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Optical Coherence Tomography of Chorioretinopathy Caused by Mucopolysaccharidoses

Ocular changes in some types of the mucopolysaccharidoses (MPS) include corneal clouding, glaucoma, pigmentary retinopathy, optic disc edema, and optic atrophy.[1,2] Pigmentary retinopathy has been reported in MPS I (Hurler disease), MPS I-S (Scheie syndrome), MPS I-H/S (Hurler/Scheie), MPS II (Hunter disease), MPS III (Sanfilippo syndrome), and MPS IV A (Morquio A syndrome).[1,2] Clinical signs of retinopathy include atrophy of the retinal pigment epithelium (RPE), arteriolar narrowing, and later bone spicules. The electroretinographic abnormality is a pattern of rod−cone dystrophy.[2] Histopathologic examinations have demonstrated widespread loss of RPE and photoreceptors.[3] However, there have been no histopathologic descriptions of the retinas in mild forms of MPS. Using optical coherence tomography (OCT), we have attempted to provide a detailed morphologic description of the retina and the choroid in cases with MPS.

Institutional review board approval was obtained. A total of 42 eyes of 21 consecutive patients with MPS were enrolled in this study, including 3 patients with MPS I (2 male, 1 female), 5 patients with MPS II (all male), 8 patients with MPS IV A (2 male, 6 female), and 5 patients with MPS VI (3 male, 2 female). Patients underwent infrared fundus imaging and spectral-domain (SD) OCT with enhanced depth imaging (Heidelberg Engineering Co, Heidelberg, Germany).

Of 3 patients with MPS I, one (28 years old) exhibited multifocal depigmented retinopathy in both eyes. Another (12 years old) had mild parafoveal retinal folds and mild swollen discs in both eyes. A third (33 years old) had a myelinated nerve fiber layer in the right eye. In the first patient, SD OCT showed focal choroidal thinning in the depigmented retinopathy areas (Fig 1, available at www.aaojournal.org). In the other 2 patients, the SD OCT showed a fuzzy and thickened external limiting membrane (ELM) at the fovea.

Among the 5 MPS II patients, 2 (9 and 20 years old) had multifocal depigmented retinopathy. The SD OCT showed focal choroidal thinning in the pigmentary retinopathy areas. A mild, fuzzy, and thickened ELM, widening of the distance between the RPE and ellipsoid zone at the fovea, and disruption of ellipsoid zone at the extrafoveal area were also noted (Fig 2). One 18-year-old man had a history of retinoschisis and was now showing mild retinal folds. The SD OCT showed mild retinal folds, a fuzzy and thickened ELM at the fovea, and some small cystic changes. The final 2 participants (46 and 49 years old) had retinopathy resembling retinitis pigmentosa. The SD OCT showed some cystic spaces, a fuzzy ELM, disrupted ellipsoid zone, and diffuse loss of choriocapillaris. The SD OCT did not show any anomalies in the 8 MPS IV patients.

Among 5 MPS VI patients, 2 (10 and 15 years old) had multifocal depigmented retinopathy, 1 (28 years old) had parafoveal retinal folds and a blurred disc margin in the right eye, and the final 2 (both 28 years old) showed no definite anomaly. The SD OCT revealed focal choroidal thinning in areas of depigmented retinopathy in the first 2 patients (Fig 3, available at www.aaojournal.org), and irregular RPE, ellipsoid zone, and ELM in the patient with parafoveal retinal folds.

Pigmentary retinopathy has been reported in MPS I, MPS I-S, MPS I-H/S, MPS II, MPS III, and MPS IV A, but has never been reported in MPS VI.[1] In contrast, our study found that the chorioretinal changes were noted not only in MPS I and II, but also in MPS VI.

Retinal pigmentary changes caused by MPS are identical morphologically to those of retinitis pigmentosa syndromes. The mechanism was unknown, but a primary disturbance of metabolic dysfunction owing to accumulation of glycosaminoglycan (GAG) in the RPE has been suggested. Because the choroidal circulation supplies the outer third of the retina and plays an important role in the metabolism of the RPE−photoreceptor complex,[4] the choroid was investigated in our study.

The study showed that the choroid was particularly thinned at areas of hypopigmentation, likely owing to focal scleral thickening/protuberances caused by GAG deposits. This finding has important implications; the choroidal and scleral pathology is located outside the external blood−retinal barrier. There is ongoing debate about whether or not enzyme replacement therapy is effective for ocular complications of MPS, and one major argument is that enzymes cannot pass the blood−retinal barrier to exert an influence. Based on our assumption, and considering the degenerative nature of MPS, enzyme replacement therapy performed in the early stages of the disease might prevent choroidal thinning caused by GAG accumulation in the sclera, and slow down the progression of retinal changes caused by MPS.

A fuzzy ELM at the fovea was noted in MPS I and II patients. Parafoveal retinal folds were noted in 1 MPS I, II, and VI patients. The ELM is formed by the attachment site of the Müller cells and the photoreceptor cells, and the internal limiting membrane is formed by the end-feet of Müller cells. In a mice model, the accumulation of nondegraded macromolecules from dysfunctional lysosomes activates astrocytes and Müller cells in the retina.[5] Therefore, it is possible that accumulation of GAG might lead to the activation of the Müller cells, and hence parafoveal retinal folds and a fuzzy ELM in our MPS patients.

Several small cystoid spaces and loss of ellipsoid zone beyond the parafovea were noted in 4 of the 5 MPS II patients, but not in patients with MPS I, IV, and VI. Although the composition of these cystic spaces remains unknown, the cystic changes might be reversible, as seen in one of our MPS II patients. In contrast, loss of the ellipsoid zone outside the fovea might indicate photoreceptor atrophy and irreversibility.

In conclusion, our study has demonstrated the presence of parafoveal retinal folds, a fuzzy and thickened ELM, and thinning of the choroid at depigmented retinopathy areas. These chorioretinal changes were noted in the MPS type I, II, and VI, but not in MPS IV A. The SD OCT with enhanced depth imaging might help to investigate the pathophysiology and follow the disease course of the chorioretinopathy caused by MPS.

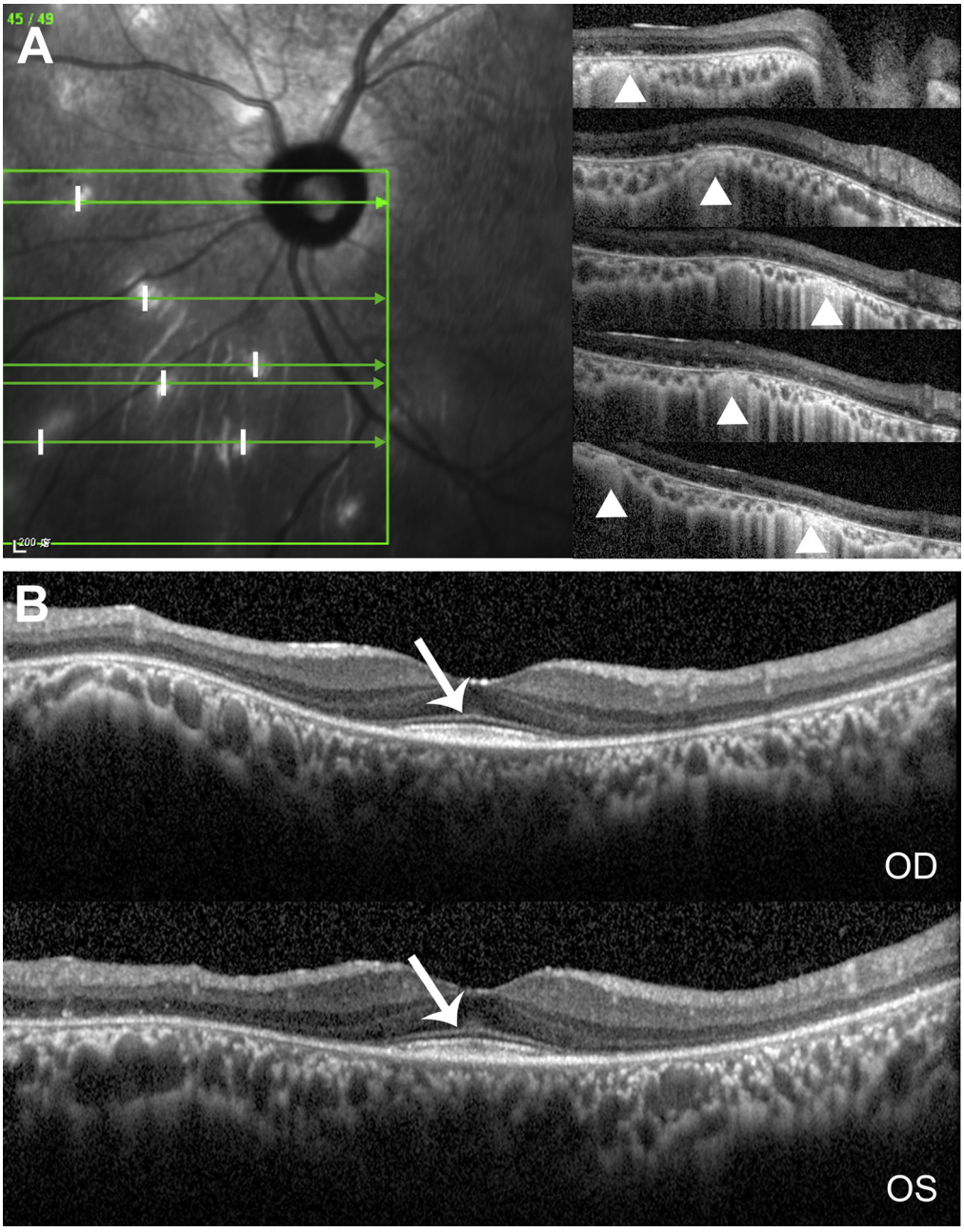

Figure 2. Fundus infrared and spectral-domain optical coherence tomography (SD OCT) images of pigmentary retinopathy in a 20-year-old patient with mucopolysaccharidoses II. The SD OCT demonstrated (**A**) focal choroidal thinning (arrowheads) in the depigmented retinopathy areas (short vertical lines) and (**B**) a fuzzy and thickened external limiting membrane (arrows), widening of the distance between retinal pigment epithelium and ellipsoid zone at the fovea, and loss of ellipsoid zone at the extrafoveal area.

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