EUROPEAN OPHTHALMIC PATHOLOGY SOCIETY

Date of meeting: 11-14June2025
Place of meeting: Basel, Switzerland
Member's name: Claudia Auw-Haedrich
Eye Clinic
University Hospital Basel
Mittlere Str. 91, 4056 Basel, Switzerland
claudia.auw-haedrich@usb.ch
Case number: 241346
Material distributed: None, scan accessible via https://eopsarchive.eu
User: EOPS
Pass: Castroviejo99

Vitreous opacities in a 56-year-old female with inherited Transthyretin amyloidosis

Clinical History

A 56-years old female patient noticed increasing visual disturbances of her right eye due to floating filaments for two years. At the age of 41, a liver transplant had been performed for familial transthyretin (TTR) amyloidosis with p.(Val50Met) mutation of the *TTR* gene with polyneuropathy and cardiomyopathy. The TTR protein altered by the mutation with beta-sheet structure is deposited in various organs, possibly with consecutive dysfunction. Medication included irbesartan, bisoprolol, rivaroxaban and tacrolimus. The best-corrected visual acuity was 0.5 OD and 1.25 OS. Slit lamp and OCT examinations revealed acellular vitreous opacities in the right eye; the iris and retina, as well as the left eye, were unremarkable. After removal of the vitreous opacity by vitrectomy, visual acuity increased to 1.0.

Ocular Pathology

Macroscopy
Slightly turbid vitreous fluid undiluted in a syringe and diluted in a bag.

Light microscopy
Vitreous fibrils and eosinophil amorphous material, which stains Congo red positive and shows apple green birefringence under polarized light indicating the presence of amyloid.

Diagnosis

Vitreous amyloidosis in p.(Val50Met) transthyretin (TTR) amyloidosis

Discussion

Liver transplantation reduces systemic amyloid deposition in *TTR* mutation-related amyloidosis, as the diseased liver is the primary site of TTR production[1]. However, vitreous amyloidosis occurred in our patient 13 years after liver transplantation[2]. The incidence of vitreous amyloidosis in familial transthyretin amyloidosis, particularly post-liver transplantation, is even higher compared to those without systemic treatment[1]. This aligns with the detection of TTR production in the retinal pigment and ciliary body epithelium of rats, suggesting intraocular synthesis of pathological TTR in our patient[3]. Another extrahepatic TTR production site is the intracerebral choroid plexus[4].
In recent years, TTR-stabilizing substances such as Tafamidis, as well as TTR-specific siRNA and antisense oligonucleotides with fewer side effects, have become available as main treatments for *TTR* mutation-related systemic amyloidosis, in addition to liver transplantation[1]. Nevertheless, these newer therapies may not reduce the frequency and severity of intraocular involvement in TTR mutation-related systemic amyloidosis, as this body compartment is generally difficult to access for systemic medications. This aligns with the findings of Monteiro et al., who have shown that the ratio of Tafamidis to TTR is lower intraocularly and in cerebrospinal fluid compared to plasma[5].

References

1. Buxbaum JN, Brannagan T 3rd, Buades-Reinés J, Cisneros E, Conceicao I, Kyriakides T, Merlini G, Obici L, Plante-Bordeneuve V, Rousseau A, Sekijima Y, Imai A, Waddington Cruz M, Yamada M. Transthyretin deposition in the eye in the era of effective therapy for hereditary ATTRV30M amyloidosis. Amyloid. 2019 Mar;26(1):10-14. doi: 10.1080/13506129.2018.1554563. Epub 2019 Jan 24. PMID: 30675806.
2. Auw-Haedrich C, Neß T. Vitreous opacities in familial transthyretin amyloidosis. DtschArztebl Int 2025; 122: 172; DOI: 10.3238/arztebl.m2024.0225
3. Cavallaro T, Martone RL, Dwork AJ, Schon EA, Herbert J. The retinal pigment epithelium is the unique site of transthyretin synthesis in the rat eye. Invest Ophthalmol Vis Sci. 1990 Mar 1;31(3):497-501. PMID: 1690688.
4. Herbert J, Wilcox JN, Pham KT, Fremeau RT Jr, Zeviani M, Dwork A, Soprano DR, Makover A, Goodman DS, Zimmerman EA, et al. Transthyretin: a choroid plexus-specific transport protein in human brain. The 1986 S. Weir Mitchell award. Neurology. 1986 Jul;36(7):900-11. doi: 10.1212/wnl.36.7.900. PMID: 3714052.
5. Monteiro C, Martins da Silva A, Ferreira N, Mesgarzadeh J, Novais M, Coelho T, Kelly JW. Cerebrospinal fluid and vitreous body exposure to orally administered tafamidis in hereditary ATTRV30M (p.TTRV50M) amyloidosis patients. Amyloid. 2018 Jun;25(2):120-128. doi: 10.1080/13506129.2018.1479249. Epub 2018 Jul 11. PMID: 29993288; PMCID: PMC6177313.