

Ocular Manifestations of Fabry Disease

By Pinakin Davey OD, PhD, FAAO.

Fabry's disease is a rare lysosomal disorder that has a prevalence of 1 in 40,000 males.[1] This disease follows x-linked inheritance and the individuals affected with the disease show multi system disorders that are present at birth and signs and symptoms worsen with time. The *GLA* gene mutation leads to the deficiency of an enzyme alpha galactosidase A which leads to the progressive accumulation of globotriaosylceramide (GB3) deposits in a variety of cells including those in kidneys, and the autonomic the cardiovascular systems . [2-4]

The ocular manifestations of Fabry disease includes a cornea verticillata which is a "vortex whorl" like corneal opacity (see figure). It is the most common finding and is seen in all hemizygotes and majority (up to 70%) of heterozygotes.[5] The cornea verticillata is the outcome of the deposit of GB3 in the basal layer of the corneal epithelium . The cornea verticillata is visible using a slitlamp microscope and in-vivo confocal microscopic studies have shown that even when the cornea verticillata may not be visible using a slitlamp there are intracellular inclusion bodies in the basal epithelial cells.[6] To a lesser degree and fewer Fabry disease patients have subtle lenticular deposits which is the Fabry cataract.[7] The Fabry cataract tends to be off axis dendritic or subcapsular opacities along the posterior suture lines. It is believed that patients with cornea verticillata will have any visual symptoms due to the deposits.[7-9]

The role of the cornea and the crystalline lens is to provide the eye with necessary refractive power and unhindered path to the light rays that pass through them. To this accord the corneal physiology is finely tuned and causes the least amount of scatter of light rays in ocular healthy individuals. It can be hypothesized that individuals with Fabry disease could have problems with visual function given that both the cornea and the crystalline lens have deposits of GB3 and opacities. It can further be

hypothesized that the vision problems would be present and worst at night time when compared to the day time, with patients with Fabry disease having additional problems of glare, blurry vision or dim vision (contrast sensitivity issues).

The patients with Fabry disease also experience anhydrosis or hypohydrosis as one of the symptom. This is due to the neurological manifestations of the disease. Prior reports have suggested that patients with Fabry disease may have deposits of GB3 in the ganglia or the lacrimal gland itself.[10-12] It can be hypothesized that patients with Fabry disease could also have symptoms of dry eyes.

In a recent publication from Davey PG [13] investigated 75 patients with Fabry disease against healthy controls using a survey instrument. The study concluded that patients with Fabry disease may experience difficulty in seeing particularly in dim light, experience glare issues, may have a mild dry eye and ocular fatigue. Further studies are continued in this area to gauge and quantify severity of the problem. Optometrists and Ophthalmologists are likely to see cornea verticillata during routine exam and should suspect Fabry disease in that individual and should perform further investigation using blood tests to determine enzyme activity of alpha galactosidase A and recommend genetic testing as needed.

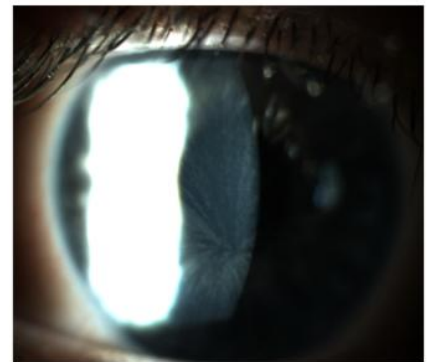


Figure 1: Cornea verticillata: "vortex whorl" like corneal opacity common in Fabry disease.

References

- 1) Meikle PJ, Hopwood JJ, Clague AE, et al. Prevalence of lysosomal storage disorders. *JAMA* 1999;281:249-54.
- 2) MacDermot KD, Holmes A, Miners AH. Anderson-Fabry disease: clinical manifestations and impact of disease in a cohort of 98 hemizygous males. *J Med Genet* 2001;38:750-60.
- 3) MacDermot KD, Holmes A, Miners AH. Anderson-Fabry disease: clinical manifestations and impact of disease in a cohort of 60 obligate carrier females. *J Med Genet* 2001;38:769-75
- 4) Branton MH, Schiffmann R, Sabnis SG, et al. Natural history of Fabry renal disease: influence of α -galactosidase A activity and genetic mutations on clinical course. *Medicine* 2002;81:122-38
- 5) Desnick RJ, Brady RO. Fabry disease in childhood. *J Pediatr* 2004;144:20-26.
- 6) Wasilica-Poslednik J, Pfeiffer N, Reinke J, Pitz S. Confocal laser-scanning microscopy allows differentiation between Fabry disease and amiodarone-induced keratopathy. *Arch Clin Exp Ophthalmol* (2011) 249:1689-1696
- 7) Samiy N. Ocular Features of Fabry Disease: Diagnosis of a Treatable Life-threatening Disorder. *Surv Ophthalmol* 53:416-423, 2008.
- 8) Sodi A, Ioannidis A, Pitz S. Ophthalmological manifestations of Fabry disease. In: Metha A, Beck M, Sunder-Plassmann G, eds. *Fabry disease. Perspectives from 5 years of FOS*. Oxford, UK: Oxford Pharmagenesis Ltd, 2006:249-61.
- 9) Sivley MD. Fabry Disease: A Review of Ophthalmic and Systemic Manifestations. *Optom Vis Sci* 2013;90:e63-e78
- 10) Cable WJ, Kolodny EH, Adams RD. Fabry disease: impaired autonomic function. *Neurology* 1982;32:498-502.
- 11) Hilz MJ. Evaluation of peripheral and autonomic nerve function in Fabry disease. *Acta Paediatr Suppl* 2002;91:38-42.
- 12) Kolodny EH, Pastores GM. Anderson-Fabry disease: extrarenal, neurologic manifestations. *J Am Soc Nephrol* 2002;13(Suppl. 2):S150-3.
- 13) P Davey. Fabry disease: a survey of visual and ocular symptoms. *Clinical Ophthalmology* 2014 Aug 19;8:1555-60

Dr. Pinakin Davey OD is a tenured Professor Western University of Health Sciences, College of Optometry in Pomona CA. He received his Bachelor of Science in Optometry from the Elite School of Optometry, India (1999). He received his Ph.D. from Anglia Ruskin University in Cambridge, England, in the area of corneal measurements and its influence on glaucoma (2003). His post-doctoral research fellowship was focused on improving imaging techniques in glaucoma at the University of Louisville (2003-2006). He graduated with Doctor of Optometry from Southern College of Optometry in 2010. He



is a fellow of the American Academy of Optometry since 2003. Dr. Davey has authored over 40 journal publications, and has given over 100 conference and invited presentations both nationally and internationally. He is an editorial board member for 10 journals and additionally a reviewer for 15 journals in the fields of ophthalmology, optometry and biomedical sciences. Dr. Davey serves as a grant reviewer for the National Institute of Health of Scotland, Medical Research Council and The College of Optometrists, United Kingdom.