

Intraocular amyloidosis with multifocal iris and anterior chamber translucent spherules

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Ocular amyloidosis, although a rare entity, is known to affect the conjunctiva, extraocular muscles, orbit, lacrimal gland, and skin around the eyes. Intraocular deposition of amyloid mainly confines to the vitreous and cornea. In this report, we describe two cases of intraocular amyloidosis presenting as multiple iris and anterior chamber cysts. Histopathological examination with special stain like Congo Red and Transmission Electron Microscopy confirmed the diagnosis of amyloidosis. Systemic investigations ruled out systemic association confirming the diagnosis of primary ocular amyloidosis.

Key words: Amyloid, anterior chamber, eye, iris

Amyloidosis is a rare disease characterized by extracellular deposition of abnormally folded proteins.^[1] Ocular involvement is uncommon and typically represents a manifestation of systemic multiorgan disease. Classification of amyloidosis has moved from "primary" and "secondary" to "light chain amyloidosis" and "amyloid A protein amyloidosis."^[1] Clinically, amyloidosis can be further classified as localized or systemic. Localized intraocular amyloidosis is exceptional with observations only as single case reports.^[2,3] Herein, we describe localized intraocular amyloidosis in two patients, manifesting with multifocal iris and anterior chamber spherules and secondary glaucoma.

Case Reports

Case 1

A 19-year-old healthy Indian female noted blurred vision, redness, and pain in the right eye (RE) for 6 months. On

examination, visual acuity (VA) was counting fingers in RE and 20/20 in left eye (LE). The RE demonstrated shallow anterior chamber with 360 degrees peripheral anterior synechiae. Approximately 400 translucent spherules of 50-200 micron diameter were embedded in the iris stroma and anterior chamber angle [Fig. 1a and b]. Other findings included posterior subcapsular cataract, elevated intraocular pressure (IOP) of 30 mm Hg, and advanced glaucomatous damage with C:D ratio of 0.9:1. The LE was normal. Iris biopsy demonstrated acellular, amorphous hyaline deposits within the iris stroma, weakly staining with Congo red, suggestive of amyloid [Fig. 1c]. Transmission electron microscopy (TEM) confirmed amyloid fibrils [Fig. 1d]. Results of analysis with *in situ* hybridization for subtyping were inconclusive due to the presence of heavily melanized melanocytes. Systemic evaluation including complete blood count, liver and kidney function tests, serum and urine protein electrophoresis, serum and urine light chain protein, bone marrow biopsy, and PET CT scan were normal. Over the following 3 years, the patient developed cataract, uncontrolled glaucoma, and corneal decompensation, requiring cataract surgery, glaucoma valve surgery, and penetrating keratoplasty, with final VA at 20/30 in affected eye [Fig. 1e and f].

Case 2

A 70-year-old Caucasian male was diagnosed with iris deposits and elevated IOP LE. On examination, VA was 20/25 RE and 20/30 LE. IOP was 10 mm Hg RE and 16 mm Hg LE, on topical anti-glaucoma medication LE. Gonioscopy revealed ~200 translucent spherules of 200-400 microns diameter in the angle LE [Fig. 2a and b]. Glaucomatous optic disc cupping with superior and inferior arcuate field defects were noted LE. Fine needle aspiration biopsy revealed amorphous material with mild Congo red staining, consistent with amyloid [Fig. 2c]. Systemic evaluation was normal. Medication compliance was poor with eventual glaucoma progression and refusal of surgical intervention. At 10-year follow-up, phthisis bulbi with no light perception was noted. The RE examination was normal all throughout.

Discussion

Amyloidosis is characterized by deposition of misfolded proteins within the extracellular space of affected organs. Ocular amyloidosis can be localized or systemic.^[2-4] The more common ocular manifestations include vitreous floaters or corneal dystrophy.^[5,6] Iris or anterior segment involvement is exquisitely uncommon.^[2,4,6] Char *et al.* reported an amelanotic iridociliary mass, diagnosed as plasmacytoma with early amyloidosis and kappa light chain deposition.^[2] Mansour *et al.* described localized iris and trabecular meshwork amyloidosis, confirmed following enucleation.^[3] Nodular deposits were,

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_812_19

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Received: 25-Apr-2019

Revision: 20-Jul-2019

Accepted: 15-Aug-2019

Published: 22-Nov-2019

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Cite this article as: Das S, Tiple S, Pegu J, Dubey S, Mathur U, Mulay K, *et al.* Intraocular amyloidosis with multifocal iris and anterior chamber translucent spherules. Indian J Ophthalmol 2019;67:2078-80.

however, not visible on examination, instead the iris showed diffuse gelatinous surface on gross examination. Both patients in our series demonstrated localized unocular amyloid deposits with multifocal, translucent iris, and angle spherules. These features have not been previously reported.

Histopathology is essential for diagnosis of amyloidosis. Congo red staining typically reveals apple-green birefringence under polarized light with fairly high specificity, but factors such as amount of available tissue, biopsy site, and type of stain and

tissue fixation can affect this stain.^[7] Congo red stain was weak in both patients and did not show characteristic apple-green birefringence in case 1, but TEM confirmed amyloid deposits.

The mechanism of glaucoma in anterior segment amyloidosis is due to involvement of the trabecular meshwork and secondary synechial angle closure. The glaucoma is usually unresponsive to medical management and needs surgical intervention as was indicated in both our patients. Washing the angle cysts might be effective in controlling the IOP. This management modality was discussed with our second patient who refused any surgical intervention and had uncontrolled IOP leading to phthisis bulbi.

Systemic amyloidosis and clonal plasma cell proliferation need to be ruled out in ocular amyloidosis. Neither patient had systemic abnormalities at mean 6.5-year follow-up.

Conclusion

In conclusion, we describe two cases of isolated anterior chamber amyloidosis manifesting as iris and angle spherules, ipsilateral glaucoma, and without systemic involvement. To the best of our knowledge, this presentation of ocular amyloidosis has not been reported previously in literature and thus adds to the list of differential diagnosis of iris and anterior chamber nodules.

Acknowledgements

We acknowledge Dr. Hardeep Singh Mudhar, Sheffield, UK, for his help with TEM.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Support provided by the Eye Tumor Research Foundation, Philadelphia, PA (CLS). The funders had no role in the design and conduct of the study, in the collection, analysis and interpretation of the data, and in the preparation, review or approval of the manuscript. Sima Das, M.S. has had full access to all the data in the study and takes

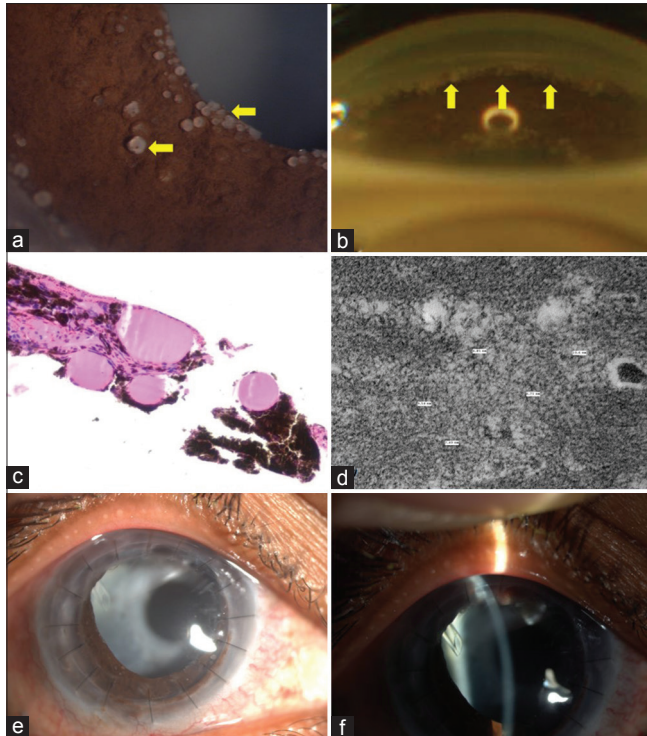


Figure 1: Clinical, histopathology, and electron microscopic photographs of iris amyloid deposits in Patient 1. (a) Slit-lamp and (b) goniophotograph of the right eye showing multiple translucent spherules (arrows) embedded in the iris and inferior anterior chamber angle. (c) Light microscopy of iris biopsy showing amorphous acellular deposits within stroma (HE, x100). (d) Amyloid deposits on high-power transmission electron microscopy (TEM) showing amyloid fibrils ranging from 6.85 to 10.6 nm size (TEM, direct magnification, x33,000). Follow-up picture showing a clear corneal graft (e) and glaucoma drainage implant *in situ* (f)

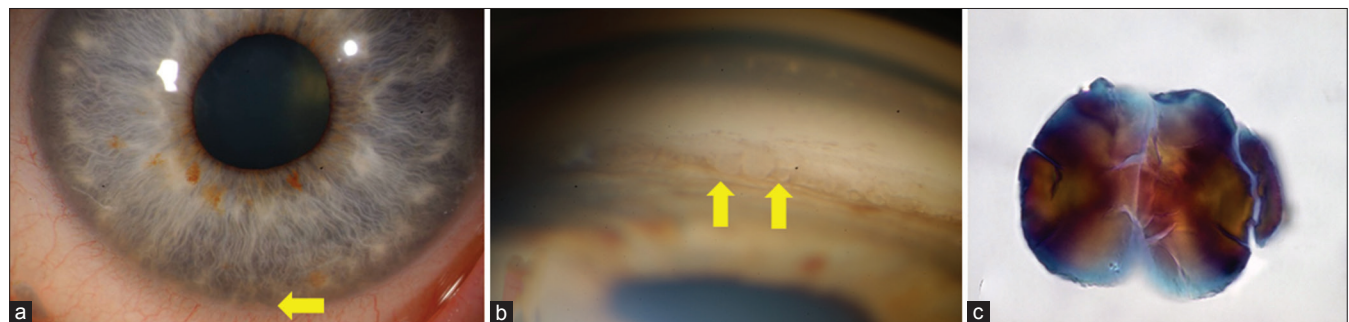


Figure 2: Clinical and histopathology photographs of the iris amyloid deposits in Patient 2. (a) Slit-lamp photograph and (b) goniophotograph showing confluent small translucent spherules (arrows) distributed on the iris and anterior chamber angle. (c) Positive Congo red staining of the fine needle aspiration biopsy of the iris spherule, suggestive of amyloid deposit

responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of interest

There are no conflicts of interest.

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