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 workup 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).

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 stratum 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 spectrometry, 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 complaint 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 immunohistochemical, immunofluorescence, and differential diagnosis of conjunctival amyloidosis includes lymphoma, leukemia, metastatic carcinoma, sarcoïdosis and other types of granulomatous inflammation, papilloma, pyogenic granuloma, nevus, melanoma and sebaceous carcinoma [5].

**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 result in chronic discomfort [6]. The clinical differential diagnosis of conjunctival amyloidosis includes lymphoma, leukemia, metastatic carcinoma, sarcoïdosis and other types of granulomatous inflammation, papilloma, pyogenic granuloma, nevus, melanoma and sebaceous carcinoma [5].

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].
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.

**REFERENCES:**

1. Moorman CM, McDonald B: Primary (localized non-familial) conjunctival amyloidosis: three case reports. Eye, 1997; 11: 603–6
2. Lee HM, Naor J, DeAngelis D, Rootman D: Primary localized conjunctival amyloidosis presenting with recurrence of subconjunctival hemorrhage. Am J Ophthalmol, 2000; 129: 244–45
3. Shields JA, Shields CL: Conjunctival amyloidosis: Atlas of Eyelid and Conjunctival Tumors. Philadelphia, Lippincott Williams and Williams, 1999; 324–25
4. Birwend ML, Menke DM, Calaminia KT: The spectrum of localized amyloidosis: a case series of 20 patients and review of the literature. Amyloid, 2006; 13(3): 135–42
5. Gertz MA: How to manage primary amyloidosis. Leukemia. Leukemia, 2012; 26(2): 191–98
6. Hill VE, Brounstein S, Jordan DR: Ptsis secondary to amyloidosis of the tarsal conjunctiva and tarsus. Am J Ophthalmol, 1997; 123: 852–54
7. Jain NS, Gupta AN: Amyloidosis of the conjunctiva. Br J Ophthalmol, 1966; 50(2): 102–4
8. Demirci H, Shields CL, Eagle RC Jr, Shields JA: Conjunctival amyloidosis: report of six cases and review of the literature. Surv Ophthalmol, 2006; 51(4): 419–33
9. Sainz-Esteban A, Saornil-Alvarez MA, Mendoza-Diaz MC, Blanco-Mateos G: Primary localized conjunctival amyloidosis: two case reports. Arch Soc Esp Oftalmol, 2005; 80(1): 49–52
10. Mesa-Gutierrez JC, Huguet TM, Garcia NB, Ginebreja JA: Primary localized conjunctival amyloidosis: A case report with a ten-year follow-up period. Clin Ophthalmol, 2008: 2(3): 685–87
11. Shields JA, Eagle RC, Shields CL et al: Systemic amyloidosis presenting as a mass of the conjunctival semilunar fold. Am J Ophthalmol, 2000; 130(4): 523–25
12. Iijima S: Primary amyloidosis: a unique case complaining of diffuse eyelid swelling and conjunctival involvement. J Dermatol, 1992; 19(2): 113–18
13. Purcell JJ Jr, Birkenkamp R, Tsai CC, Riner RN: Conjunctival involvement in primary systemic nonfamilial amyloidosis. Am J Ophthalmol, 1983; 95(6): 845–47
14. Glass R, Scheir HG, Vanoff M: Conjunctival amyloidosis arising from a plasma cytoma. Ann Ophthalmol, 1971; 3(4): 823–25
15. Brorou CG, Baglio E, de Gotrau P et al: Chronic hypopyon revealing primary ocular amyloidosis. Klin Monbl Augenheilkd, 2003; 220(3): 196–98
16. O’Donnell B, Wuebbolt G, Collin R: Amyloidosis of the conjunctiva. Aust NZJ Ophthalmol, 1995; 23(3): 267–12
17. Marsh WM, Streeter BW, Hoepner JA et al: Localized conjunctival amyloidosis associated with extranodal lymphoma. Ophthalmology, 1987; 94(1): 61–64
18. Hubbard AD, Brown A, Boshekar RE, Leatherbarrow B: Surgical management of primary localized conjunctival amyloidosis causing ptosis. Br J Ophthalmol, 1995; 79(7): 767
19. Dhurwar S, Linke RP, Kolling G et al: Ptsis from localized A-symptomatic amyloid deposits in the levator palpebrae muscle. Ophthalmology, 2004; 111(5): 1043–47
20. Borodic GE, Beyer-Machule CK, Millin J et al: Immunoglobulin deposition in localized conjunctival amyloidosis. Am J Ophthalmol, 1984; 98(5): 617–22
21. Madangopal AV: Conjunctival amyloidosis. Br J Ophthalmol, 1962; 46(12): 749–52
22. Fraunfelder FW: Liquid nitrogen cryotherapy for conjunctival amyloidosis. Arch Ophthalmol, 2009; 127(5): 645–48
23. Rodrigues G, Sanghvi V, Lala M: Conjunctival amyloidosis of both eyelids. Indian J Ophthalmol, 2001; 49(2): 116–17
24. Meisler DM, Stock EL, Wertz RD et al: Conjunctival inflammation and amyloidosis in allergic granulomatosis and angitis (Churg-Strauss syndrome). Am J Ophthalmol, 1983; 91(2): 216–19
25. Gertz MA, Lacy MQ, Dispenzieri A: Amyloidosis: recognition, confirmation, prognosis, and therapy. Mayo Clin Proc, 1999; 74(5): 490–94
26. Zojer N, Königsberg R, Ackermann J et al: Deletion of 13q14 remains an independent adverse prognostic variable in multiple myeloma despite its frequent detection by interphase fluorescence in situ hybridization. Blood, 2000; 95(6): 1925–30
27. Avet-Loiseau H, Farcot T, Daviet A et al: 14q32 translocations and monosomy 13 observed in monoclonal gammopathy of undetermined significance delineate a multistep process for the oncogenesis of multiple myeloma. Intergroupe Francophone du Myélome. Cancer Res, 1999; 59(18): 4546–50
28. Harrison CJ, Mazzullo H, Ross FM et al: Translocations of 14q32 and deletions of 13q14 are common chromosomal abnormalities in systemic amyloidosis. Br J Haematol, 2002; 117(2): 427–35
29. Imamura J, Miyoshi I, Koeffler HP: p53 in hematologic malignancies. Blood, 1994; 84(8): 2412–21
30. Drach J, Ackermann J, Fritz E et al: Presence of a p53 gene deletion in patients with multiple myeloma predicts for short survival after conventional-dose chemotherapy. Blood, 1998; 92(3): 802–9