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Case Report

Primary Localized Conjunctival Amyloidosis Mimicking Lymphoma

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Abstract

A 27-year-old healthy male presented to our clinic with complaints of redness and burning in his left eye for the past 6 months. Biomicroscopic examination revealed a salmon-colored, elevated, painless mass lesion involving the entire lower fornix conjunctiva of the left eye. A conjunctival incisional biopsy was performed due to suspicion of lymphoproliferative disease. Histopathological examination confirmed amyloidosis. Further investigations did not reveal any evidence of systemic amyloidosis, lymphoma, or other lymphoproliferative diseases. During the 18-month follow-up after surgery, no recurrence or new findings were observed in the patient's ophthalmologic or systemic evaluations. Amyloidosis in the periocular region can present with various clinical findings. Although a classic salmon-colored conjunctival mass initially may suggest lymphoproliferative diseases, conjunctival amyloidosis should be considered in the differential diagnosis.

Keywords: Conjunctiva, Lymphoma, Primary amyloidosis

Introduction

Conjunctival lesions range from benign, simple degenerative changes to malignant conditions such as lymphoma and melanoma. While the typical clinical features of these lesions can guide differentiation during examination, similarities can sometimes be misleading. Primary localized conjunctival amyloidosis is one of the rarest conditions among conjunctival lesions. Clinically, it can present with recurrent subconjunctival hemorrhage, a yellow-colored conjunctival mass, or lesions resembling pterygium (1). However, it is important to note that conjunctival amyloidosis can also present with conjunctival lesions of varying appearances. Herein, we present a case of primary localized conjunctival amyloidosis, which clinically resembled a lymphoproliferative lesion but was histopathologically diagnosed as amyloidosis.

Case Report

A 27-year-old male presented to our clinic with complaints of redness, swelling, stinging, and watering in the inner part of the left lower eyelid for the past 6 months. Biomicroscopic examination revealed a painless, elevated, salmon-

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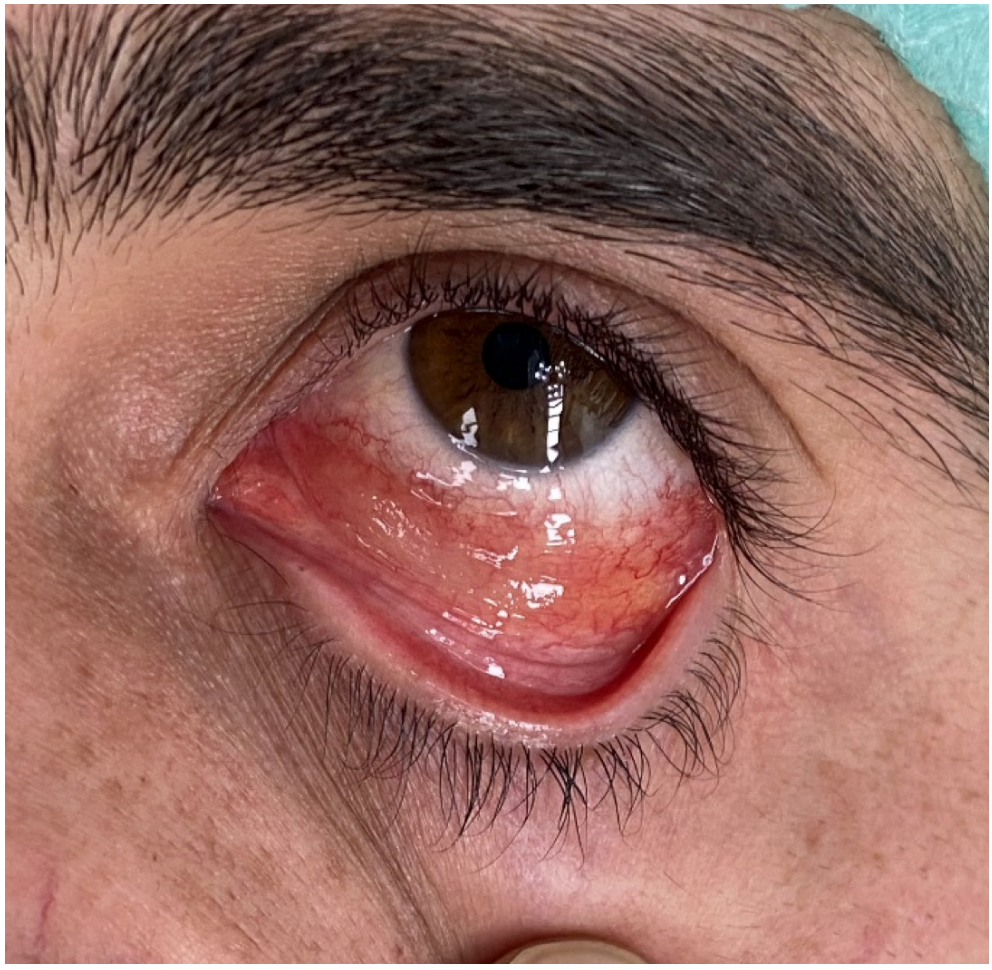

Figure 1. A salmon-colored, elevated lesion involving the entire inferior fornix conjunctiva and extending to the bulbar conjunctiva.

colored conjunctival mass lesion involving the entire lower fornix conjunctiva and extending to the bulbar conjunctiva on the left side, with indistinct borders and minimal surrounding hyperemia (Fig. 1). The other anterior segment and fundus examinations, as well as ocular movements, were normal bilaterally. Orbital magnetic resonance imaging showed no signs of orbital involvement. Due to its salmon color and rubbery consistency, an incisional biopsy was planned with a preliminary diagnosis of lymphoproliferative disease. The visible portion of the lesion along the lower fornix was excised, and the area was primarily closed. Histopathological evaluation revealed widespread and dense eosinophilic material throughout the stroma and vessel walls beneath the epithelium. An immunohistochemical study showed diffuse staining with Congo red, confirming a diagnosis of amyloidosis (Fig. 2). Figure 3 also demonstrates staining with Congo red with apple green birefringence. The patient was referred to the internal medicine clinic to investigate systemic involvement. Complete blood count (CBC), serum electrophoresis, β-2 microglobulin level, 24-h urine protein level, kidney and liver function tests, echocardiography, and abdominal ultrasonography were all normal, leading to a diagnosis of primary localized conjunctival amyloidosis. At the 4-month post-operative follow-up, there was no adhesion in the fornix, and the cosmetic appearance was satisfactory (Fig. 4). During the 18-month follow-up, no recurrence was observed. Written informed consent of the patient was taken for the publication of his clinical findings.

Discussion

Amyloidosis is a clinical condition characterized by the extracellular accumulation of a pathological protein material called amyloid. This material consists of amorphous, insoluble, misfolded fibrils with a beta-sheet structure and can accumulate in various tissues and organs. Depending on the extent of involvement, amyloidosis is classified as either systemic or localized. Based on the underlying etiology, it is further classified as either primary or secondary (2).

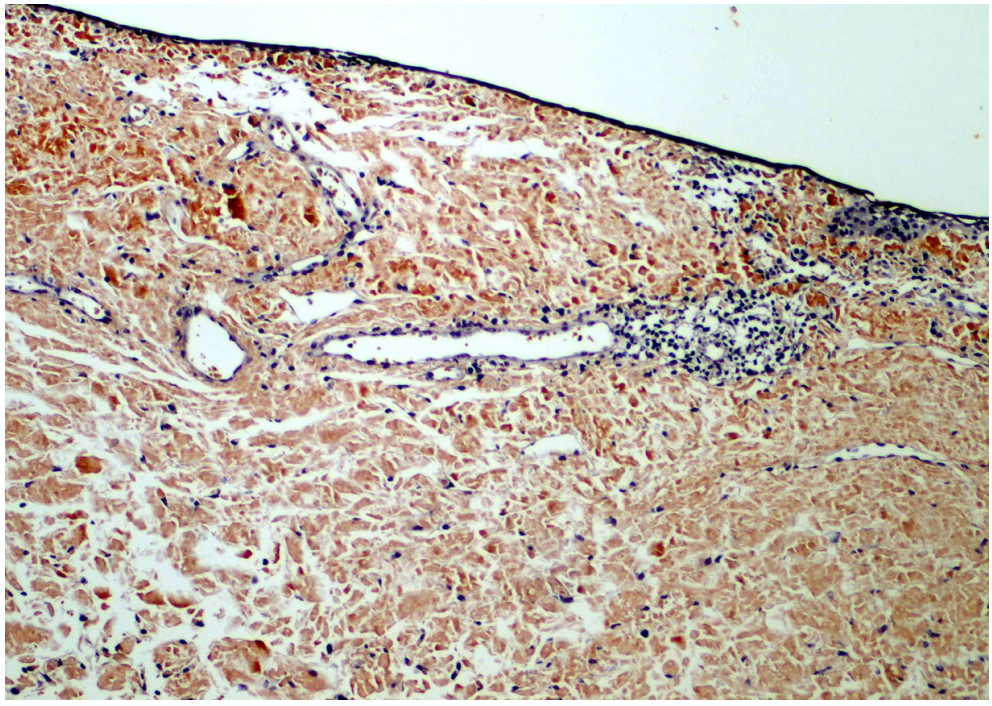

Figure 2. Brick red staining reaction with Congo red (×40).

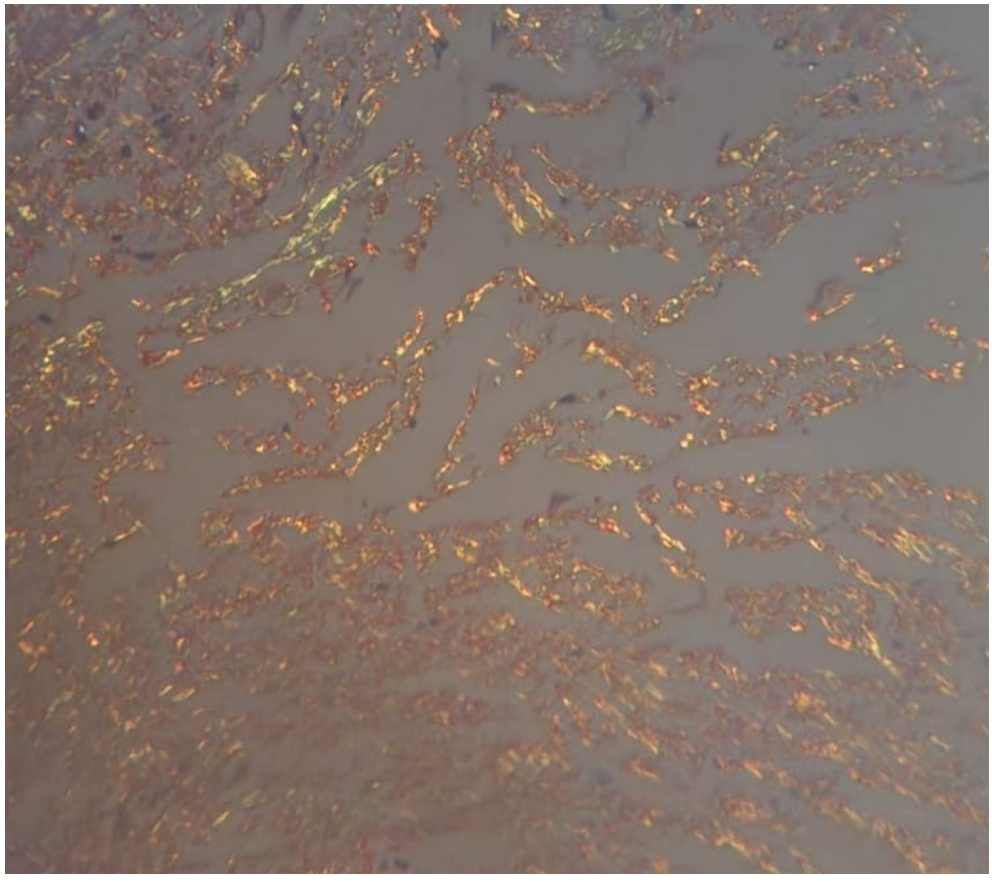

Figure 3. Congo red staining with apple green birefringence.

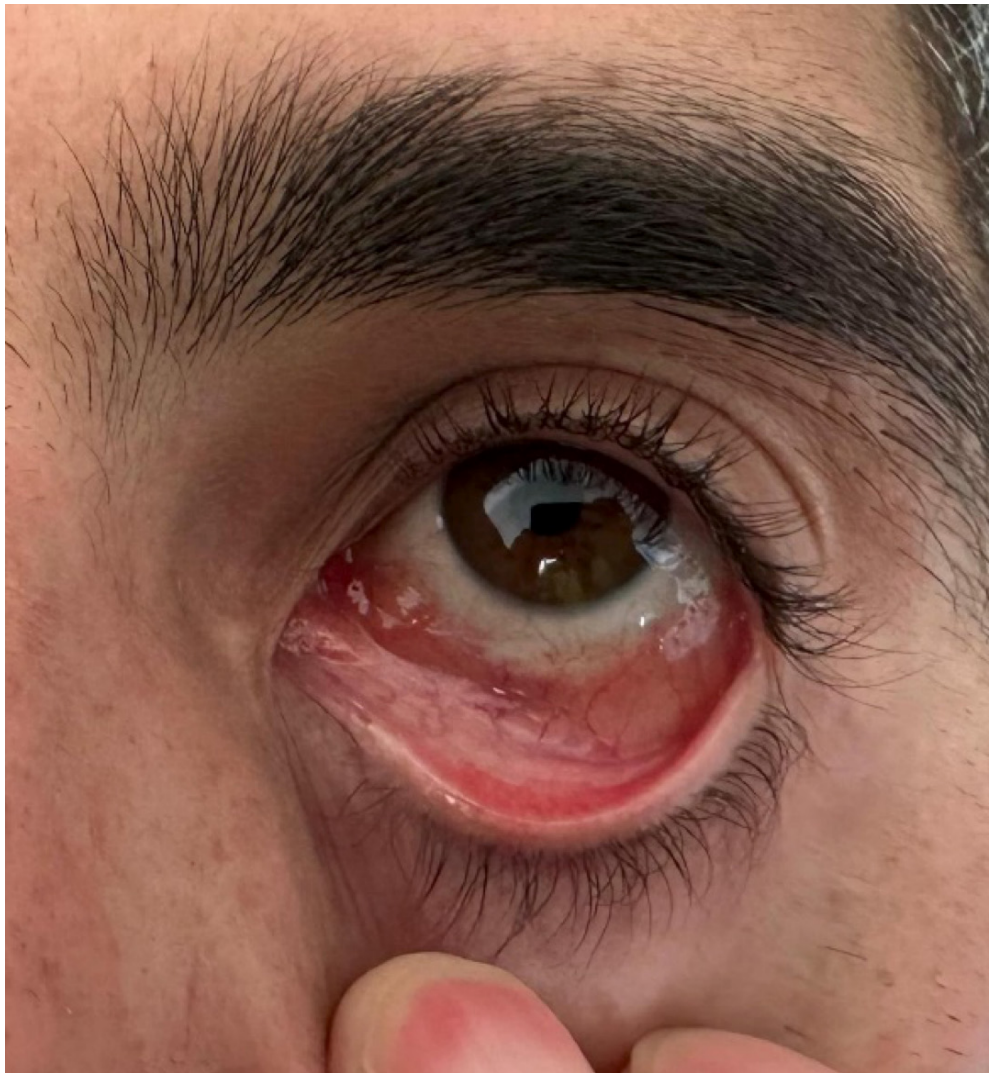

Figure 4. 4th month follow-up after surgery.

Localized conjunctival amyloidosis is a very rare form of the disease that can be either primary or secondary. Most commonly, conjunctival amyloidosis presents as primary localized, typically unilateral, and rarely shows systemic involvement. Secondary localized amyloidosis can develop due to chronic inflammation or as part of systemic conditions such as multiple myeloma, rheumatoid arthritis, leprosy, and familial Mediterranean fever. It is characterized by the accumulation of immunoglobulin-related protein (light chain amyloid) in the conjunctiva (1,3,4). Conjunctival amyloidosis generally occurs in middle-aged adults and shows no significant gender difference (2). The most common sites are the fornices (upper > lower) and the tarsal conjunctiva (5). Patients may present with conjunctival masses, pterygium-like lesions, or subconjunctival hemorrhage (1,3). Other ophthalmological involvements include the eyelid and orbit. These patients may present with blepharoptosis, entropion, eyelid masses, periorbital ecchymosis, periorbital edema, lacrimal gland involvement, extraocular muscle involvement, and proptosis (2). In this case, because the lesion exhibited a classic appearance suggestive of lymphoma, primary localized conjunctival amyloidosis was not initially considered due to its extreme rarity. The decision to perform a biopsy was primarily driven by the lesion's rapid development and characteristic "salmon patch" morphology. This case report highlights that, despite its uncommon occurrence, conjunctival amyloidosis can clinically mimic malignant lesions such as lymphoma, thereby posing a diagnostic challenge. Spitellie et al. (6) suspected lymphoproliferative disease in a 39-year-old female patient due to a painless, salmon-colored mass located under the left upper eyelid and involving the anterior orbit. The histopathological diagnosis was consistent with amyloidosis, and no systemic involvement was observed. In our case, only the lower fornix was involved with no orbital involvement. The lesion exhibited a salmon-colored appearance suggestive of lymphoproliferative disease. Since the lesion developed over a short period of 6 months,

orbital involvement may not yet have been observed. Cases where localized amyloidosis progresses to systemic disease have been reported, so this possibility should be kept in mind when monitoring a patient presumed to have localized amyloidosis (6). No systemic involvement was observed during the 18-month follow-up of our patient. In addition, Marsh et al. (7) reported a case of a 62-year-old patient diagnosed with localized conjunctival amyloidosis who subsequently developed extranodal lymphoma during follow-up. Therefore, long-term follow-up of these patients is crucial.

Histopathological evaluation is essential for diagnosis. Hematoxylin-eosin-stained sections show nodular accumulations of amorphous, homogeneous eosinophilic deposits in the substantia propria. Staining with Congo red reveals brick-red coloring, and under polarized light, amyloid deposits exhibit apple-green birefringence (8,9). Setoguchi et al. (10) detected low-grade B-cell lymphoma along with amyloid accumulation in the histopathological evaluation of a conjunctival lesion affecting the upper and lower eyelid fornices. They interpreted this as lymphoma cells transforming into plasma cells that produce amyloidogenic immunoglobulin light lambda chains.

Systemic evaluation of patients diagnosed with conjunctival amyloidosis is important. A comprehensive systemic evaluation at diagnosis should include CBC, serum protein electrophoresis with immunofixation, β-2 microglobulin level measurement, 24-h urine protein analysis, kidney and liver function tests, serum free light chain assay, abdominal ultrasonography, and echocardiography to thoroughly assess potential cardiac involvement. If clinically indicated, additional investigations such as bone marrow biopsy or PET-CT may be performed to exclude systemic or hematologic disorders (7).

Treatment options for adnexal and orbital amyloidosis include monitoring, excision, ocular surface reconstruction with amniotic membrane, cryotherapy, and even radiotherapy (3,9,11). Different treatment approaches can be applied depending on the location of the involvement, the presence of functional defects, and cosmetic expectations. In our case, the entire visible lesion was excised during the incisional biopsy stage. The ease of closing the conjunctiva in the fornix area allowed for ocular surface reconstruction without the need for an amniotic membrane. Follow-up examinations showed no recurrence or complications requiring intervention, such as symblepharon.

Ophthalmologic follow-up should include systematic slit-lamp examinations of the conjunctiva and fornices, detailed documentation, and sequential photography of any residual or newly developed conjunctival lesions. Evaluation should also address potential complications such as symblepharon or amyloid recurrence, along with assessment of intraocular pressure and posterior segment status to rule out secondary ocular involvement.

Importantly, conjunctival involvement may be the first clinical manifestation of systemic amyloidosis, with the ophthalmologist often being the first physician to recognize the disease. Therefore, ophthalmologists play a crucial role in initiating the diagnostic workup for this potentially systemic condition. All conjunctival lesions – especially those that mimic malignant processes or persist despite treatment – should be thoroughly evaluated with a high index of suspicion.

Conclusion

Conjunctival amyloidosis can present with various clinical features. Although rare, it should be considered in the differential diagnosis of all benign and malignant lesions of the conjunctiva. Since conjunctival involvement can occasionally be the first clue to a systemic amyloid disease, ophthalmologists have a vital role in early diagnosis. All diagnosed patients should be evaluated for systemic involvement or accompanying lymphoproliferative diseases and followed long-term.

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