoma to aggressive, life-threatening malignancies such as melanoma or Kaposi's sarcoma.[1] Myxomas are benign connective tissue tumors that arise in the heart, skin, bones, skeletal muscles, nasal sinuses, gastrointestinal system, and genitourinary system.[2] Ocular myxoid lesions are rare tumors documented to occur in conjunctiva, cornea, and lacrimal glands.[3–5] Myxoid tumors of the conjunctiva have controversial nosology and overlapping morphology. Various terms have been applied to conjunctival myxoid lesions, including ''conjunctival myxoma,'' ''conjunctival stromal tumor (COST),'' and, more recently, ''conjunctival myxoid stromal tumor (COMST)'' based on their morphologic, ultrastructural, and immunohistochemical patterns.[6] As in myxomas of other sites, the origin of these tumors, their neoplastic or non-neoplastic nature had been debated.[6–8]

Phlyctenulosis and phlyctenular keratoconjunctivitis are hypersensitivity reactions to a foreign antigen.[9,10] It is a nonspecific allergic response in the cornea or conjunctiva to a variety of distinct conditions. The ocular findings may be evidence of the presence of systemic tuberculosis.[11] In developed countries, staphylococcal infections and worm infestations are important etiological associations.[9]

This is a case report of a patient with a conjunctival myxoid stromal tumor (COMST), mimicking a phlyctenulosis.

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2. Case report

A 64-year-old male presented with six-month history of non-painful lump in the conjunctiva of the left eye. He had noticed a rapid enlargement of the lump for the preceding two months. He was seen at a local eye clinic and was said to have a pterygium on the temporal conjunctiva, requiring no specific treatment unless it grows over the cornea. At presentation to us there was slightly elevated, inflamed granular nodule extending from temporal mid conjunctiva to the limbus. It was a mobile, non-tender, non-ulcerated, non-hemorrhagic, non-pigmented lesion and was not adherent to the sclera. The differential diagnosis of phlyctenulosis or a soft tissue tumor was considered. At the presentation, its dimensions were 3mm × 2 mm × 2 mm. His uncorrected visual acuity was 6/36 bilaterally and best corrected vision was 6/6 in each eye. Extraocular movements were full and painless. Bilateral anterior segment and dilated fundus examinations were unremarkable. Both lacrimal apparatuses were normal (Fig. 1).

The lesion was completely excised under local anesthesia using conjunctival scissors with approximately 2mm wide margin. No sclerotomy was required as it was a non-adherent mobile lesion. The conjunctival gap was approximated and closed using vicryl 8-O' sutures. Topical mitomycin was not applied during surgery. The surgical sample received was a white color tissue piece admixed with mucus measuring 6mm × 5mm × 3mm. The microscopy showed an ill-defined hypocellular myxoid lesion composed of stellate and spindle-shaped cells with eosinophilic cytoplasm, containing round-ovoid and spindle-shaped nuclei with a vesicular chromatic pattern. The tumor cells lied in an abundant myxoid stroma with fibrillary and ropy collagen strands, diffusely distributed mast cells, and a thin capillary network. The tumor cells were diffusely and strongly positive for vimentin and CD 34 and were negative for S100 (Fig. 2). The immunomorphological features were compatible with a conjunctival myxoid stromal tumor.

Complete systemic evaluation excluded the possible association with systemic myxomas. There were no unusual areas of pigmentation or clinical evidence of endocrine abnormalities. Echocardiogram, chest x-ray, ultrasound scan of the abdomen and thyroid, excluded the possible association with Carney Complex and Zollinger-Ellison syndrome.

There were no signs of recurrence following the six-month post-excision.

3. Discussion

Myxomas are rare in the conjunctiva, accounting for 0.2% of all conjunctival lesions.[6] The mean age at presentation is 45 years.[5,12,13] Conjunctival myxomas typically present as slow-growing, painless, well-circumscribed, yellow-pink, cyst-like masses, with fibrous, vascular, soft tissue trunks.[3,14] They are often asymptomatic. This leads to a delay in presentation for medical advice and the mean time frame before patients presented for ophthalmic review of their conjunctival myxoma was 34 months. The lesions have been reported to range between 4 mm and 20 mm in diameter.[15] Most cases were painless, although there were few reported cases of conjunctival myxoma with ocular pain.[5] Most of the reported myxomas occurred in the bulbar conjunctiva, with the majority being temporal.[15]

Although the neoplastic nature of myxomas has been previously questioned, its association with multiple endocrine neoplasia syndromes and recent molecular genetic data firmly establish the myxoma's identity as a true neoplasm.[6]

Histologically, myxomas resemble Wharton's jelly, the loose mucoid tissue found within the umbilical cord.[4] The characteristic histopathological features of conjunctival myxoma are, sparsely scattered stellate and spindle-shaped cells distributed throughout a mucinous matrix, with delicate reticulin fibers, minimal blood vessels, and mature collagen fibers.[3,12,16,17] The mucinous matrix is predominantly composed of hyaluronic acid, with a lesser amount of chondroitin sulphate, that reacts to Alcian blue stain. The cells react for vimentin, CD 34, alpha-smooth-muscle actin, Bcl2 immunomarkers, and partially stain for CD 68 suggesting a fibroblastic cell phenotype.[12,13] It is non-reactive to S-100 protein, desmin, myoglobulin, and digested Periodic-acid-Schiff (PAS) staining.[12]

Before the emergence of COST as an entity in 2012, all primary myxoid proliferations were diagnosed as myxomas. According to the characterization of histopathologic and immunohistochemical features of COST by Herwig and associates the diagnosis of COST was rendered to conjunctival tumors composed predominantly of spindle cells with occasional pseudonuclear inclusions and multinucleated giant cells in a background of ropey collagen and a scant myxoid matrix.[7] The recent study by Qin and associates, however, demonstrated overlapping clinical and histopathologic features and an identical immunophenotype for conjunctival myxomas and COST, leading the authors to suggest the term that "conjunctival myxoid stromal tumor-COMST'' may be more

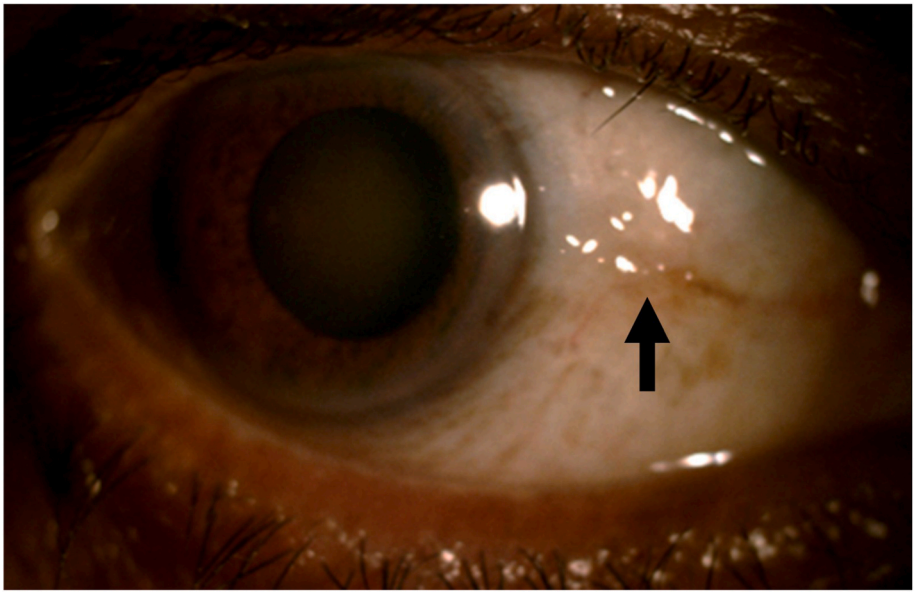

Fig. 1. Magnified Macroscopic view of the lesion-Arrowhead.

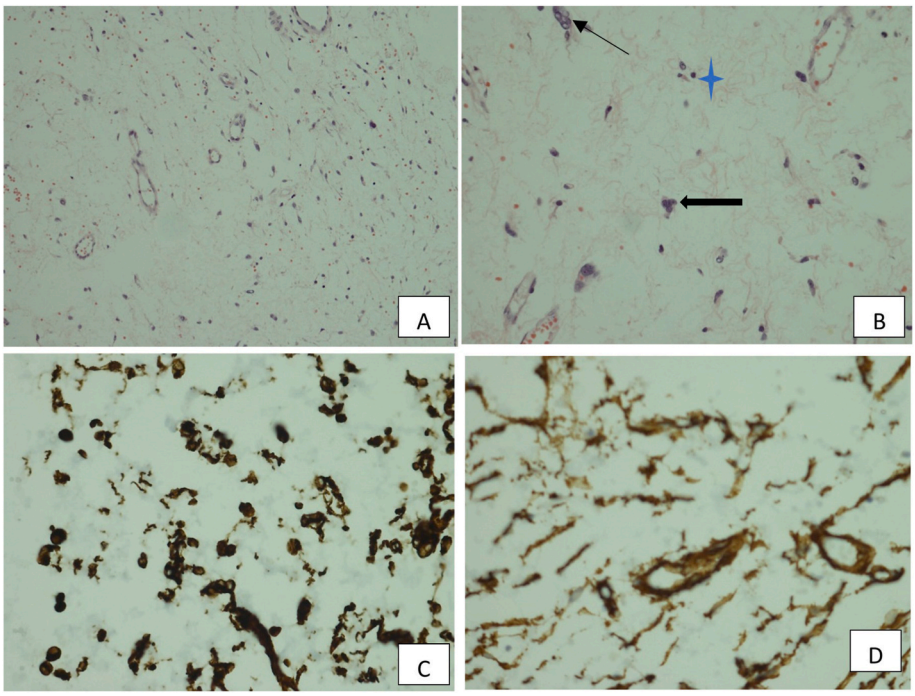

Fig. 2. Immunomorphological features of the tumor. A. Stellate and spindle-shaped cells lying in an abundant myxoid background containing fibrillary collagen (H & E x200). B. The cell with intranuclear inclusions (thin arrow), multinucleated cells (thick arrow), and mast cells (blue star) in the stroma (H & E x400) C. The lesional cells strongly and diffusely stained for vimentin (x400). d. The cells show diffuse and strong immunoreactivity for CD 34 (X400).

appropriately descriptive for this entity.[8]

The differential diagnosis of myxoid tumors of conjunctiva includes amelanotic naevus, amelanotic melanoma, fibrous histiocytoma, lymphangioma, myxoid neurofibroma, spindle-cell lipoma, rhabdomyosarcoma, and liposarcoma.[5,12,18] Histologically, an absence of pigmentation, the presence of sparse vascular structures, characteristic cellular morphology, and mucin staining, differentiate conjunctival myxoid tumors from these lesions.[15]

All reported cases of conjunctival myxoma have been treated with excision.[5,17] There was no documentation of malignant transformation in a mean follow-up time of 30 months.[3,5,12] The high recurrence rate that has been noted in orbital and cardiac myxomas was not a feature of these conjunctival myxoid tumors. With an average follow-up of 29 months, a single excision appeared to be an adequate treatment.[14] In general, the recurrence rate of all myxomas is documented as being relatively low. A review of 58 patients with soft tissue myxomas found a 3% incidence of recurrence 8–10 months post-excision.[3] The recurrences are more likely as a part of Carney Complex.[12]

The Carney Complex is an autosomal dominant syndrome with the presence of myxomas, spotty mucocutaneous pigmentation, endocrine overactivity, and psammomatous melanotic schwannomas.[12,19,20] Ophthalmic manifestations of the Carney Complex include eyelid lentigines, conjunctival or caruncle spotty pigmentation, and eyelid or conjunctival myxomas. Carney reported that greater than 50% of patients with the Carney Complex suffered a significant embolic event in their life related to cardiac myxomas.[20] Ophthalmic manifestations of the Carney Complex, not limited to myxoma, have been shown to precede embolic events.[19,20] Therefore, it is important to identify ocular myxomas and to screen and monitor for cardiac myxomas.

Conjunctival myxoma has been associated with pancreatic gastrinoma in Zollinger-Ellison syndrome. Zollinger-Ellison syndrome may be a manifestation of the Carney Complex, given the neural crest origins of myxomas, schwannomas, and gastrinomas.[19] Other systemic diseases, such as Mazabraud syndrome and McCune-Albright syndrome have not been associated with conjunctival myxomas.[5] In this patient, possible syndromic associations were excluded, and the tumor is more likely to be a non-syndromic, sporadic case.

Histologically, phlycten is an aggregation of lymphocytes and occasional polymorphonuclear cells. Conjunctival phlyctenulosis are usually transient and asymptomatic, but occasionally, larger phlyctens cause frank pustular conjunctivitis with subsequent penetration into deeper structures, leading to permanent scar formation. It is a morphologic expression of delayed hypersensitivity to diverse antigens, that arises as an expression of altered immune mechanisms.[21]

4. Conclusion

Myxoid tumors of the conjunctiva are benign tumors, however, they can mimic other benign conditions like phlyctenulosis or more sinister lesions like malignant tumors. Therefore, it is important to do an excisional biopsy to ascertain the definitive pathology of an indeterminate conjunctival lesion. COMST may be the index presentation for the detection of previously undiagnosed myxoma syndromes. One such association is with cardiac myxomas, which can result in vascular embolic events. Therefore, it is important to do cardiac screening in all patients diagnosed with a COMST.

Patient consent

The patient provided both oral and written consent for use of his medical history and images in this publication.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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