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Case report

Ocular findings in a patient with fucosidosis

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ABSTRACT

Purpose: To describe the ocular findings in a patient with fucosidosis, a rare inborn lysosomal storage disease.

Observations: A 14 year-old female presented with *angiokeratomas corporis diffusum*, coarse facial features, poor verbal skills, hearing impairment and mild developmental delay. A lysosomal storage enzyme screen confirmed absent activity of α-L-fucosidase consistent with a diagnosis of fucosidosis. Her eye exam was remarkable for telangiectatic vessels in the inferior conjunctiva and mild corneal stromal haze bilaterally. Spectral domain–optical coherence tomography scans of the macula and a full-field electroretinogram were normal.

Conclusions and importance: We describe the findings in a 14 year-old patient with fucosidosis and review the systemic and ocular manifestations of this rare lysosomal storage disease.

1. Introduction

Fucosidosis is a rare inborn lysosomal storage disease caused by α-L-fucosidase deficiency in which absent enzyme activity causes incomplete breakdown of fucose-containing compounds. These partially broken down glycolipids and glycoproteins gradually accumulate within various tissues throughout the body and cause cellular dysfunction. Less than 120 cases have been documented in the literature worldwide and only a few describe the detailed ocular phenotype. We describe the ocular findings in a patient with fucosidosis.

2. Case report

A 14 year-old female was referred to the pediatric ophthalmology clinic at University of California, San Francisco. The patient had previously presented to the dermatology department with pink patches on her hands and legs since birth which had progressed to involve her torso and extremities and a clinical diagnosis of *angiokeratomas corporis diffusum* was made (Fig. 1). She also had coarse facial features, poor verbal skills, hearing impairment, and mild developmental delay.

Both of her parents were from Mexico with no known history of consanguinity. She had 4 healthy brothers. She had two female cousins born from a consanguineous marriage among maternal cousins with developmental delay, one who died at age 3 and the other at age 40. The older cousin had seizures, severe speech and language delay, and an odd facial appearance. There was no clinical information about the younger cousin. They both died without a diagnosis.

A lysosomal storage enzyme screen confirmed absent activity of α-L-fucosidase consistent with a diagnosis of fucosidosis. The results of enzyme analysis of the patient's parents were consistent with their carrier status.

On examination, her best corrected visual acuity was 20/50 in the right eye and 20/40 in the left eye. Cycloplegic refraction in the right eye was $-4.50 + 2.00 \times 90$ and $-6.75 + 2.75 \times 90$ in the left eye. Color vision was normal in each eye when tested with the Hardy-Rand-Rittner plates. She had an 18 prism diopter exophoria in primary gaze at distance with a latent component fine jerky vertical nystagmus. Her ductions were full with the exception of a slight limitation in right abduction. She had 100 seconds of arc

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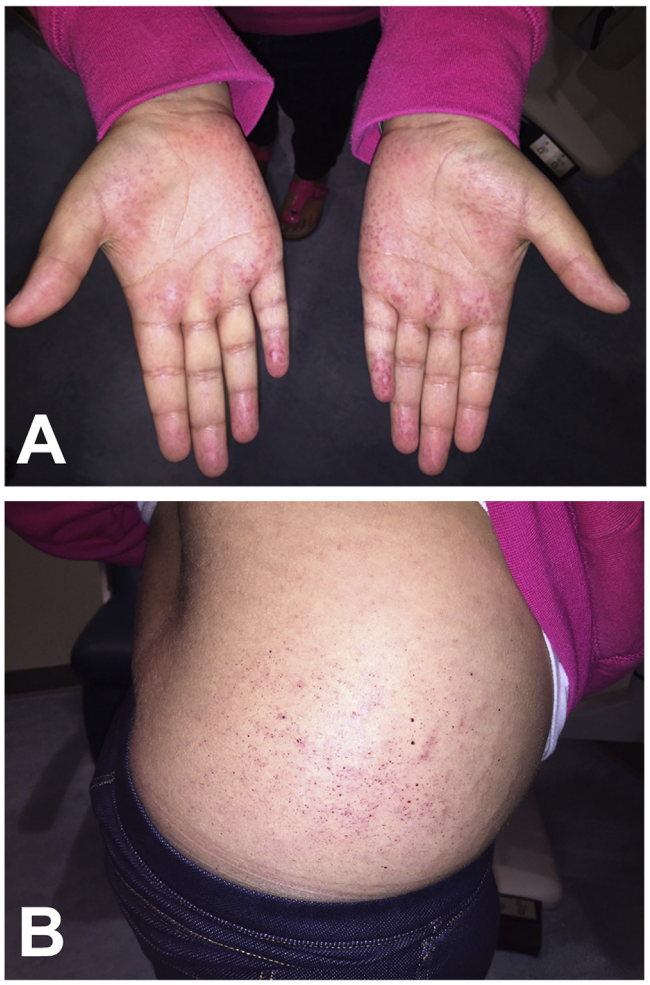

Fig. 1. Skin findings in fucosidosis. Angiokeratomas *corporis diffusum* in palms (A) and abdomen (B).

stereopsis. Both pupils reacted normally to light with no afferent pupil defect.

Slit lamp examination revealed telangiectatic vessels in the inferior conjunctiva and mild corneal stromal haze bilaterally proportional to her slightly decreased best corrected visual acuity (Fig. 2). The remainder of the anterior and posterior segment examination was normal in both eyes. Spectral domain–optical coherence tomography (SD-OCT) scans of the macula were normal (Fig. 3). Scotopic and photopic full-field electroretinography (ERG) performed with Burian-Allen electrodes according to the International society of Clinical Electrophysiology of Vision (ISCEV) standard were within normal limits in each eye. This was performed under anesthesia preceding an otolaryngologic procedure.

3. Discussion

Fucosidosis is a rare form of lysosomal storage disease associated with α-L-fucosidase deficiency that leads to impaired degradation of fucose and subsequent accumulation of fucosylated glycoproteins and glycolipids in a variety of tissues.[1] Fucosidosis is inherited as an autosomal recessive inheritance pattern and is caused by mutations in the *FUCA1* gene on chromosome 1p36.11.[2] The clinical course is characterized by progressive cognitive and motor deterioration, coarse facies, growth retardation, recurrent infections, dysostosis multiplex, *angiokeratoma corporis diffusum*, visceromegaly and seizures.[1,2] The neurological phenotype is variable, with some affected individuals showing rapid neurologic deterioration and death before 5 years of age (<30% of patients) whilst others have a slower neurologic deterioration with survival into the second or third decade.[1–3] Our patient presented within the mildly affected spectrum of neurological disease. She has not developed seizures or motor deterioration to date.

A relatively high incidence of fucosidosis has been reported in both Italians and the Mexican-Indian population of New Mexico and Colorado.[1] Although this patient was born in United States, her parents are from the same town in Mexico and her two cousins with developmental delay were born from a consanguineous marriage among maternal cousins.

Since the first clinical, histochemical, and microscopic findings were described by Durand in 1966,[4] the ocular findings in fucosidosis have not been reported in detail. Borrone et al. reported two affected siblings: one with corneal clouding, strabismus, papilledema with congestion and tortuosity of retinal vessels, and the other with thin and tortuous vessels.[5,6] Subsequently, Snodgrass described macular changes resembling bull's eye retinopathy along with conjunctival vessel changes in a single patient with fucosidosis.[7]

Ophthalmic abnormalities previously described in association with fucosidosis include dilated and tortuous retinal veins (54%), dilated and tortuous conjunctival vessels (53%), microaneurysms of conjunctival vessels (41%), corneal opacities (11%), and pigmentary retinopathy (7%).[1,5–7] Our patient demonstrated the majority of those anterior segment findings but had a normal fundus appearance in both eyes. Furthermore, she had a normal full field ERG and macula SD-OCT.

Histopathologic studies of the ocular ultrastructure in patients with fucosidosis have revealed lysosomes filled with a fibrilogranular and multilaminated material. The corneal epithelial cells, corneal endothelial cells, keratocytes, fibroblasts, retinal ganglion cells, inner segments of photoreceptors and glial cells of the optic nerve have all shown evidence of deposition of this abnormal material.[8]

Despite these findings, severe visual impairment is not a common finding in fucosidosis, Willems et al. reported loss of visual acuity in only 5 of 77 patients (6%).[1] This is in contrast to lysosomal storage disorders where corneal clouding, pigmentary degeneration of the retina, and glaucoma may be associated with severe visual disability. Our patient had mildly reduced visual acuity from corneal deposits but normal retinal structure and function.

Presently, treatment of fucosidosis is supportive. Increased enzyme activity has been reported in fucosidase-deficient dogs following bone marrow transplantation,[9] and bone marrow transplantation has been carried out in a small number of patients with fucosidosis early in the disease course.[10] Additional experimental work is being conducted using intracisternal enzyme replacement therapy,[11] though in general, the long-term outcome of such approaches is unclear and further experimental studies are ongoing.[12]

4. Conclusions

Fucosidosis is a rare inborn lysosomal storage disease cause by α-L-fucosidase deficiency with less than 120 cases documented in the literature worldwide. The ocular phenotype is varied, but can include both anterior (dilated and tortuous conjunctival vessels, corneal opacities) and posterior segment (tortuous retinal veins, pigmentary retinopathy) findings. Severe visual impairment is uncommon.

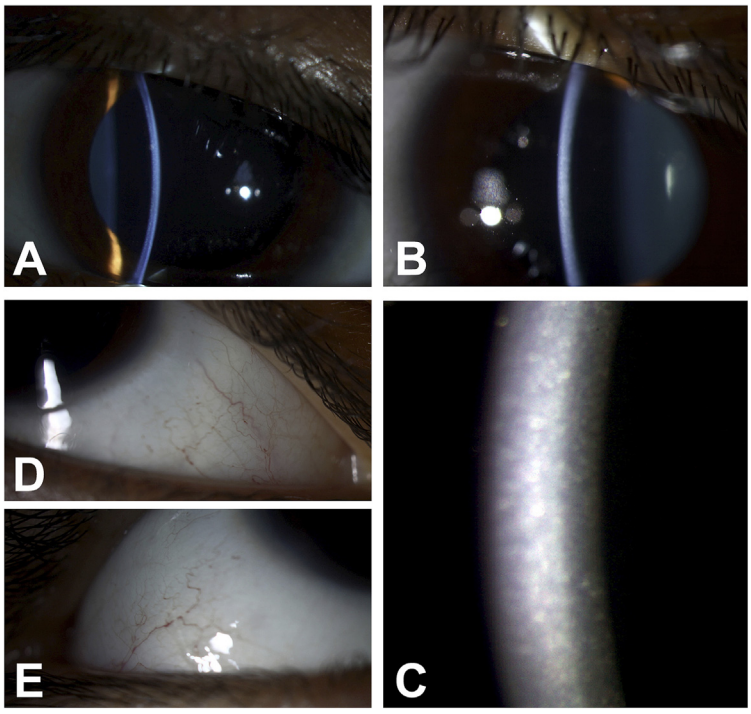

Fig. 2. Slit lamp findings in fucosidosis. Anterior segment with normal iris and clear lens (A); corneal stromal haze (B); corneal stromal haze magnification (C); tortuous conjunctival vessels along with microaneurysms of conjunctival vessels (D, E).

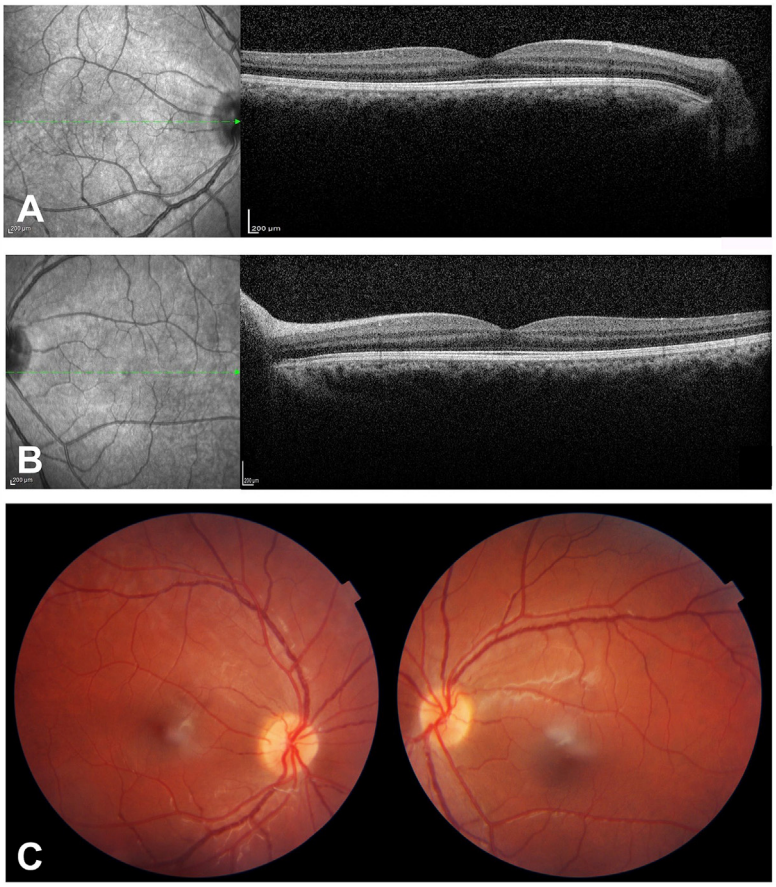

Fig. 3. Spectral domain–optical coherence tomography images of each macula showing normal inner and outer retinal layers and normal retinal pigment epithelium of right eye (A) and left eye (B). Color fundus photography showed healthy optic discs, normal retinal vasculature and normal macular appearance. The slightly abnormal-appearing foveal light reflex bilaterally is a photography flash artifact (C).

5. Patient consent

The patient's mother provided written consent for publication of personal identifying information including medical record details and photographs.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflict of interest

The following authors have no financial disclosures: LR, JTO, JLD, SP, ATM.

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