

En face optical coherence tomography findings in a case of Alport syndrome

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Alport syndrome is a rare hereditary disease that is associated with retinal abnormalities such as dot-and-fleck retinopathy and temporal macular thinning. The main pathophysiological process of Alport syndrome is loss of the collagen network in the basement membrane. However, the alterations in each retinal layer have not been fully evaluated. In the case presented here, we evaluated the retina of a patient with Alport syndrome using *en face* optical coherence tomography (OCT). The findings suggested that the primary alterations occur in the internal limiting membrane and the retinal pigment epithelium basement membrane which is a part of the Bruch's membrane. The adjacent retinal layers are damaged subsequently. In conclusion, *en face* OCT could be useful in evaluating retinal abnormalities and understanding their underlying pathophysiology in Alport syndrome.

Key words: Alport syndrome, collagen, *en face* optical coherence tomography, multifocal electroretinogram (mfERG)

Alport syndrome is a rare hereditary disease that is caused by mutations in the genes for the collagen Type IV alpha chain (COL4A3-5).^[1] These mutations result in loss of the $\alpha 3(IV)$ - $\alpha 5(IV)$ collagen network in the basement membrane,^[2] which in turn produces retinal abnormalities such as dot-and-fleck retinopathy, temporal macular thinning, disturbances in foveal pigmentation, and macular hole.^[3] Till date, alterations in each retinal layer have not been fully evaluated in Alport syndrome. However, recent advances in *en face* optical coherence tomography (OCT) have enabled noninvasive layer-by-layer analysis. Herein, we report the case of a patient with Alport syndrome who was evaluated using *en face* OCT and mfERG.

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Case Report

A 24-year-old man who had hematuria for 10 years was diagnosed with Alport syndrome after renal biopsy. A further genetic test confirmed a COL4A3 gene mutation, and the patient underwent a renal transplant. His best-corrected visual acuity was 20/25 in the right eye and 20/20 in the left eye. A slit lamp examination revealed recurrent corneal erosion. His intraocular pressure was within normal range in both the eyes. Slit lamp examination of the anterior segment revealed posterior polymorphous corneal dystrophy, recurrent corneal erosion, and corneal guttata. A dilated fundus examination revealed perimacular and peripheral dot-and-fleck lesions in both eyes.

Fundus photography confirmed bilateral foveal sparing perimacular dot-and-fleck retinopathy [Fig. 1a and b]. In an autofluorescence image, there were

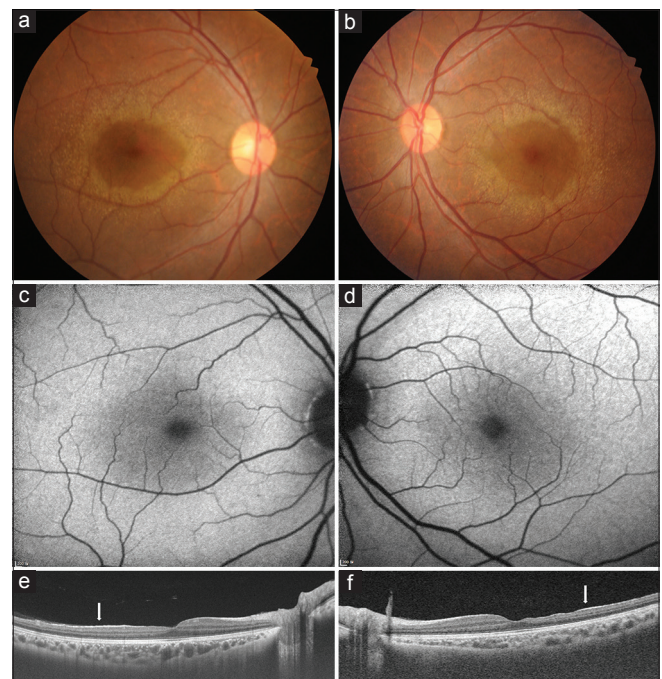


Figure 1: (a and b) Fundus photography showing bilateral foveal sparing perimacular dot-and-fleck retinopathy. (c and d) Autofluorescence image showing bilateral splotchy hyperautofluorescences in perimacular area corresponding to the perimacular dot-and-fleck lesions. (e and f) Horizontal scan of the swept source optical coherence tomography demonstrated the accumulation of hyperreflective materials on the internal limiting membrane surface (arrows) with symmetrical temporal retinal thinning

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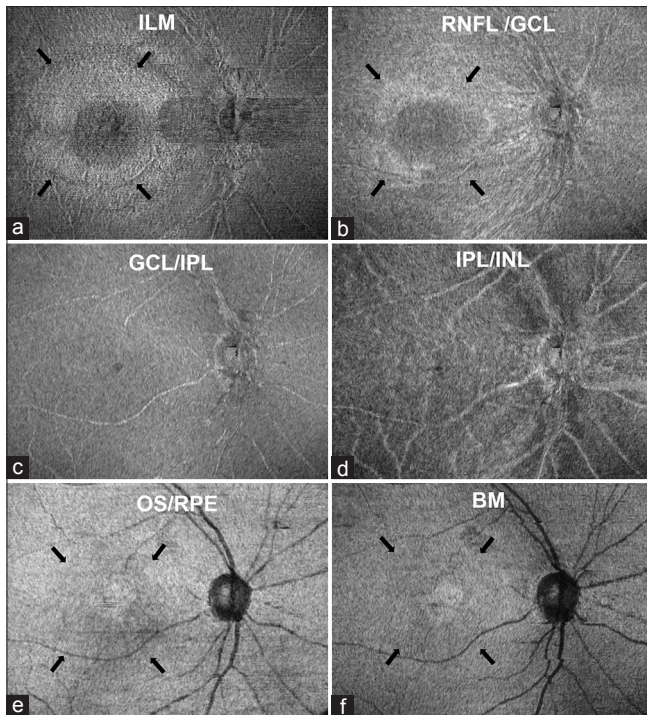


Figure 2: (a-f) *En face* OCT findings in the right eye. (a and b) At the level of internal limiting membrane and retinal nerve fiber layer/ganglion cell layer, hyperreflective area (arrows) was observed corresponding to the perimacular dot-and-fleck lesions (arrows). (c and d) At the level of the ganglion cell layer/inner plexiform layer and inner plexiform layer/inner nuclear layer, retinal structures were normal. (e and f) At the level of the outer segment/retinal pigment epithelial cell layer and Bruch's membrane layer, hyporefective areas in a circular pattern (arrows) were observed

splotchy, hyperautofluorescent regions in the perimacular areas of both the eyes; these corresponded to the perimacular dot-and-fleck lesions, suggesting that the retinal pigment epithelium (RPE) had been altered [Fig. 1c and d]. A horizontal scan of swept source OCT (SS-OCT; Topcon, Tokyo, Japan) demonstrated the accumulation of hyperreflective materials on the surface of the internal limiting membrane (ILM) [arrows in Fig. 1e and f], with symmetrical, temporal, and perimacular thinning. At the level of the ILM, the *en face* OCT findings showed hyperreflective areas that corresponded to the perimacular dot-and-fleck lesions [arrows in Fig. 2a]. The hyperreflective area was still observed at the level of the retinal nerve fiber layer (RNFL)/ganglion cell layer (GCL) [arrows in Fig. 2b]. The GCL/inner plexiform layer (IPL) and IPL/inner nuclear layer showed normal retinal structures [Fig. 2c and d]. However, the outer segment (OS)/RPE layer, as well as Bruch's membrane (BM), demonstrated hyporefective areas in a circular pattern, suggesting that these layers were damaged [arrows in Fig. 2e and f]. Trace arrays and three-dimensional topography of the mfERG response density in both the eyes demonstrated a decrease in the P1 amplitudes of the temporal perimacular areas in both the eyes; this decrease corresponded to the perimacular thinning [Fig. 3a and b]. The N1 amplitude in the temporal perimacular areas was within the normal range [Fig. 3a and b]. The patient was prescribed antibiotics and artificial tears for his recurrent corneal erosion; he then attended regular follow-up

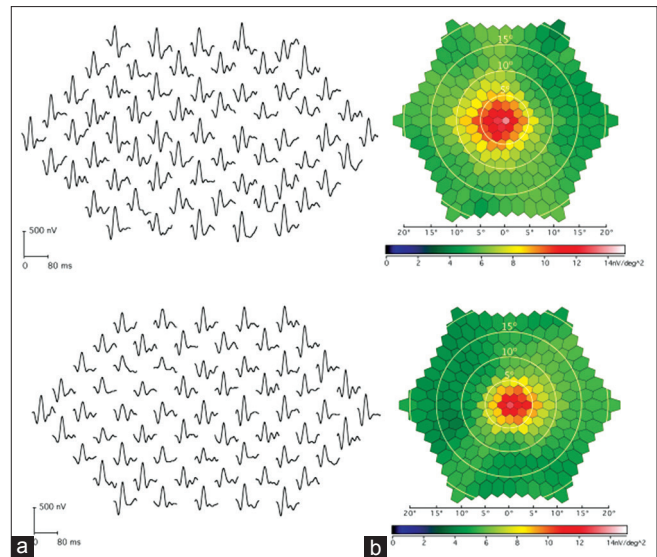


Figure 3: (a and b) Trace arrays and three-dimensional topography of the response density of multifocal electroretinogram in both the eyes showed decrease of P1 amplitudes in temporal macula areas corresponding to the temporal outer and inner retinal thinning

visits at the departments of nephrology and ophthalmology in our hospital.

Discussion

In the normal retina, $\alpha 3\alpha 4\alpha 5$ type IV collagen networks are distributed throughout the ILM and the RPE basement membrane which is a part of the BM. Mutations in the *COL4A3* gene result in loss of collagen networks and subsequent thinning or lamellation of these layers.^[4] The ILM, which comprises the footplates of the Muller cells, acts as a physical barrier protecting the retina from toxins and the tractive forces of the vitreous. The BM primarily regulates the passage of nutrients and metabolites between the RPE and the underlying choriocapillaris. The thinning of these layers may subsequently cause damage to the adjacent retinal layers. In the present case, *en face* OCT demonstrated hyperreflective areas in the ILM and RNFL/GCL, as well as several hyporefective areas in the OS/RPE and BM. These findings suggested that the primary effects of the gene mutation were on the ILM and RPE basement membrane and that the adjacent retinal layers, such as the RNFL/GCL and OS/RPE, were damaged subsequently. In previous reports, various OCT findings have been reported, including temporal retinal thinning, macular hole, lamellar hole,^[3] and increased reflectivity in the ILM/RNFL.^[4] However, to the best of our knowledge, no reports have described *en face* OCT findings in Alport syndrome.

It may be that the splotchy hyperautofluorescence seen on the autofluorescence image of the temporal perimacular area in the present study, and which corresponded to perimacular dot-and-fleck lesions, represented alterations in the RPE layer. In addition, a previous study suggested that dot-and-fleck lesions in the perimacular area, which indicate hyperreflective materials, are caused by cellular production of an abnormal form of $\alpha 5$ Type IV collagen and that foveal sparing of these lesions reflects the distribution of Muller cells.^[5] The same

study reported retinal abnormalities even though the ERG and electrooculogram findings were within the normal range.^[5] In the present case, we found that the P1 amplitude of the temporal perimacular area was decreased in the mfERG, suggesting localized retinal dysfunction.

Conclusion

In summary, *en face* OCT findings in the case described here suggested that the primary alterations in Alport syndrome occur in the ILM and the RPE basement membrane and that the adjacent retinal layers are damaged subsequently. *En face* OCT may be useful in evaluating retinal abnormalities and understanding the underlying pathophysiology of Alport syndrome.

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Conflicts of interest

There are no conflicts of interest.

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