Ocular Findings of a Patient with Fabry Disease

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ABSTRACT

The aim of this report is to describe the ophthalmic findings of a 27-year-old patient with Fabry disease. Best corrected visual acuity was 20/20 and intraocular pressure was 19 mmHg in both eyes. There was an infiltrate on cornea bilaterally (cornea verticillata), increased tortuosity in conjunctival vessels, a hemangioma on the lower lid of the right eye. The temporal paleness of both optic nerves was noticed with slit lamp biomicroscope and colored fundus photography. Also, there was mild venous tortuosity in retinal vessels. Visual field test, tear function tests, SdOCT findings were all normal in both eyes. In Fabry disease, clinical manifestations begin in childhood, and it affects multiple organ systems which can lead to an early death. Ocular findings are an early onset of the disease, so clinical examination of these findings are important to suspect and request consultations from other clinical disciplines to establish a definitive diagnosis earlier.

Keywords: Cornea verticillata, Fabry disease, Globotriaosylceramide, Glycosphingolipid, Vascular tortuosity.

INTRODUCTION

Fabry disease is an X-linked lysosomal storage disease. The estimated incidence of Fabry disease is about one per 80,000 to 117,000.[1] Due to X-linkage, the disease affects both males and females. Males usually have an earlier onset and a more severe form of the disease whereas some female gene carriers are asymptomatic.[2] The most common mechanism is the mutations in GLA gene which provides instructions for making an enzyme called alpha-galactosidase A. Alpha-galactosidase A breaks down a molecule called globotriaosylceramide. Alpha-galactosidase deficiency results in accumulation of glycosphingolipids, particularly globotriaosylceramide (GL3) in tissues throughout the body and multi-organ system disease. Age of onset can range from early childhood to the fifth decade.[3, 4]

Progressive cardiomyopathy, nephropathy, renal failure, and cerebrovascular events are the most important organ complications, contributing to significant morbidity and mortality.[5] Ocular involvement in Fabry disease is characterized by corneal and lens opacities as well as vascular abnormalities. Although Fabry-related ocular lesions typically do not affect vision, they are often an early sign of the disease and can be detected in a routine eye examination.[2] Cornea verticillata is an almost obligate ophthalmic finding. The brownish-yellow Bowman membrane-related corneal deposits and telangiectatic conjunctival vessels are early ophthalmic slit lamp markers of the disorder. Fundus vessel tortuosity is observed in many patients, in particular of the retinal venules.[6]

CASE REPORT

A twenty-seven-year-old woman was referred to our clinic for a routine ophthalmic examination. In her medical history, it was noticed that she was a carrier for Fabry disease, had the diagnoses of Sjogren syndrome and Hashimoto thyroiditis, used levothyroxine and hydroxychloroquine for three years. There was no consanguineous marriage between her parents. Her mother had Fabry disease, chronic renal failure, and glaucoma while her sister had Fabry disease and Hashimoto thyroiditis. Her father was normal. She underwent a full ophthalmic examination including best corrected visual acuity (BCVA) with Snellen chart, intraocular pressure (IOP), slit lamp biomicroscope inspection for the anterior and posterior segment, tear function tests, visual field test, spectral domain optic coherence tomography (SdOCT),

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colored fundus photography, and fundus autofluorescence (FAF) imaging.

BCVA was 20/20 with -0.50 myopic correction and IOP was 19 mmHg in both eyes. In biomicroscopic slit lamp there was an infiltrate on cornea bilaterally (cornea verticillata), increased tortuosity in conjunctival vessels, and a hemangioma on the lower lid of the right eye (Figure 1). The temporal paleness of both optic nerves was noticed with slit lamp biomicroscope by dilatation of the pupils with %1 tropicamide, than documented by colored fundus photography and FAF imagines. Also, there was mild venous tortuosity in retinal vessels (Figure 2). Visual field test, and tear function tests were normal. SdOCT findings showed that the thickness of cornea, retina, optic nerve head, and ganglion cell complex were all normal in both eyes (Figure 3).

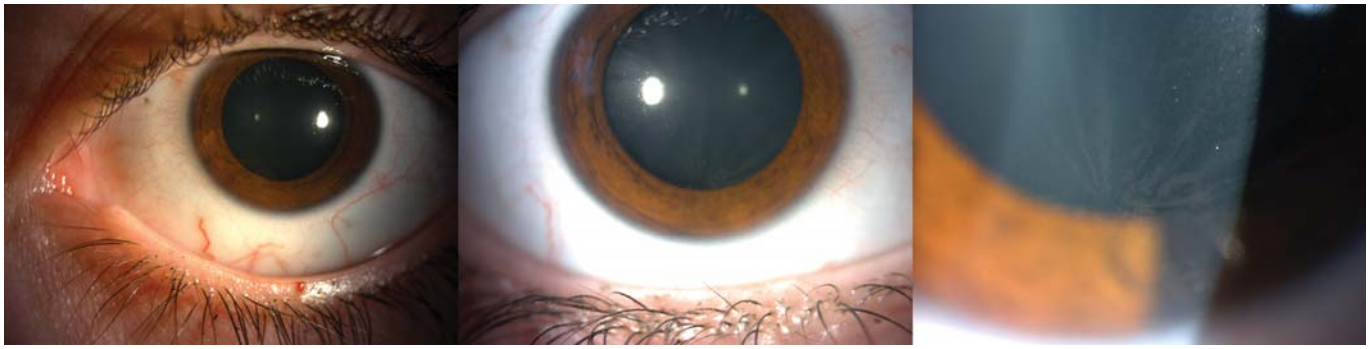

Figure 1: *Increased tortuosity in conjunctival vessels, a hemangioma on the lower lid and cornea verticillata can be seen.*

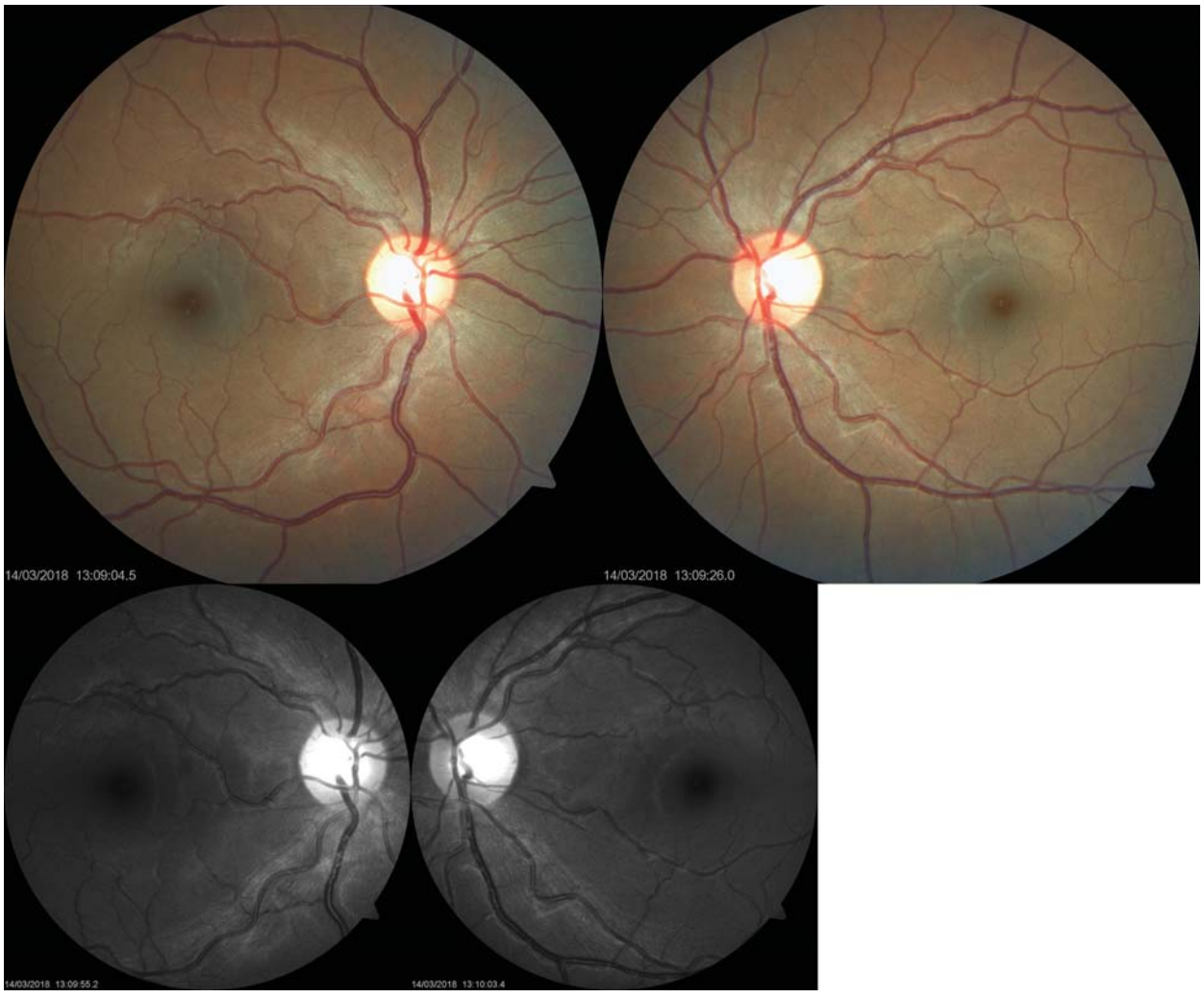

Figure 2: *Colored fundus photography and fundus autofluorescence images showed the temporal paleness of both optic nerves and mild venous tortuosity in retinal vessels.*

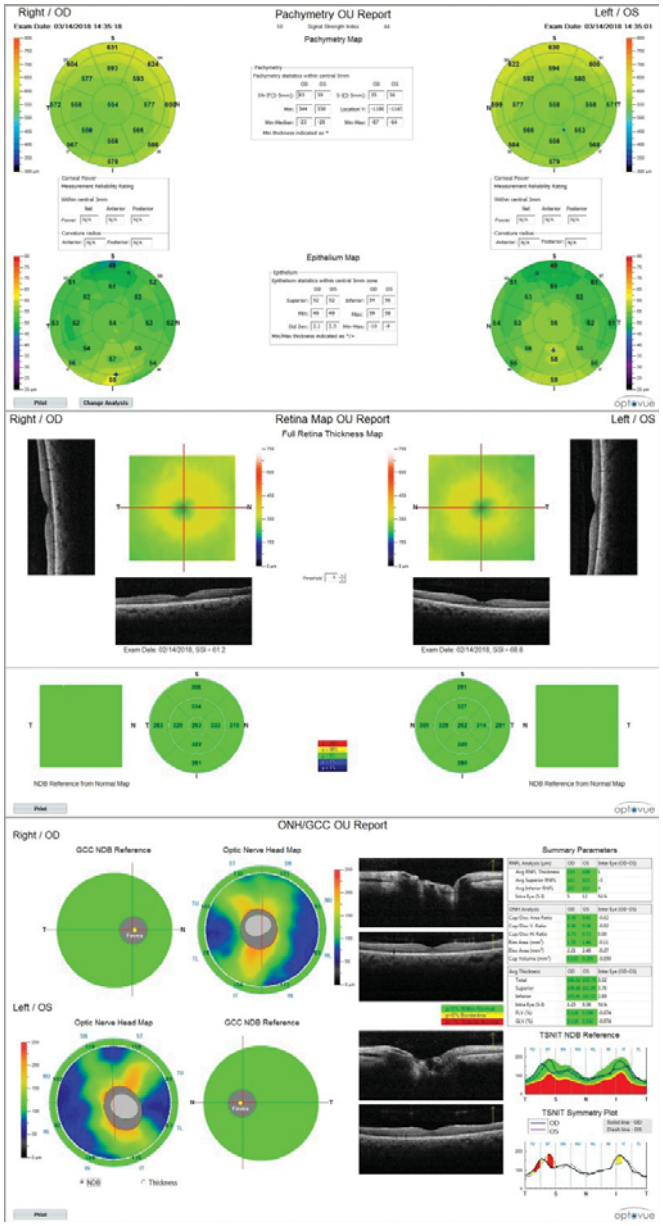

Figure 3: *Thickness of cornea, retina, optic nerve head, and ganglion cell complex were all normal in both eyes in SdOCT* images.*

** SdOCT: Spectral Domain Optic Coherence Tomography*

CONCLUSION

In Fabry disease, ocular findings are frequently seen due to the accumulation of glycosphingolipid into the tissues. Glycosphingolipid deposits have been noted in the endothelial, perivascular, and smooth muscle cells of ocular and orbital vessels, in the smooth muscle of the iris and ciliary body, in perineural cells, and connective or epithelial tissues of the lens, conjunctiva, and cornea of patients with Fabry disease. [7]

The most common and specific findings include increased conjunctival vascular tortuosity, corneal opacities (corneal verticillata), lens opacities and retinal vascular anomalies. The rare findings are retinal artery vein occlusions, anterior ischemic optic neuropathy, optic disc pale or atrophy, papillary edema, myelinated nerve fiber, valvular edema, angioma-angiokeratoma in the valves, and tear disorders.[2]

Cornea verticillata is the most common and earlier ocular manifestation of Fabry disease, detection of the characteristic corneal lesion should prompt consideration of Fabry disease as a diagnosis. The patient should be examined for the extra-ocular findings such as progressive cardiomyopathy, nephropathy, renal failure, and cerebrovascular events.[5]

Delays in the diagnosis of Fabry disease may be fatal. Therefore the early diagnosis is very critical. In a retrospective analysis of 105 patients with Fabry disease, 13 patients were diagnosed by an ophthalmologist among 50 patients with no family history of the disease.[8] Any patient with corneal haze, cornea verticillata, or Fabry cataract, especially in combination with retinal vascular tortuosity, conjunctival vascular telangiectasis, should be considered as a Fabry suspect and consulted with other clinical disciplines.

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