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SHORT COMMUNICATION

Optical coherence tomography in enhanced S-cone syndrome: Large macular retinoschisis with disorganized retinal lamination

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PURPOSE. The authors previously reported clinical and molecular features of a boy (at age 17) with enhanced S-cone syndrome (ESCS) who had bilateral cystoid maculopathies. The purpose of the current study was to describe the patient's optical coherence tomography (OCT) findings.

METHODS. OCT was performed when the patient was 23 years old.

RESULTS. OCT images revealed formations of single large hyporeflective cystic spaces in the cystoid maculopathies of both eyes. The cystic spaces were much larger than those of previously reported cases. In the temporal region of each cystic space, symmetric disorganized retinal lamination was observed with the retina lacking well-defined and hyporeflective bands of the inner nuclear layer and the outer nuclear layer, which are seen in normal retina. Splitting in the retinal thickness was at the level of the outer retinal layer rather than at the inner retinal layer in both eyes.

CONCLUSIONS. Splitting is likely to occur close to the outer plexiform layer in which the cleavage plane of familial juvenile retinoschisis is identified. The unique OCT manifestation of symmetric large macular retinoschisis with disorganized retinal lamination may indicate a severe form of ESCS. (Eur J Ophthalmol 2005; 15: 643-6)

KEY WORDS. Enhanced S-cone syndrome, Hereditary retinal disorder, Autosomal recessive inheritance, Optical coherence tomography, Macular retinoschisis

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INTRODUCTION

The human retina has three separate classes of cone photoreceptor cells: the short-wavelength sensitive (S or blue), middle-wavelength sensitive (M or green), and long-wavelength sensitive (L or red) cones. Enhanced S-cone syndrome (ESCS) is a rare inherited retinal dystrophy with autosomal recessive transmission and is characterized by hyperfunction of S cones with severely impaired L/M cone and rod functions (1, 2). Recently, Haider et al (3) demonstrated that ESCS is caused by mutations in the NR2E3 gene, which encodes a photoreceptor cell-specific nuclear receptor. Clinically, patients with ESCS have relatively good visual acuity and normal central color vision (1, 4). Loss of visual acuity and central color vision in ESCS patients is mostly due to cystoid maculopathy. Therefore, it is important to assess the macular regions of ESCS patients.

Our previous study documented clinical and molecular features of a boy diagnosed with ESCS (5). Funduscopy showed that he had certain cystoid maculopathies in both eyes. In this report, using optical coherence tomography (OCT), we focused on evaluating cross-sectional retinal images of the cystoid maculopathies and their location in the ESCS patient.

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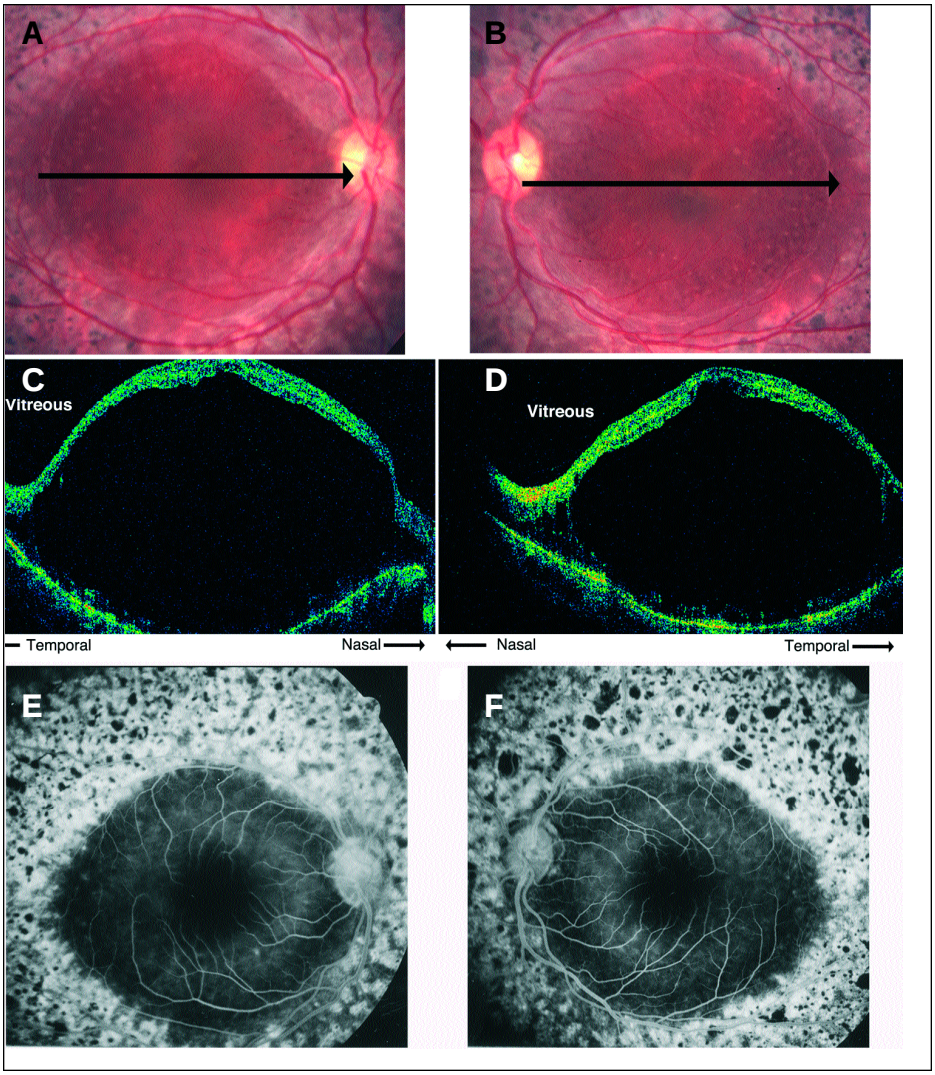

Fig. 1 - Color fundus photographs of the right **(A)** and left **(B)** eyes. Solid black arrows indicate locations and directions for optical coherence tomography (OCT) scans. Horizontal 9 mm OCT scans of the right **(C)** and left **(D)** eyes, corresponding to the arrows, demonstrate symmetric single large hyporeflective cystic spaces. Slight fluorescein leakage in the macula is seen in the right **(E)** and left **(F)** angiograms at age 23 years.

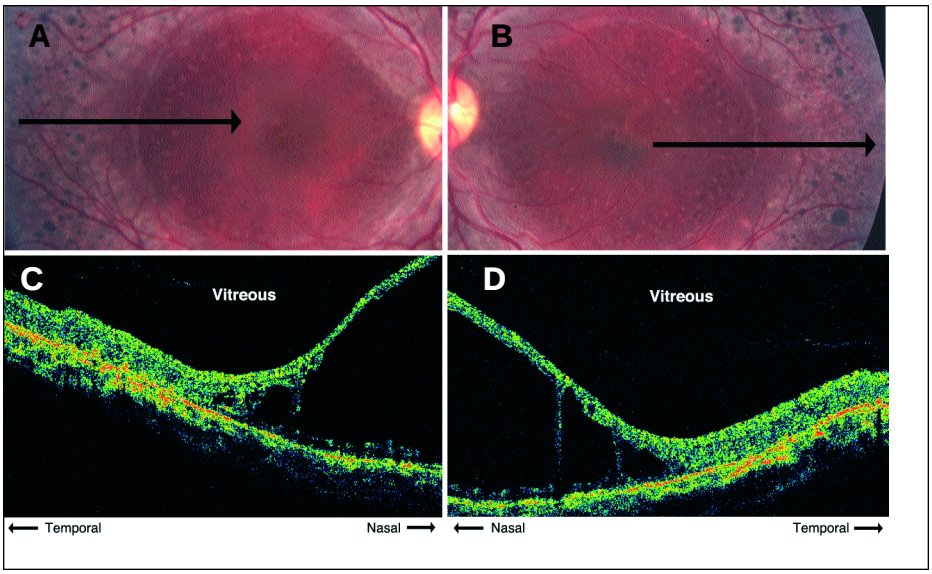

Fig. 2 - Color fundus photographs of the right **(A)** and left **(B)** eyes. Solid black arrows indicate locations and directions for optical coherence tomography (OCT) scans. In the temporal retinae of the cystic spaces, horizontal 5 mm OCT scans of the right **(C)** and left **(D)** eyes reveal symmetric disorganized retinal lamination. Splitting in the retinal thickness is at the level of the outer retinal layer rather than at the inner retinal layer in both eyes.

Case report

We previously reported a 17-year-old boy who was diagnosed with ESCS on the basis of psychophysical and electroretinographic examinations (5). In addition, molecular analysis demonstrated that the patient had a homozygous nonsense mutation (Q350X) in the NR2E3 gene (5). His best-corrected visual acuity (BCVA) was 0.1 in the right eye and 0.7 in the left eye. Funduscopy showed bilateral cystoid maculopathies and pigmentary degenerations in the vascular arcade and midperipheral retina (5). The maculopathies exhibited slight leakage in the fluorescein angiograms. Subsequently, the patient has been followed up for more than 6 years after his first ophthalmic evaluation at age 17. During this 6-year time period, visual loss of his left eye has been progressive. At his current age of 23, his BCVA has decreased to 0.1 in the left eye but remained at 0.1 in the right eye. Fundus examinations have revealed that the cystoid maculopathy of the left eye has markedly expanded in comparison with that of the initial examination, while the fundus finding for the right eye has not changed. To define the cystoid maculopathies of both eyes, we evaluated the cross-sectional retinal images with OCT (OCT3 Model 3000, Carl Zeiss Meditec AG, Japan). The OCT images horizontally scanned through the foveae and optic discs (a transverse width of 9 mm) showed formations of single large hyporeflective cystic spaces within the neurosensory retina of both eyes (Fig. 1). Each cystic space is symmetric and assumes the form of a circle with a radius that is the length of the distance between the fovea and optic disc. The fluorescein angiograms (at age 23 years) in the mid to late phase showed slight hyperfluorescence in the macular lesions of both eyes (Fig. 1). In addition, the OCT images (spanning a transverse width of 5 mm) in the temporal regions of the cystic spaces disclosed disorganized retinal lamination, as the inner nuclear layers (INL) and the outer nuclear layers (ONL), which are usually seen in relatively hyporeflective bands in normal retina (6), became indistinct within certain retinal thicknesses (Fig. 2). Splitting in the retinal thickness was at the level of the outer retinal layer rather than at the inner retinal layer in both eyes (Fig. 2).

DISCUSSION

We describe two main OCT findings for an ESCS patient with the NR2E3 mutation (Q350X). First, it was demonstrated that the cystoid maculopathies were due to the large hyporeflective cystic spaces in both eyes (Fig. 1). Our previous study showed that the maculopathies exhibited only slight fluorescein leakage (5). Three years later, the angiogram findings (Fig. 1) remain unchanged. Splitting in the retinal thickness was at the level of the outer retinal layer but not at the subretinal space, as certain scattered retinal elements were noticed at the back (scleral side) of the cystic spaces in both eyes (Fig. 2). In addition, the angiogram findings (Fig. 1) are differentiated from leakage in the subretinal space or cystoid macular edema. In the maculopathies, splitting is, therefore, likely to occur close to the outer plexiform layer in which the cleavage plane of familial juvenile retinoschisis has been identified (7). Taken together we consider the symmetric cystic space to be due to macular retinoschisis in the patient. Second, it was found that the laminar structure in the temporal retina of the cystoid maculopathy was disorganized (Fig. 2), with the retina lacking the well-defined and hyporeflective INL and ONL bands that are found in normal retina.

In two original reports regarding ESCS patients (1, 2), 7 of 11 patients had cystoid maculopathies. Of these, 4 of the 7 patients with cystoid maculopathies exhibited no fluorescein leakage (1). Milam et al (8) histopathologically studied a postmortem retina of an ESCS patient who was homozygous for the NR2E3 R311Q mutation, showing that the retina was disorganized with densely packed cones intermixed with inner retinal neurons (8). Thus, these findings suggest that the cystoid maculopathy and disorganized laminar structure are distinctive retinal findings of ESCS. There are only two reports (3, 9) that have described the cross-sectional retinal OCT images across the fovea in two ESCS patients with NR2E3 mutations. The OCT data of these reports documented foveal cystic lesions, which were much less than the cystic spaces of our patient, but no information concerning the retinal laminar architecture was described (3, 9).

Recently, Jacobson et al (10) investigated retinal thickness using OCT images in 17 patients with NR2E3 mutations. Although the number of patients diagnosed with ESCS was not related, it was shown that each NR2E3-mutant retina in patients who were not referred regarding retinae with macular retinoschisis had a foveal depression with a large annular increase in retinal thickness, and two patients exhibited abnormal retinal lamination around the fovea (10).

In this report we present the unique OCT finding in which the symmetric large macular retinoschisis with disorganized retinal lamination was observed in an ESCS pa-

tient. A previous study demonstrated that this patient had the homozygous nonsense NR2E3 mutation (Q350X) (5) that led to a truncated NR2E3 protein lacking 61 amino acids of the ligand-binding domain (LBD), which is of functional importance.

The clinical course has exhibited a rapid deterioration of visual acuity since the onset at age 17, when he initially realized there was visual impairment (5).

We conclude that the OCT manifestation of this patient may indicate a severe form of ESCS and can be correlated with the defective NR2E3 protein with the null function for the LBD.

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