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Vitreous Amyloidosis

Ocular, Systemic, and Genetic Insights

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Purpose: To report the unique clinical and surgical characteristics encountered in eyes with vitreous amyloidosis. Systemic evaluation and visual outcome after vitrectomy are discussed. A novel mutation in the transthyretin gene (*TTR*) in Indian patients with familial amyloid polyneuropathy (FAP) is described.

Design: Retrospective, observational study.

Participants: Ten eyes of 5 patients from 2 pedigrees with a diagnosis of vitreous amyloidosis.

Methods: Detailed history, pedigree charting, systemic and ocular examination of 10 eyes (5 patients from 2 pedigrees) were carried out. Tests were performed to rule out vitreitis, retinal vasculitis, vitreous hemorrhage, and systemic amyloidosis. Genetic analysis to identify the mutation was performed in 1 patient. Vitreous biopsy, followed by 25-gauge pars plana vitrectomy, was performed in the same sitting in all cases. Samples were sent for Congo red staining and polarized microscopy. Patients were followed up on days 1, 7, and 28 and then every 2 months. Visual acuity assessment, intraocular pressure measurement, and fundus examination were performed each time.

Main Outcome Measures: Mutations in *TTR* and postoperative visual acuity.

Results: Mean age at presentation was 32 years, with a 3:2 male-to-female distribution. Family history was positive in all patients. Nine eyes had pseudopodia lentis, whereas all 10 had glass wool–like vitreous. Glaucoma developed in 1 patient (2 eyes). Waxy paper-like vitreous with firm vitreous adhesions beyond major arcades and along retinal vessels was noted during surgery in all eyes. Congo red staining and apple green birefringence demonstrated vitreous amyloidosis. The mean preoperative best-corrected visual acuity (BCVA) was 1.39±0.64 logarithm of the minimum angle of resolution (logMAR), whereas the postoperative BCVA improved to 0.17±0.07 logMAR ($P = 0.004$). Gene sequencing revealed a phenylalanine→isoleucine mutation in the 33rd position of exon 2 of *TTR* in 1 patient of 1 pedigree, confirming the diagnosis of FAP. Two patients subsequently were found to have sensorimotor autonomic neuropathy, whereas 2 others had subclinical autonomic dysfunction.

Conclusions: The clinical clues, management strategy, surgical characteristics, vitrectomy outcomes, and significance of systemic evaluation in vitreous amyloidosis are highlighted. A novel single mutation (Phe33Ile) in a case of FAP with vitreous amyloidosis from India is reported. *Ophthalmology 2017;■:1–9 © 2017 by the American Academy of Ophthalmology*

Amyloidosis is a disorder of protein misfolding leading to the formation of extracellular aggregates of insoluble fibrillar proteins. Ocular amyloidosis has been associated with serum amyloid A, immunoglobulin light chain, immunoglobulin heavy chain, transthyretin, gelsolin, keratoepithelin, and lactoferrin fibril proteins.[1] Familial amyloid polyneuropathy (FAP) is a type of amyloidosis with autosomal dominant inheritance[2] with incomplete penetrance and variable expressivity. Thus, in cases of FAP with vitreous amyloidosis, extraocular systemic features may be absent on initial presentation and there can be a lack of concurrent manifestations in relatives. Such cases of vitreous amyloidosis may have clinical or subclinical neurologic symptoms or signs. In a few cases of FAP, cardiac and gastrointestinal abnormalities also have been reported.[3]

Ocular manifestations are observed in only 10% of cases of FAP.[4] The incidence of vitreous opacities in FAP varies from 5.4% to 35%.[5] Vitreous amyloidosis is almost always related to mutant transthyretin (TTR), which is a plasma protein carrier of thyroxine and vitamin A. Herein, we report the unique clinical and surgical characteristics encountered in 10 eyes of 5 patients who underwent pars plana vitrectomy for clearing media haze resulting from suspected amyloid in the vitreous. The cytopathologic features of the vitreous in our patients confirmed the diagnosis of amyloidosis. Further systemic evaluation unraveled the underlying systemic disease: FAP in both

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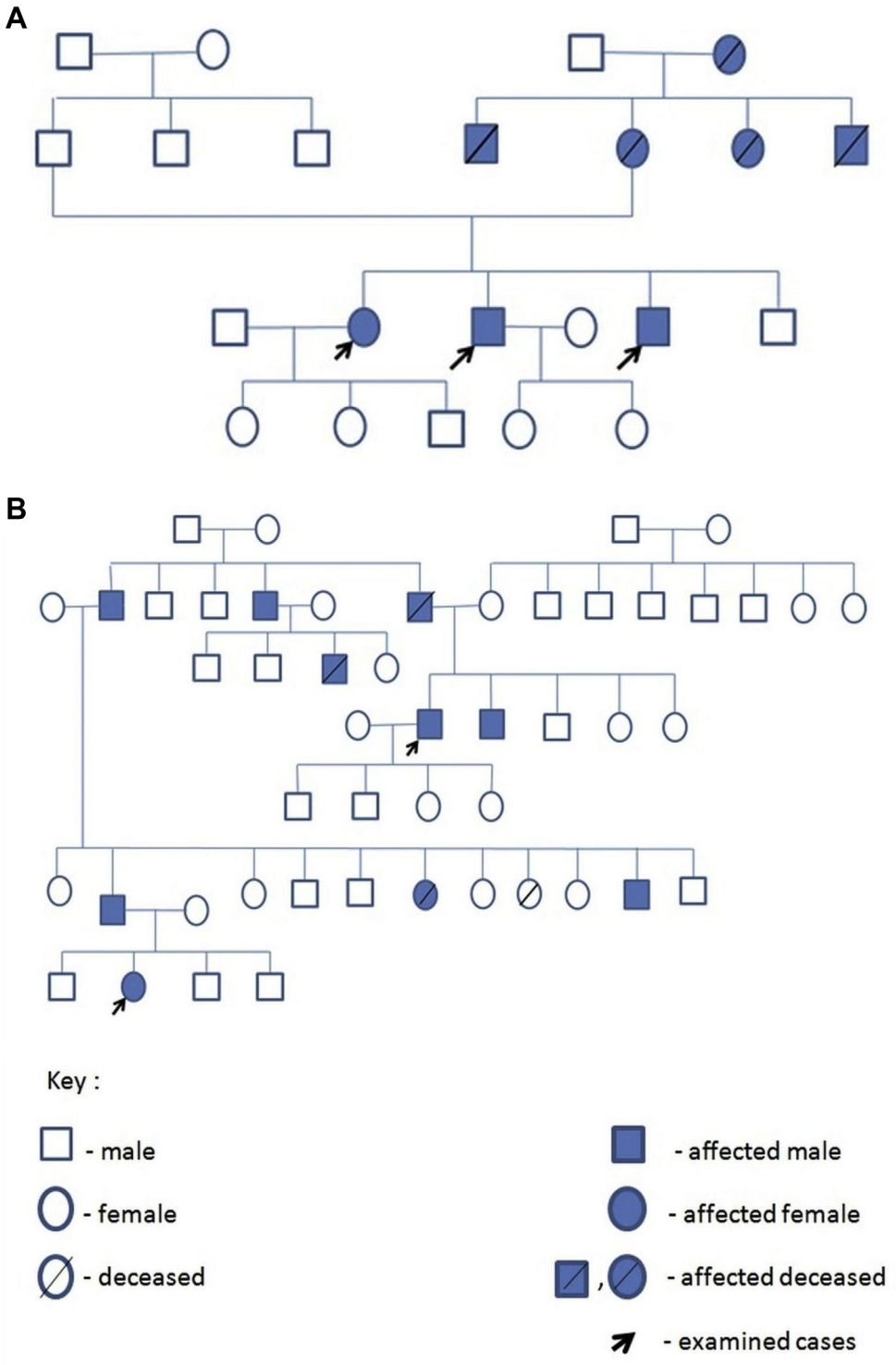

Figure 1. **A**, Pedigree for patients 1, 3, and 5. **B**, Pedigree for patients 2 and 4.