Accepted Manuscript

Ocular Manifestations of Familial Transthyretin Amyloidosis

Margaret M. Reynolds, Kevin K. Veverka, Morie A. Gertz, Angela Dispenzieri, Steven R. Zeldenrust, Nelson Leung, Jose S. Pulido

PII: S0002-9394(17)30378-1

DOI: 10.1016/j.ajo.2017.09.001

Reference: AJOPHT 10249

To appear in: *American Journal of Ophthalmology*

Received Date: 24 February 2017

Revised Date: 29 August 2017

Accepted Date: 1 September 2017

Please cite this article as: Reynolds MM, Veverka KK, Gertz MA, Dispenzieri A, Zeldenrust SR, Leung N, Pulido JS, Ocular Manifestations of Familial Transthyretin Amyloidosis, *American Journal of Ophthalmology* (2017), doi: 10.1016/j.ajo.2017.09.001.

Abstract

Purpose: Among patients with familial amyloidosis, mutation in the transthyretin (TTR) protein is the most common type. Patients with TTR amyloidosis have been noted to have ocular, especially vitreous, involvement. In this report, an analysis of the types and frequency of ocular manifestations in TTR amyloidosis is presented.

Design: Observational case series.

Methods: Two hundred and sixty-three patients who presented to Mayo Clinic with TTR amyloidosis between January 1, 1970, and November 1, 2014, consented to be included in the Mayo Clinic amyloidosis database maintained by the Department of Hematology. Fifty-four patients had ocular examinations at a mean of 4.25±3.93 months after systemic symptoms.

Results: Of 108 examined eyes in 54 patients with TTR amyloidosis, there were 26 eyes (24%) in 13 patients with ocular involvement. Patients with ocular involvement were more likely to be women than those without ocular involvement (46% vs. 15%, respectively, p=0.008) and have significantly worse visual acuity (VA) at presentation (logMAR 0.24 [Snellen equivalent 20/30] vs. logMAR 0.00 [Snellen equivalent 20/20], p=0.017). The ophthalmic findings included vitreous amyloid (26/26, 100%), neurotrophic keratitis (2/26, 8%), glaucoma (5/26, 19%), and tortuous retinal vessels (4/26, 15%). The glaucoma was classified as open-angle (2/26), exfoliative (2/26), and neovascular following central retinal vein occlusion from amyloidosis (1/26). Ten patients underwent vitrectomy for visually significant vitreous amyloidosis, which significantly improved visual acuity from a baseline of logMAR 0.70 [Snellen equivalent 20/100] to logMAR 0.05 [Snellen equivalent ~20/20], p=0.003. Three TTR mutations, Glu89Lys, Gly47Arg, homozygous Gly6Ser, not previously described, were associated with vitreous amyloid.

Conclusion: In this large cohort of patients with TTR amyloidosis, female sex and decreased VA were associated with ocular amyloid. Three mutations which have not been previously reported to have vitreous involvement were described: Glu89Lys, Gly47Arg, and homozygous Gly6Ser.

Key words: familial amyloidosis; transthyretin amyloidosis; vitreous amyloidosis; vitreous opacities; systemic amyloidosis