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Spectral optical coherence tomography in a patient with type I sialidosis

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Summary

Background:

The aim of our study was to analyze spectral optical coherence tomography (SD-OCT) findings in a patient with clinical signs of sialidosis.

Case Report:

Fluorescein angiography and spectral optical coherence tomography was performed in a 37-year-old woman using a SD-OCT device with axial resolution of 6 µm. Enzyme assay followed. The patient was diagnosed with type I sialidosis by enzymatic assay. Besides a normal angiogram, a thickened nerve fiber layer was observed on spectral optical coherence tomography.

Conclusions:

The thickened nerve fiber layer was probably caused by accumulation of metabolic products such as sialylated oligosaccharides and glycopeptides, suggesting that SD-OCT, due to its enhanced resolution, can be a useful tool for diagnosis of rare neurological conditions.

key words:

sialidosis • spectral domain optical coherence tomography • neuraminidase • cherry-red spot • SOCT

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BACKGROUND

Cherry-red spots in the macula may be observed in several lysosomal storage disorders, including sialidosis, a rare autosomal recessive disease caused by isolated deficiency of neuraminidase (sialidase) 1. Sialidosis type II is the early-onset variant with dysmorphic changes. Type I sialidosis, rare compared to type II, is a relatively mild disease with onset in the second or third decades of life and slower progression. It manifests with myoclonus syndrome, ataxia, gait abnormalities, epilepsy and impairment of vision. We present a case study, including spectral optical coherence tomography, in 38-year-old female affected with type I sialidosis.

CASE REPORT

A previously healthy 15-year-old girl developed sudden, jerky movements of the upper limbs. She was born to non-consanguineous parents and her early development and progress in school was normal. She had no siblings and her family history was unremarkable. The jerkiness gradually generalized to the lower extremities. Her gait was disturbed and her speech became slurred. At the age of 20, myoclonus of the face was present and ophthalmography revealed the opsoclonus. When she was 22-years-old generalised clinic-tonic and partial seizures occurred. The epilepsy was well controlled with valproate. Between 20 and 31 years she was several times evaluated ophthalmologically and fundus examination did not reveal any abnormalities. However, corneal opacities were noted at that time. Visual acuity dropped from 1.0 to 0.7 on Snellen charts during that time. Intraocular pressure was normal. At the age of 35 cherry-red spots in the maculae were observed for the first time (Figure 1) suggesting diagnosis of type I sialidosis.

Ophthalmological evaluation and neurological examination

Around the cherry-red spots in the macula we observed a slightly oval, pale perimacular area, about 1.5 disc diameters in size. Besides this finding, the clinical examination was normal. Fluorescein angiography was also performed and no abnormal leakage was observed. Neurological examination at age 38 years revealed severe myoclonus and dystonic movements of the trunk, exaggerated by voluntary movements and emotion, in all 4 extremities, head and face. Generalised ataxia was present. Her speech was dysarthric and explosive. Horizontal nystagmus was observed. Deep tendon reflexes were hyperactive. Because of involuntary movements and ataxia she was unable to feed and dress herself and she was wheelchair-bound. Neuropsychological evaluation revealed mild impairment of cognitive functions and adaptive depressive reaction. The brain MRI was normal. EEG occasionally showed discharges of sharp waves and diffuse theta waves. Visual acuity dropped to 0.1 in both eyes at that time. During the fundus examination, the cherry-red spots on the macula and a normal optic nerve head were observed. Fluorescein angiography was unremarkable (Figure 1). Spectral optical coherence tomography (SD-OCT, Spectralis, Heidelberg Engineering, Germany) was additionally performed (Figure 2). SD-OCT is a novel technique providing information about the internal structure of an object by measuring the interferometric signal detected as a function of optical frequencies. This allows

for high speed and high resolution cross-sectional imaging of the human retina, enabling more exact visualization of retinal layers, especially photoreceptors and external limiting membrane. The SD-OCT used in this study provides 3.9 μm axial and 12–18 μm transverse resolution, and 3-dimensional scanning is also possible. The examination revealed increased paracentral retinal thickness with normal central retinal thickness. All retinal layers seemed normal except the thickened nerve fibre layer, including an intact photoreceptor layer and external limiting membrane.

Enzyme assay

Sialidase activity in blood leucocytes was measured against artificial fluorogenic substrate 2'-(4-methylumbelliferyl)- α -D-N-acetylneuraminic acid (4MU-NeuAc; Sigma). Isolated cells ($2\text{--}5 \times 10^6$) were homogenized by sonication in 0.20 ml of 0.05 M sodium acetate buffer, pH 4.4 and incubated with 0.125 mM 4MU-NeuAc at 37°C for 1 h. The reaction was terminated by addition of 1.9 ml of 0.4 M glycine buffer, pH 10.5. Liberated 4-methylumbelliferone was measured using a Shimadzu RF-5301 spectrofluorometer with excitation at 355 nm and emission at 460 nm. Protein concentration was measured using a protein assay kit (Bio-Rad). The measured sialidase activity 0.08 nmol/hr mg of protein was approximately 10-fold less than the level detected in normal controls (from 0.07 to 2.1 nmol/hr mg, n=56). Beta galactosidase activity was in the normal range, which excluded diagnosis of galactosialidosis.

DISCUSSION

There have been few descriptions of patients with cherry-red spot syndrome with a normal optic disc in adult patients with myoclonus, without mental retardation. First it was reported by Anderson et al in 2 sisters, ages 16 and 19, manifesting adult-onset myoclonus with bilateral cherry-red spot syndrome [1] and diagnosed with mucopolipidosis type I [2]. Titarelli et al further reported a 24-year-old man with similar symptoms, additionally presenting a visual field impairment. A few years later several more studies were published, confirming increased levels of sialylated oligosaccharides in urine and defects of acid sialidase (neuraminidase) in skin fibroblasts and leukocytes in patients with similar symptoms [3–5]. O'Brien and Lowden classified those symptoms as sialidosis type I, or the cherry-red spot myoclonus syndrome, characterized with normal intelligence and a defect of neuraminidase 1.

This report describes the first spectral optical coherence tomography performed in a patient diagnosed with sialidosis type I.

The whitish perimacular region in sialidosis patients was until now explained as a thickening of the retina. SD-OCT, presenting high-resolution images of the retinal structure, brings new insight into understanding the morphology of the thickened retina. As can be seen on the images, not all retinal layers are thickened, only the nerve fibre layer. Some authors have stated that changes in brain MRI may correspond to nerve fibre layer thickness, for example in sclerosis multiplex [6]. As the eye is an extension of the brain, some products that accumulate in the brain may be visible in the eye. We believe that the thickening of the nerve fibre

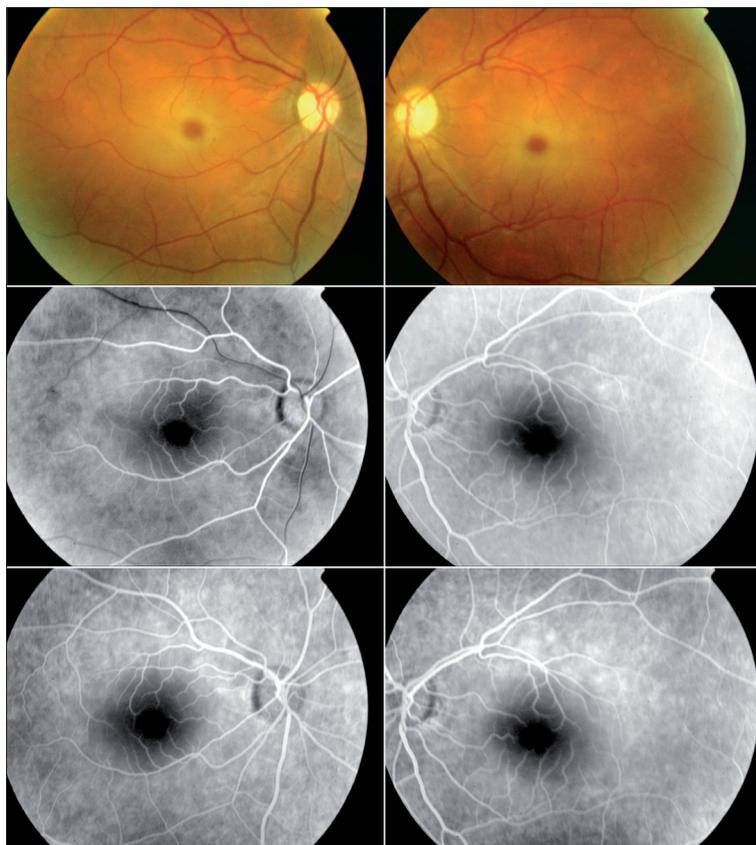


Figure 1. Spectral Domain Optical Coherence Tomography. Right eye on the right side and left eye on the left side. A normal fovea contour and thickened nerve fibre layer are visible.

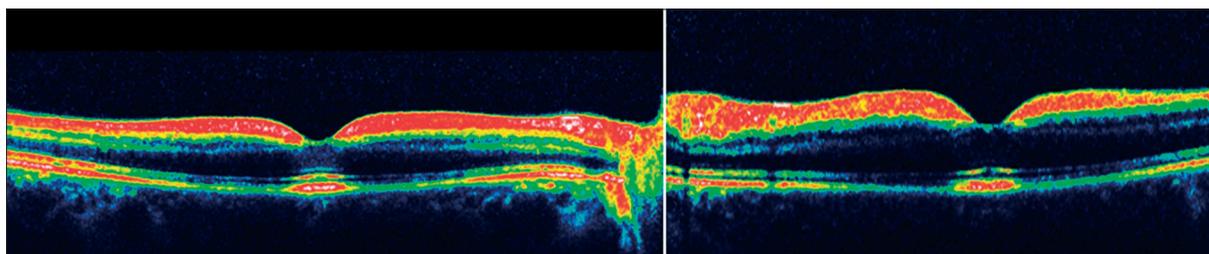


Figure 2. Fundus photograph and fluorescein angiography of both eyes. Cherry-red spots are visible on both fundus images. Fluorescein angiography is normal.

layer observed in SD-OCT in the presented case of sialidosis could be due to accumulation of metabolic products, as sialic-acid-containing oligosaccharides and glycopeptides.

CONCLUSIONS

SD-OCT is an easy and non-invasive approach to confirm metabolic diseases such as sialidosis. In particular, multiple eye-tracking systems such as the one used in this study help to achieve high-quality images even in patients with heavy nystagmus and involuntary movements. SD-OCT images therefore not only help to suggest or confirm correct diagnosis, but it additionally brings new insight into our understanding of the pathological changes in the retinal structure occurring in sialidosis patients.

Conflict of interest

We declare no proprietary interest of any author.

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