Case Report

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Optical coherence tomography features in a case of Type I sialidosis

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Abstract:

A 15-year-old boy presented with progressive myoclonic epilepsy and unbalance gaits for 4 years. Slit lamp examination showed a punctate cataract and funduscopic examination revealed bilateral macular cherry-red spots. Macular scan of spectral domain optical coherence tomography (SD-OCT) showed hyperreflectivity of the inner retinal layer and apparent hyperreflectivity of the photoreceptor layers in the foveal region. The clinical presentations were consistent with a Type I sialidosis which led to genetic analysis and revealed NEU1 mutation in this patient. He was under regular follow-up by ophthalmologist and neurologist. Sialidosis is a rare lysosomal storage disease resulting from a deficiency of alpha-N-acetyl neuraminidase caused by a mutation in the NEU1 gene. This results in abnormal intracellular accumulation of sialyloligosaccharides in brain neurons and ganglion cells of the retina. SD-OCT is a useful tool in detecting macular cherry-red spot and has a role in evaluating the extent of ganglion cell damage. It can aid in the differential diagnosis and long-term follow-up of the neurological metabolic disorders.

Keywords:

Cherry-red spot myoclonus syndrome, sialidosis, Type 1, optical coherence tomography

Introduction

Sialidosis Type I, also known as cherry red spot myoclonus syndrome, is a rare lysosomal storage disease. Patients of Type 1 sialidosis typically develop symptoms of myoclonus, seizure, and visual problems in their second or third decade of life.[1] Macular cherry-red spots are always detected and are a characteristic finding that assists in diagnosis of this rare disease.

Cherry-red spot is an ocular manifestation of central retinal artery occlusion, traumatic retinal edema, and many inherited metabolic storage disease including Tay–Sachs disease, Sandhoff disease, GM1 gangliosidoses, Niemann–Pick disease, Farber's disease, metachromatic leukodystrophy, and sialidosis.[2] In these metabolic storage diseases, the cherry-red spots are bilateral and have insidious onset of symptoms. Careful fundus examination of suspected victims is necessary to detect its presence.

Optical coherence tomography (OCT) is a noninvasive technology that uses laser light to acquire high-resolution images. Today's spectral-domain (SD) OCT can provide an axial resolution of 3–6 μm within tissues. The increased speed and resolution provide an enhanced ability to visualize retinal layers.[3] OCT has the advantages of providing objective measurements of the affected structures, allowing direct comparison with previous values, and also suitable for use in older children. Therefore, it is a useful tool for diagnosis and follow-up in patients of metabolic storage diseases presenting with cherry-red spots.

Here, we presented a case of Type 1 sialidosis with cherry-red spots and its OCT features.

Case Report

A 15-year-old boy suffered from progressive myoclonic epilepsy and unbalance gaits for

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4 years. He was admitted due to increased frequency of seizure attacks recently, accompanied with visual impairment. Tracing back his history, he was a healthy boy with normal intelligence as well as unremarkable birth and family history until 4 years ago, frequent unexpected fall brought him to seek for medical help. Difficult to walk, progressive myoclonic epilepsy, and ataxia developed thereafter. Ophthalmologist was consulted during this admission for detecting any ocular abnormality.

His best-corrected visual acuity was 20/60 in the right eye (OD) and 20/200 in the left eye (OS). Intraocular pressure was normal in both eyes (OU). Extraocular movement was full and free (OU). His cornea was clear and perinuclear punctate cataract was detected (OU). Fundus examination revealed reddish fovea with perifoveal whitening appearance compatible with cherry-red spots (OU) [Figure 1]. Macular scan of SD-OCT (Cirrus, Carl Zeiss Meditec) showed hyperreflectivity of the inner retinal layer (the nerve fiber layer plus ganglion cell layer without clear boundary between the two layers) and apparent hyperreflectivity of the photoreceptor layers in the foveal region (OU) [Figure 2a]. The central macular thickness was 248/242 μm (OD/OS). Average macular thickness and cube volume were 261/268 μm and 9.4/9.6 mm^3, respectively [Figure 2b]. Ganglion cell analysis showed irregular thickness and apparent thinning [Figure 2c]. The Goggle visual evoked potential study revealed small amplitude and mild prolonged P100 latency in both eyes, indicative of bilateral visual pathway dysfunction.

After thorough ancillary tests to rule out other differential diagnosis of progressive myoclonic epilepsy including neuronal ceroid lipofuscinosis, Unverricht–Lundborg disease, and Lafora disease, his clinical presentations were compatible with Type I sialidosis. Genetic analysis was done which revealed NEU1 mutation, 544A>G (Ser182Gly), and 619C>T (pGln2007) point mutation in our patient. He was under regular follow-up by ophthalmologist and neurologist. Although intractable seizure still happened, his ocular condition was stable at 6-month follow-up.

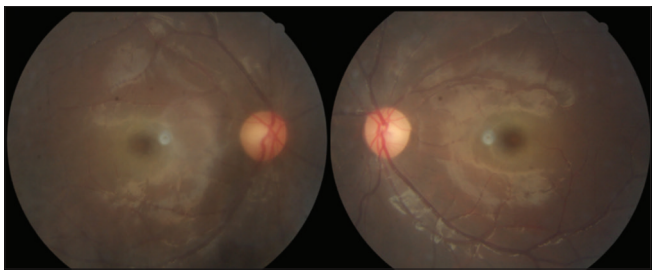

Figure 1: Fundus examination revealed cherry-red spot in both eyes

Discussion

Sialidosis is a rare inherited lysosomal storage disease caused by NEU1 mutation, resulting in isolated deficiency of alpha-N-acetyl neuraminidase (sialidase). This enzyme deficiency interrupts the normal catabolic pathways for degradation of sialylated glycoconjugates, causing their accumulation in the lysosome and excretion in urine,[4] and affects mostly central nervous system, skeletal system, and the reticuloendothelial system. To

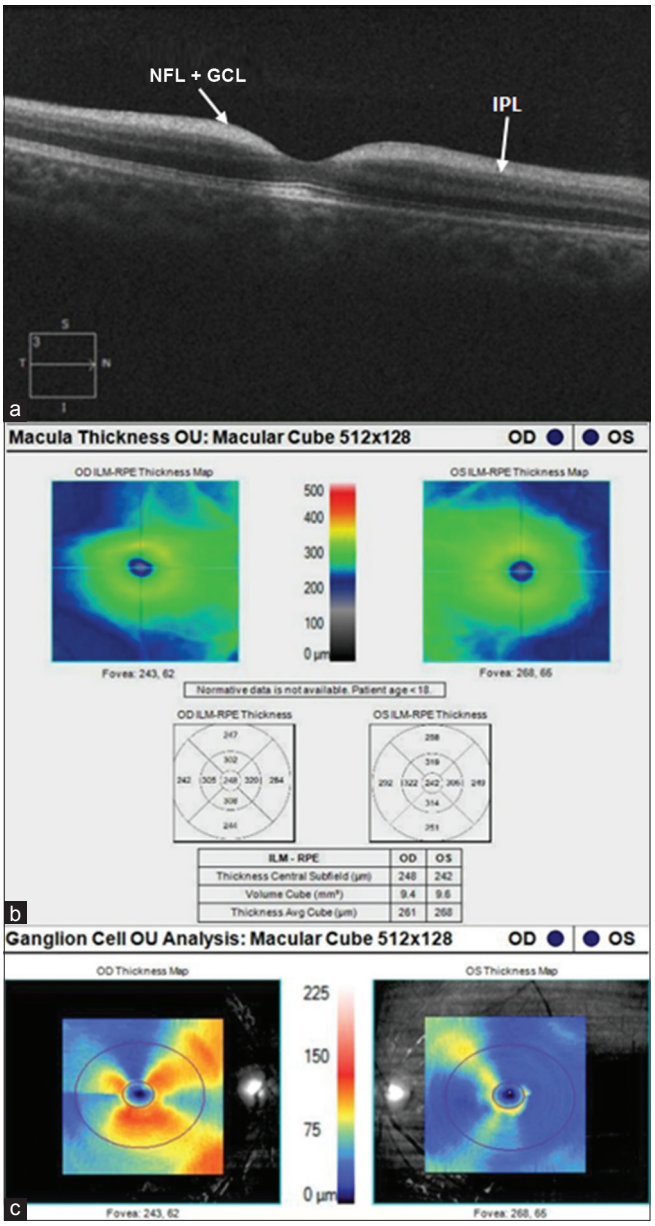

Figure 2: Macular scan of spectral domain optical coherence tomography, (a) increased reflectivity of the inner retinal layer and apparent hyperreflectivity of the photoreceptor layers in the foveal region in the right eye (NFL: Nerve fiber layer, GCL: Ganglion cell layer, IPL: Inner plexiform layer). The same finding was also detected in the left eye. (b) Macular thickness map and value (ILM: Internal limiting membrane, RPE: Retinal pigment epithelium). (c) Ganglion cell analysis, it showed irregular thickness and apparent thinning in both eyes

date, more than 40 NEU1 disease-causing mutations have been identified.[5] There are two main clinical variants. Type 1 or the nondysmorphic type is a relatively mild, late-onset form. Patients usually present on the second or the third decade of life and develop gait abnormalities, progressive impaired vision, bilateral macular cherry-red spots, and myoclonus syndrome. Ataxia and seizures have also been reported.[4] Type 2 or the dysmorphic type is the early-onset form, which is also associated with Hurler-like phenotype, dysostosis multiplex, short stature, developmental delay, mental retardation, and hepatosplenomegaly.[4] Our teenage patient presented with myoclonic epilepsy and bilateral macular cherry-red spots, which were typical in Type I sialidosis.

Macular cherry-red spots that may fade later in the course of the disease[5] are important clinical hallmark of sialidosis. The reported incidence of cherry-red spots was thought to be <75% in Type 2 patients and virtual 100% in patients with the Type I form.[1] However, in a study of 17 Taiwanese patients with sialidosis Type 1, distinct characteristics of phenotype with infrequent (only 17.6%) cherry-red spot was found.[6] Fading or late appearance of the cherry-red spots had been proposed by previous studies. Another hypothesis was that diversity of genotype and residual enzyme activity may affect the phenotype.[5,6] In their study,[6] all patients had a mutation at 554A>G in exon 3 of the NEU1 gene causing Ser182Gly substitution, which was also found in our patient. Ser182Gly mutation is known to have higher residual enzymatic activity with nonshorter half-life, and causes no obvious structural change of lysosomal multienzyme complex.[7] Fifteen patients in their study were homozygous and fourteen of them did not have cherry-red spots. Two patients with heterozygous as well as our patients presented with cherry-red spots. If there was any subtle change in the macula that can be detected by modern technology such as OCT could also be considered.

The SD-OCT can help us to detect and understand the pathophysiology of the formation of cherry-red spot. The characteristic finding of cherry-red spot in OCT is increased reflectivity of the inner retinal layer and apparent hyperreflectivity of the photoreceptor layers in the foveal region.[8-12] The hyperreflective inner retina, as can be seen in our case [Figure 2a], composed of nerve fiber layer and ganglion cell layer without clear boundary between the two layers.[11] In previous reports, some stated that only the retinal nerve fiber layer was thickened was probably an unprecise description.[9,12] The presumed accumulation of sialyloligosaccharides in the ganglionic cells at the macula[8-12] results in increased reflectivity of the inner retina found in OCT and the corresponding perifoveal white patch pattern visualized by fundoscopy. The foveal pit which lacks of ganglion cells continues to retain its reddish appearance named as cherry-red spot. In OCT, the apparent, not true, hyperreflectivity of the photoreceptor layers in the foveal region is due to the relative hyporeflectivity of the outer retinal layers caused by masking effect of the increased reflectivity of the nerve fiber layer and ganglion cell layer at the perifoveal area.[12] This feature was similar in other metabolic storage disease with cherry-red spot. One case report of a patient with galactosialidosis,[13] cherry-red spot was detected and SD-OCT revealed an abnormally hyperreflective region in the retinal ganglion cell layer, the same as our patient. There has been one case series of OCT findings in three patients with Niemann–Pick disease Type B.[14] One had macular halo and SD-OCT showed hyperreflective retinal tissue at the shoulders of the foveal depression. Two had perimacular clouding and SD-OCT demonstrated an annulus of hyperreflective tissue at the retinal surface outside the foveal depression.

In evaluation of macular lesions, SD-OCT can provide the values of macular thickness and macular volume [Figure 2b]. The objective macular measurements provided by OCT are useful at any age for long-term follow-up because they allow direct comparison with previous values of the same patient.[15] In regard to the ganglion cell analysis (thickness of ganglion cell layer to inner plexiform layer) provided by Cirrus SD-OCT [Figure 2c], irregular thickness and apparent thinning were noted in both eyes. The value was probably unreliable due to unclear boundary between the hyperreflective nerve fiber layer and ganglion cell layer causing segmentation errors possible. Therefore, this is not a suitable parameter to be used in this disease.

Our case presented with bilateral macular cherry-red spots and myoclonus, which are typical in Type I sialidosis. SD-OCT is a useful tool in detecting macular cherry-red spot and plays an important role in evaluating the extent of ganglion cell damage. It can be helpful in the differential diagnosis and long-term follow-up of this kind of neurological metabolic disorders and potentially be used to evaluate the effectiveness of treatment if any progress made in the future.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

The authors have no any conflicts of interest to declare.

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