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Unilateral conjunctival AL kappa amyloidosis with trace evidence of systemic amyloidosis

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Summary

Background: Amyloidosis is a systemic disorder that results from the tissue deposition of various proteins with distinctive morphological characteristics. Conjunctival amyloidosis is a rare variant which is generally localized and not associated with systemic involvement.

Case Report: We present here a case of 47-year-old female patient with right eyelid swelling that progressed over a 12 year period and eventually underwent surgery with pathology showing AL conjunctival amyloidosis. Unlike in most other reported cases of localized amyloidosis, she was noted to have amyloid deposition in the bone marrow and gastrointestinal tract upon extensive evaluation without any evidence of underlying plasma cell dyscrasia. She has been on observation without evidence of systemic progression or recurrence of conjunctival amyloid.

Conclusions: Although it initially appeared that our case represented an isolated form of AL (kappa)-type conjunctival amyloidosis, systemic evaluation revealed trace amount of amyloid in the bone marrow and GI tract. It is feasible that upon very close scrutiny patients with seemingly localized AL amyloidosis may have trace amounts of amyloid involving other organs and based on experience from this single patient we believe that it is safe to observe such patients closely rather than pursue systemic therapy

key words: amyloidosis • multiple myeloma • Congo red

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Background

Primary ocular amyloidosis of the eye, especially conjunctival amyloidosis, is a rare clinical condition that requires histopathological confirmation and must be considered in the differential diagnosis of conjunctival neoplasms [1,2]. Conjunctival amyloidosis is usually seen in middle-aged adults. It can present as confluent fusiform lesions or polypoidal papules that have a waxy or yellow color [3]. We present a case of a patient with conjunctival amyloidosis of 12 years duration that progressively worsened; extensive work up demonstrated trace systemic involvement.

Case Report

A 47-year-old female patient presented with asymptomatic swelling of the right lower eyelid of 12-years duration. Progressive swelling decreased visual acuity and then development of ptosis during the last 8 months, prompted the patient to seek ophthalmologic evaluation (Figure 1).

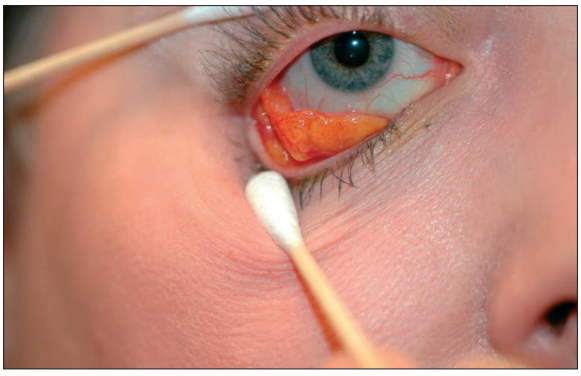

Figure 1. Right conjunctival amyloidosis.

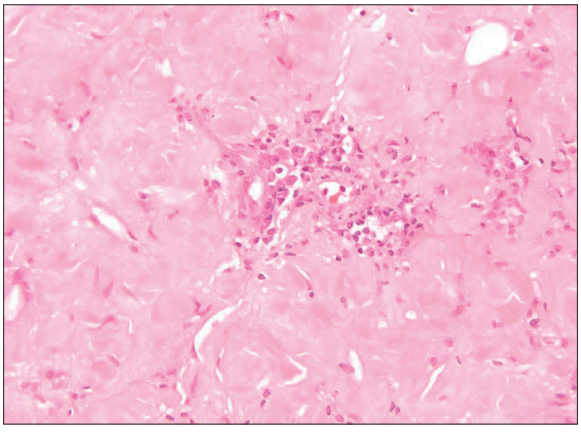

Figure 2. Histological section of conjunctiva showing stromal nodular accumulation of proteinaceous acellular material with minimal associated perivascular plasma cells and lymphocytes. (hematoxylin and eosin, ×400).

An excisional biopsy revealed multiple rounded, firm, red-yellow tissue fragments measuring 1×1×0.4 cm in aggregate. Histopathological examination demonstrated amyloid deposition within the conjunctival stroma and subconjunctival fibro-adipose tissue (Figure 2), highlighted by Congo red histochemical stain with birefringence and apple-green dichroism of extracellular deposits under polarized light (Figure 3A,B).Both kappa and lambda light chains were detected on immunohistochemical, immunofluorescence, and *in-situ* hybridization studies. Liquid chromatography, tandem mass spectroscopy, performed on micro-dissected specimen at the Mayo Clinic demonstrated a peptide profile consistent with AL (kappa) – type amyloid deposition. Normal vision returned after the procedure. She was referred to the UAMS Myeloma Institute to evaluate for systemic amyloidosis and underlying plasma cell dyscrasia (PCD). The work-up included complete blood count, urinalysis, urine and serum protein electrophoreses, PET and axial MRI scans that were all negative for PCD. The bone marrow biopsy was positive for amyloid on Congo red stain, but without evidence of PCD. Electrocardiogram, echocardiogram, BNP and NT-pro BNP results were normal. FISH results on the marrow specimen were positive for 13q14.3 and 13q34 deletion and a 17p13.1 deletion (P53 gene). Evaluation of gastrointestinal amyloid deposition was pursued for the patient's compliant of diarrhea. Colonoscopy and esophagogastroduodenoscopy was performed and biopsies showed trace amounts of amyloid by Congo red histochemical stain, interstitially and perivascularly, in the colon and duodenum, but thioflavin- T was negative, and no kappa or lambda was detected on immunofluorescence studies. Thus, although there were no signs of clinically-significant systemic amyloidosis or underlying PCD, we were able to identify the presence of amyloid in the bone marrow and traces of amyloid, colon and duodenum.

Discussion

AL amyloidosis mostly presents as a systemic disease though it may presents as a localized disease, where amyloid deposition is limited to a single organ. The specific area of the body affected depends upon the biochemical nature of the amyloid fibril protein and, as in systemic non-localized AL amyloidosis; light chain fragments may be involved. Localized AL amyloidosis may first be suspected on the basis of its location. Typical sites associated with localized AL amyloidosis include the brain, bladder, skin, urinary tract, conjunctiva, larynx and the tracheobronchial tree in the absence of systemic visceral dysfunction [4,5].

Amyloidosis of the palpebral conjunctiva is a rare condition that may results in chronic discomfort [6].The clinical differential diagnosis of conjunctival amyloidosis includes lymphoma, leukemia, metastatic carcinoma, sarcoidosis and other types of granulomatous inflammation, papilloma, pyogenic granuloma, nevus, melanoma and sebaceous carcinoma [3].

Many of the cases reports published on conjunctival amyloidosis describe localized involvement with no evidence of systemic amyloidosis. 35 of the cases with conjunctival amyloidosis were reviewed [1,2,7,8–10,11–24]. Thirty of these cases were isolated conjunctival amyloidosis with no evidence of systemic involvement [2,7,8–10,15–24]; four cases were associated with primary systemic amyloidosis [8,11–13] and one case was associated with multiple myeloma [14]. Histopathological examination as well as immunohistochemical and immunofluorescence were performed on some of these patients; however the results showed six cases AL subtype amyloidosis [13,16–20], four cases AA subtype amyloidosis [10,15,16], and three cases anti-amyloid P AB [1,12].

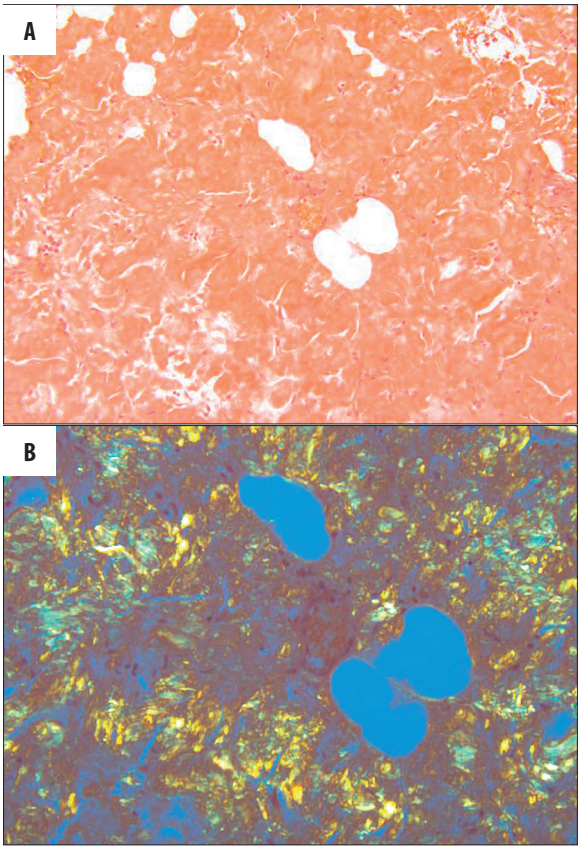

Figure 3. Characteristic dichroism of amyloid on polarized light examination. (**A**) Congo red, ×200; (**B**) Congo red (polarized), ×200).

The rest of the cases that were reviewed in the literature were indeterminate.

Four cases reviewed were associated with primary systemic amyloidosis which was well documented with bone marrow biopsy and rectal/fat biopsy [8,11–13]. Systemic work up were documented on 22 cases [1,8–10,11–14,17,19–21,23,24], four cases had bone marrow biopsy [11,12,17,21]. Five cases underwent either rectal or fat biopsy [10,12,13,17,20], rest of the cases were variable though checking CBC, UA, LFT, SPEP, and UPEP were essential**.**

Usually conjunctival amyloidosis is asymptomatic and does not require treatment, though in this case eyelid swelling had worsened over the preceding 8 months develop with symptoms that required surgical excision. Pathological and ancillary examination of the excised tissue confirmed the diagnosis of amyloidosis, AL (kappa) subtype; no underlying PCD was detected on thorough systemic examination, but trace amyloid was discovered in the bone marrow, colon and duodenum. AL type amyloidosis may develop 15% of cases of multiple myeloma [25]. Deletions of long arm of chromosome 13 commonly occur in multiple myeloma (MM), monoclonal gammopathy of undetermined significance (MGUS) and in systemic amyloidosis [26–28]. FISH chromosomal analysis on the bone marrow specimen in this case showed 13q14.3 and 13q34 deletion, indicating either monosomy 13 or 13q-. P53 mutations (also present in this case as a 17p13.1 deletion) occur moderately often in hematological malignancies. They are particularly associated with progression of disease in both lymphoid and myeloid leukemia as well as lymphomas [29]. In MM patients P53 gene deletion reflects an unfavorable prognosis [30].

Conclusions

Although it initially appeared that our case represented an isolated form of AL (kappa)-type conjunctival amyloidosis, systemic evaluation revealed trace amount of amyloid in the bone marrow and GI tract, as well as chromosomal abnormality seen commonly in multiple myeloma. It is feasible that upon very close scrutiny patients with seemingly localized AL amyloidosis may have trace amounts of amyloid involving other organs and based on experience from this single patient we believe that it is safe to observe such patients closely rather than pursue systemic therapy.

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