

Clinical & Refractive Optometry is pleased to present this continuing education (CE) article by Dr. Ron Melton and Dr. Randall Thomas entitled **Fabry's Keratopathy**. In order to obtain 1-hour of COPE-approved CE credit, please refer to page 454 for complete instructions.

Fabry's Keratopathy

Ron Melton, OD; Randall Thomas, OD

SUBJECTIVE

A 67-year-old white female presented for a routine eye examination with typical visual complaints of occasional blur at distance and near. Her current eyeglasses are four years old. She has experienced mild photophobia in bright light and while driving at night. The patient is taking ranitidine hydrochloride (Zantac) and loratadine (Claritin D) and is allergic to ibuprofen (Motrin). There is no known personal or family history of ocular disease, surgery or injury.

OBJECTIVE

- Visual acuity: 6/7.5 (20/25) OU
- Gross observation: normal OU
- Pupils: equal, round and reactive OU
- Lids: uninvolved OU
- Conjunctiva: slight injection OU
- Cornea: both corneas demonstrated a pronounced brownish-tan verticillate pattern within the sub-epithelial tissues (Fig. 1). There was no disruption of the precorneal tear film as demonstrated with fluorescein dye
- Lens: Grade I nuclear sclerotic cataracts OU
- Tension by applanation: 17/17 mm Hg at 9:30 a.m.
- Dilated fundus exam: 0.2 cup-to-disc OU with maculae clear; slight tortuosity to the retinal blood vasculature OU

ASSESSMENT

- Fabry's keratopathy OU

PLAN

- Consult with geneticist or other expert in Fabry's Disease

R. Melton, R. Thomas — Adjunct faculty members at the Pennsylvania, Pacific University and SUNY Colleges of Optometry; Consultants to the American Optometric Association and Fellows of the American Academy of Optometry; both are in clinical practice in North Carolina. Recipients of the Glaucoma Educators of the Year Award presented by the American Academy of Optometry.

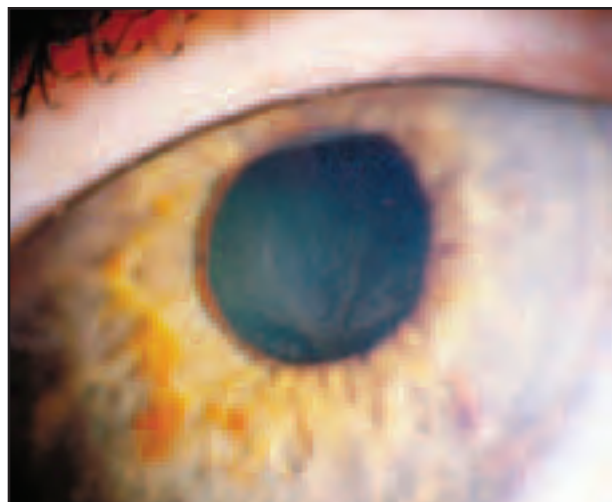


Fig. 1 This symptomatic female carrier of Fabry's disease shows the classic whorl-like deposits in the basal layer of the corneal epithelium.

Comments: A retrospective history revealed that the above patient had three brothers who all died in their 50s from heart and kidney disease. Since Fabry's is an X-linked recessive disease, males are afflicted, and females are carriers. Genetic counseling should be considered for family members of child-bearing age. In male patients with Fabry's disease, the main symptom is intermittent attacks of pain in the toes, fingers, palms or soles. There is often associated fever and increased sedimentation rate. Skin lesions that are dark-red in color are commonly seen on the hips, buttocks, thighs, and genitals. Cardiovascular and renal complications reduce the life expectancy in males to 40-50 years.

Eye care practitioners may be in a primary position to diagnose Fabry's disease. Corneal deposits are seen in males and heterozygous females when other manifestations of the disease are in their early stages. Along with the corneal opacities, posterior spoke-like cataracts are said to be pathognomonic for Fabry's disease. Conjunctival and retinal vessel changes are more nonspecific, yet suggestive of the disease. Keep in mind that all of these ocular findings may not be present with every patient.



Fig. 2 A 30-year-old male patient has the distinctive corneal verticillate (whorled streaks) extending to the periphery.

GENERAL OBSERVATIONS

- The following rare, asymptomatic, superficial corneal findings are found in Fabry's disease (a metabolic disorder):
 - Diffuse whorl-like deposits (cornea verticillate) are seen in the epithelium (basal layers); in more advanced cases, the deposits radiate from a point below the center of the cornea or as whorled streaks extending to the periphery (Fig. 2).
 - Corneal deposits similar to the classic amiodarone, chloroquine, chlorpromazine, or indomethacin verticillate keratopathy, seen in both males and females.
 - Visual acuity is generally not affected.
- Fabry's disease (angiokeratoma corporis diffusum) is a multi-system, X-linked recessive disease first reported in dermatological literature in 1898.
 - In affected males, Fabry's disease usually causes premature death (age 40-50) from kidney, cardiovascular or other systemic complications.
 - A deficiency of the enzyme α -galactosidase A causes a build-up of ceramide trihexoside in the renal and cardiovascular systems. It is different from the other sphingolipidoses because of its predilection for blood vessels.
 - Diagnosis is usually made in childhood or adolescence. Early manifestations of Fabry's

disease include intermittent fever, bouts of pain in digits, evanescent proteinuria, and telangiectases. Skin lesions (small, round vascular eruptions) that become hyperkeratotic are common. These cutaneous lesions appear in a "bathing trunk" distribution on hips, buttocks, back, and genitals.

- Lab testing: α -galactosidase is significantly decreased in plasma and urine. Conjunctival biopsy is positive.
- The female carrier is either asymptomatic or has mild systemic symptomatology. It is in these relatively healthy patients that such keratopathy is likely to be discovered in out-patient clinical settings.

- **Ocular findings**

- Corneal opacities (90% of cases)
- Retracted, unexplained edema of upper eyelids is common
- Spoke-like cataracts (50%)
- Conjunctival vascular changes (tortuosity and aneurysms in 60%)
- Retinal vessel tortuosity (55%)
- Papilledema, retinal edema, optic atrophy and renal vascular dilation are other uncommon late ocular findings

- **Management**

- There is no successful intervention ophthalmically, but the FDA has recently approved an ultra-orphan drug (Fabrazyme by Genzyme) for the treatment of the disease. Fabrazyme replaces the missing enzyme and is administered IV every 2 weeks. This treatment can slow the progression of this life-threatening disease.
- Kidney transplantation is helpful in end-stage renal disease. Penetrating keratopathy has a poor prognosis in these patients. Genetic counseling should be considered if a female patient is a heterozygous Fabry carrier.
- Websites for additional information:
www.fabryregistry.com
www.fabrycommunity.com

Disclaimer: Not every detail of every case is discussed, rather the key clinical findings are described. For example, if nothing is said about the corneal status, you should assume that the cornea is normal, etc. When vision is recorded, it should be assumed to be best corrected or pinholed. Regarding therapy, we show how we treated the particular case. Given that medicine is an art, as well as a science, therapy will — and often does — vary with each unique patient presentation depending on severity, known drug allergies, prior treatment, response to therapy, etc.