Primary Localized Conjunctival Amyloidosis
Presenting with Unilateral Ptosis

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Abstract

**Purpose:** Primary localized amyloidosis of eyelid is a localized type of amyloidosis without evidence of systemic involvement, which is a quite rare clinical condition. Here we report a case of primary localized amyloidosis of eyelid.

**Case report:** A 40-year-old woman presented with a four-month history of swelling of the left upper eyelid resulting in a mechanical ptosis. The mass had a firm bony consistency. Ocular examination revealed a firm mass in upper lid connected to the tarsus. She had no sign or history of ocular inflammation. Homogenous eosinophilic deposits with extensive foci of calcification and ossification were visible in pathologic assessment, which was consistent with amyloidosis. All evaluations were negative for systemic amyloidosis.

**Conclusion:** Primary localized amyloidosis may appear as a calcified and ossified tumoral mass.

**Keywords:** Eye, Eyelid, Amyloidosis, Primary Localized Amyloidosis, Conjunctival Amyloidosis, Ocular Amyloidosis, Hyaline Protein, Ptosis


Introduction

Amyloidosis is accumulation of heterogeneous, amorphous, proteinaceous material in extraocular space or any tissue. It has two main clinical subcategories; systemic and localized.

Systemic amyloidosis is a serious and sometimes life threatening disorder in which amyloid material accumulate in the tissue, destroying its structure and function. On the other hand, localized amyloidosis is a rare, usually benign disorder, frequently involving head and neck without systemic manifestation, with an excellent prognosis. Primary localized conjunctival amyloidosis is a rare subgroup. The abnormal amyloid material is present in substantia propria and around conjunctival vessels. These subconjunctival lesions are solitary or multiple, usually bilateral, and well-vascularized, fusiform or polypoid, and painless. It may present with subconjunctival hemorrhage, yellow subconjunctival or an orbital mass, or lid thickening and blepharoptosis.
Ptosis is attributable to several mechanisms. Frequent episodes of hemorrhage cause recurrent eyelid swelling resulting in levator aponeurosis dehiscence from the tarsal plate. On the other hand, a large amyloid mass adds considerable weight to the lid causing mechanical ptosis. Direct muscle infiltration with amyloid materials may lead to myogenic ptosis.

Continuous rubbing of the conjunctival mass against the cornea causes ocular surface irritation. Fornix shortening, symblepharons, insufficient tear lake, and dryness are some other ocular surface problems.

Various treatment methods have been proposed. Conservative surgical excision, cryotherapy and superficial radiotherapy have been attempted with partial success. We present our experience with a rare case of primary localized amyloidosis of upper palpebral conjunctiva, with presentation of ptosis.

Case report
A 40-year-old woman presented with history of ptosis for many years and diffused swelling of the left upper eyelid for 4 months and aggravation of symptoms since 2 weeks before referral (Figure 1). Upper palpebral conjunctiva was congested and the mass was subconjunctival and bulbar conjunctiva sparing, moreover, the lesion was extended posteriorly to the orbit. The patient had a high crease and poor levator function, consistent with aponeurotic ptosis. In eyelid eversion there was a 35x15 mm irregular infiltrative yellow mass with a bony consistency. Posterior extension to orbit could not be measured. The mass involved the tarsal conjunctival surface, with extension to the superior fornix and plica semilunaris. Ocular examination including visual acuity (VA), extraocular movements, pupils, intraocular pressure and fundoscopy was unremarkable.

Careful history taking did not reveal any preceding chronic ophthalmic complaints. Computerized tomography of the eye showed a hyperintense mass in upper left eyelid with intraorbital extension (Figures 2A and 2B). Mass density was similar to calcification. The extraocular muscles, eyeball, retrobulbar area and optic nerve were normal. Magnetic resonance imaging (MRI) revealed a crescent shape low T1 and T2 weighted signal lesion which showed no enhancement (Figures 3 and 4). The lesion was removed carefully from the bulbar, palpebral and fornical conjunctiva. Levator muscle and upper tarsus was invaded and was removed to some extent with the mass.

In pathologic study of the lesion, conjunctival epithelium was normal and deposition of acellular, pale, eosinophilic, hyaline material beneath the conjunctival epithelium in substantia propria was detectable. Lesion was mostly composed of foci of calcification and extensive foci of ossification near the hyaline deposits (Figure 5). There was a trace of mature plasma cells and lymphocytes.

The material was congophilic by Congo red staining, and on polarization had an apple green birefringence suggestive of amyloid deposition (Figure 6).

Urine protein analysis, complete blood count, an abdominopelvic ultrasound scan and an echocardiogram were performed in order to rule out the systemic involvement of amyloidosis, which all were normal. Immunoelectrophoresis revealed a normal electrophoretic pattern. Immunoglobulin (IgA, IgM, IgG) levels were normal. Bence-Jones proteins and monoclonal band were absent in the urine.

Figure 1. Preoperative photograph: Ptosis of the left upper lid is obviously visible
Figure 2. Computerized tomography (axial image (A) and Sagittal image (B)) shows a white mass in upper left eyelid with intraorbital extension. Its density was same as calcification and bone.

Figure 3. MRI (sagittal T1 weighted) revealed a crescent shape low signal lesion without enhancement.

Figure 4. MRI (axial T2 weighted) revealed no high signal lesion.

Figure 5. Homogenous eosinophilic material with several foci of calcification (H&E staining x100)

Figure 6. Apple green birefringent deposits of amyloid materials (Congo red staining)
Discussion

The term 'amyloidosis' was first used by Virchow in 1854 based upon the color after staining with iodine and sulfuric acid.\textsuperscript{5} In 1968, Macoul and Winter reported a case of ocular manifestation in systemic amyloidosis. Much earlier, localized ocular amyloidosis was reported in 1871 for the first time.\textsuperscript{5}

Localized amyloidosis is quite a rare disease,\textsuperscript{2,6} and only 4% of localized amyloidosis of the head and neck region occur in the orbit.\textsuperscript{2,6} Primary amyloidosis involves all ocular structures.\textsuperscript{3,5} There are some reports of amyloidosis as a cause of ptosis in the literature.\textsuperscript{3} Usually in cases of focal orbital amyloidosis, amyloid deposits are visible in eyelid or conjunctiva and in superior portions of the orbit.\textsuperscript{5,7-16} Typically, patient present with unilateral or bilateral solitary or multiple firm, rubbery, waxy appearing, painless fusiform or polypoid masses.\textsuperscript{5,17} It is found in young and middle-age individuals, and rarely appears as a painless lid mass, or exophthalmos presented for years in elderlies.\textsuperscript{2,5,10-15,18,19} Double vision, and periorbital hemorrhage sometimes occurs.\textsuperscript{2,6,14-16,18,19} Most common non familial ophthalmologic manifestation of amyloidosis is localized form in the conjunctiva. The condition is usually unilateral as in our patient, but bilateral involvement has also been reported.\textsuperscript{20,21} Involvement usually begins in the fornix with secondary extension into the bulbar and palpebral conjunctiva.\textsuperscript{5} Patients usually have a long history of slowly enlarging eyelid mass, decreased tearing with multiple biopsies and surgeries performed.\textsuperscript{22} Our patient, had ptosis for many years before detection of orbital mass. The exact pathogenesis of the ptosis is not clear. It does not seem to have neurogenic pathology as the ocular motility was normal. The amyloid deposition in the levator palpebrae superioris probably was responsible for the ptosis.\textsuperscript{10,23} (probably with either levator aponeurosis dehiscence, mechanical ptosis (upper lid weight), or myogenic mechanism (direct muscle infiltration with amyloid materials)).

Amyloidosis must be considered as a differential diagnosis in conjunctival neoplasms (Moorman and McDonald 1997; Lee et al 2000).\textsuperscript{24} Bleeding tendency is a characteristic feature of amyloidosis, which was not a feature in our case (Lee et al 2000; Pirouzmand et al 2002; Westermark et al 2002).\textsuperscript{24}

Various treatment modalities have been mentioned in literature, including conservative local excision,\textsuperscript{3,22} debulking, cryotherapy, and superficial cobalt therapy,\textsuperscript{8} all were reported with partial success.\textsuperscript{5} Previously, surgery was made difficult by the bleeding tendency and recurrence. Results were also poor. In recent years, published data showed that surgical complications has been minimized due to careful debulking of deposits with a spooned curette, preservation of anatomic planes, avoidance from normal lid tissue sacrifice\textsuperscript{1,16} and careful dissection with diathermy needle. Mass excision is the gold standard treatment but it must be as conservative as possible.\textsuperscript{5,3,22} Total excision of the lesion is usually impossible and surgery should be performed to excise main part of the lesion with preservation of the palpebral lobe of the lacrimal gland, the levator palpebrae superioris, and the extraocular muscles.\textsuperscript{14} In large amyloid masses, debulking may be needed before surgical excision. Radiotherapy has been reported useful in reducing the size of the mass before surgery in some cases.\textsuperscript{25}

Although not frequent, there are some reports of recurrence\textsuperscript{3,5,22} with persistent ocular complaints that can be attributable to conservative local excision and persistent disease.

Exact etiology and pathogenesis of the disease is still unclear.\textsuperscript{5} Amyloid is an extracellular, proteinaceous substance that can be deposited in various tissues. The best way of histopathological identification is Congo red staining. All forms of amyloid have a green birefringence under a polarizing microscope.\textsuperscript{18} Histopathological findings in our case were consistent with amyloidosis. Significant ossification and calcification were probably due to chronicity.

Systemic examination and all laboratory tests were normal which excludes systemic amyloidosis. Ptosis was the only symptom or sign due to upper lid mass, which makes diagnosis of secondary amyloidosis improbable.\textsuperscript{2}

There are some descriptions of CT appearance of orbital amyloidosis in the literature. Localized amyloidosis of the lacrimal gland\textsuperscript{9,10,12-15} and involvement of
extraocular muscles have been demonstrated.\textsuperscript{6,11-14} Changes in adjacent bones have been seen in a few cases; erosion or focal thinning\textsuperscript{12,14} and hyperostosis or focal thickening\textsuperscript{14} have also been reported. Seven of 16 cases of orbital amyloidosis revealed punctate calcifications.\textsuperscript{5,9,11,12,14} Enhancement with contrast material of the amyloid lesion in the head and neck region varies from none to marked on CT scans.\textsuperscript{2,6,7,9,11,12} CT scan in our case revealed a calcified mass in conjunctival side of the upper lid with posterior extension into the orbit, involving levator palpebrae superioris, although the posterior part was not calcified.

**Conclusion**

There are not many reports of MRI in focal amyloidosis. Hypointense signal has been observed in the lesion on T2-weighted images in a patient with focal nasopharyngeal amyloidosis.\textsuperscript{6} Amyloid deposition in other organs also appears hypointense on T2-weighted images.\textsuperscript{2} Similarly, the lesion in our case was hypointense on T2-weighted images (Figures 3 and 4).

**References**