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SHORT COMMUNICATION

Occurrence of full-thickness macular hole complicating Stargardt disease with ABCR mutation

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PURPOSE. *To report an unusual episode of full-thickness macular hole complicating Stargardt disease with an ABCR mutation.*
METHODS. *Case report.*
RESULTS. *Fundus examination of a 20-year-old healthy man showed typical fundus manifestation with yellowish-round or fish-like flecks associated with vitreous macular adhesion and a round punched-out area in the right eye. Optical coherence tomography (OCT) illustrated a full-thickness macular hole. Molecular genetic examination of the ABCR gene showed two heterozygous missense mutations: R1108C (CGC→TGC) in exon 22 and a splicing mutation IVS6-→1GT – described in the literature in association with Stargardt disease.*
CONCLUSIONS. *Macular hole was once described in other inherited retinal degenerations (Best disease and Bietti crystalline retinopathy). The pathogenesis gives rise to a host of speculations: widespread alteration of the retinal pigment epithelium; inflammatory mechanisms; a minor trauma which might cause subretinal fibrosis. Surgical procedures were not performed on our patient after his ophthalmologic history and findings were considered. (Eur J Ophthalmol 2006; 16: 335-8)*

KEY WORDS. *ABCR gene, Macular dystrophy, Macular hole, Stargardt disease*

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INTRODUCTION

Stargardt disease is a usually autosomal recessive macular dystrophy whose presentation is mostly revealed during the first or second decade of life.

A relatively poor visual prognosis is usually designated.

Histopathologic studies report diffuse lipofuscin storage affecting the retinal pigment epithelium (RPE) and focal central atrophy of photoreceptors and RPE cells.

In most cases, the ailment is clinically characterized by a typical fundus manifestation with yellowish-round or fish-like flecks associated with macular degeneration.

Fluorescein angiography often confirms the typical aspect of dark choroid, caused by the diffuse lipofuscin deposits in the RPE masking the underlying choroidal fluorescence.

Autosomal recessive Stargardt disease has been associated with mutations of the ABCR gene, encoding an ATP-binding cassette transporter protein expressed in rod and cone photoreceptors and involved in the visual cycle. In the absence of a functional ABCR gene, the metabolite A2-E, the major component of lipofuscin, accumulates within the outer segment of the photoreceptors.

In Stargardt disease the materialization of a macular hole has never been described in the literature.

We report a 20-year-old healthy man who developed a macular hole 7 years after the initial Stargardt diagnosis.

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Case report

A 20-year-old man was referred to our Eye Clinic in April 2003 with a history of Stargardt disease and central visual loss in both eyes, which had happened 6 years earlier. The patient did not report any ocular trauma or eye infection. Both the medical history and family history were unremarkable.

Fundus photography dated May 2000 showed that both eyes possessed a macular atrophy surrounded by widespread flecks (Fig. 1). Fluorescein angiography (Fig. 2) evidenced bilaterally a central ovoid zone of hyperfluorescence due to severe atrophy of the RPE at the posterior pole. Retinal vessels were much better visible than normal because of the "choroidal silence" phenomenon. EOG and ERG findings were within normal limits.

In December 2002, the patient visited an ophthalmologist complaining of persistent metamorphopsia in his right eye. Fundus examination revealed a vitreomacular traction in the right eye with a visual acuity of 20/400. The patient was then referred to our department for further investigation.

On examination, the best-corrected visual acuity was 20/800 in both eyes. Examination of the anterior segments was unremarkable in both eyes. The Goldmann applanation tonometer measured 14 mmHg in the right and 16 mmHg in the left eye respectively. No signs of ocular inflammation were detected.

Ophthalmoscopy of the right eye showed an epiretinal membrane determining a strong vitreous macular adhesion associated with a round punched-out area, about one-third of the disc diameter, in the center of the macula.

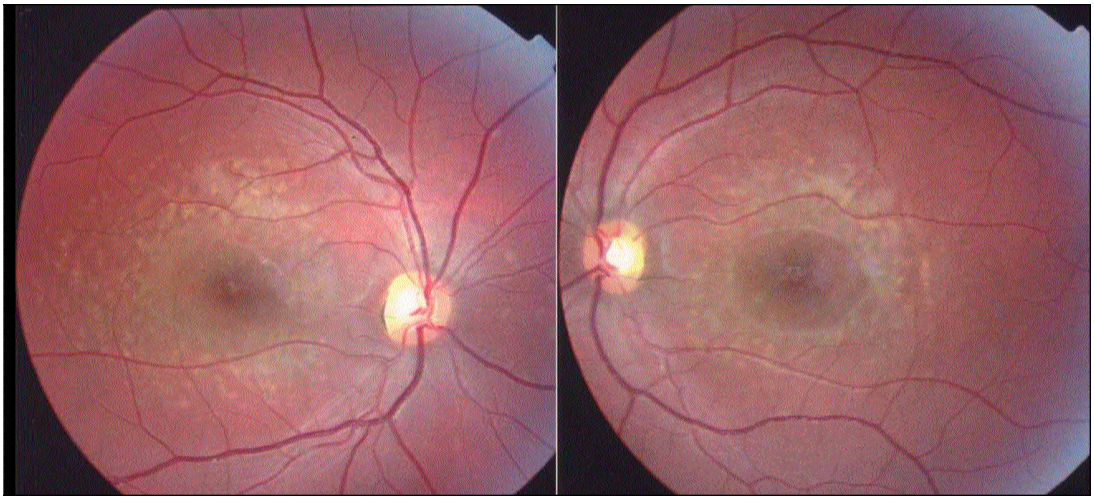

Fig. 1 - *Fundus photograph (May 2000) showing in both eyes a macular atrophy surrounded by widespread flecks.*

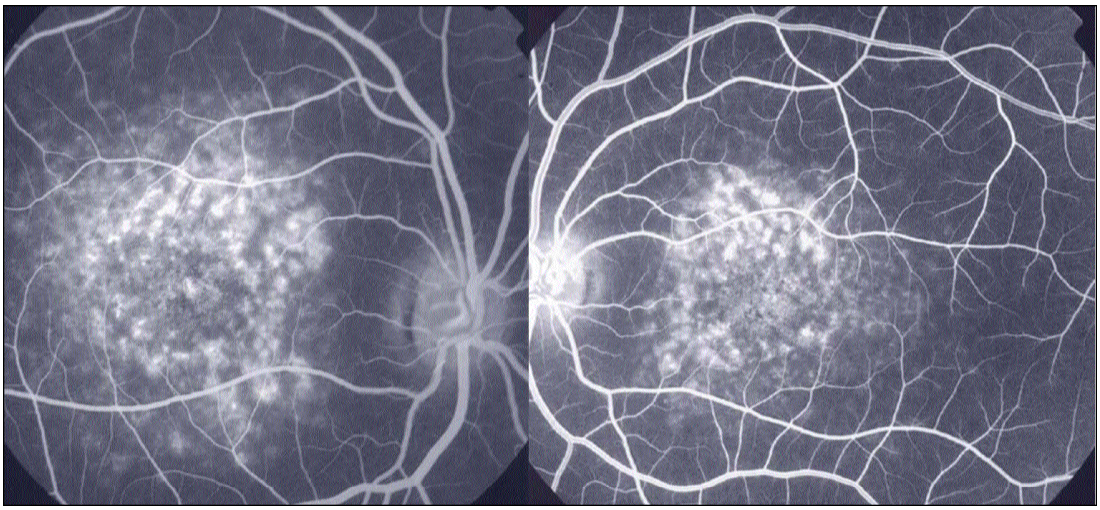

Fig. 2 - *Fluorescein angiography (May 2000) showing bilaterally a central ovoid zone of hyperfluorescence due to severe atrophy of the retinal pigment epithelium at the posterior pole. Retinal vessels are much better visible than normal because of the "choroidal silence" phenomenon.*

Some white drusen-like spots were clearly visible at the bottom of the macular hole. These findings are commonly observed in full-thickness holes.

A Watzke-Allen test was positive and a Weiss ring was visible in front of the optic nerve head. The macular area was surrounded by yellow-white flecks scattered throughout the posterior pole. The left eye examination revealed a similar distribution of multiple flecks around an atrophic macula (Fig. 3).

Optical coherence tomography (OCT) showed that the right eye had a full-thickness macular hole, vitreofoveolar adherence at the margin of the hole, and partial separation of the vitreous cortex from the retinal surface.

In the left eye, the OCT scan showed a dramatic decrease of foveal thickness mainly due to the disappearance of sensory retina elements, and the cellular loss was concentrated in the fovea without any significant yielding of the perifoveal area (Fig. 4).

The patient and his parents underwent molecular genetic examination of the ABCR gene. DNA samples were analyzed for mutations in all 50 exons of the ABCR gene employing the DHPLC method (with optimization of the DHPLC conditions for mutation analysis, Transgenomics, San Jose, CA, USA).

Two heterozygous mutations in the proband were identified: a missense mutation R1108C (CGC→TGC) in exon 22 and a splicing mutation IVS6-1G→T. These alterations have been described in the literature in association with Stargardt disease.

The father of the proband was a healthy carrier of the R1108C mutation. IVS6-1G→T was identified in the mother.

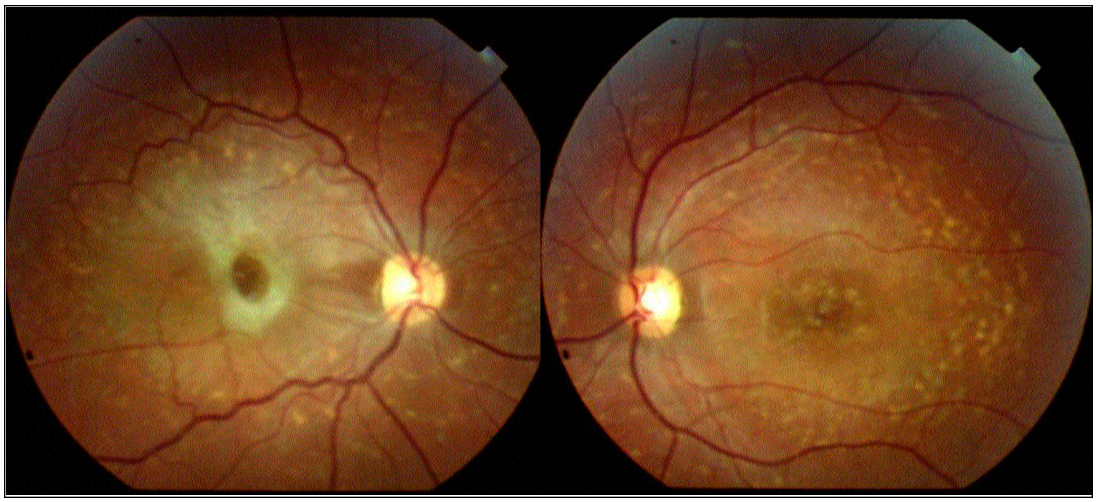

Fig. 3 - *Fundus photograph (April 2003) showing vitreous macular adhesion associated with a round punched-out area in the right eye and, in addition, a macular atrophy surrounded by widespread flecks in the left eye.*

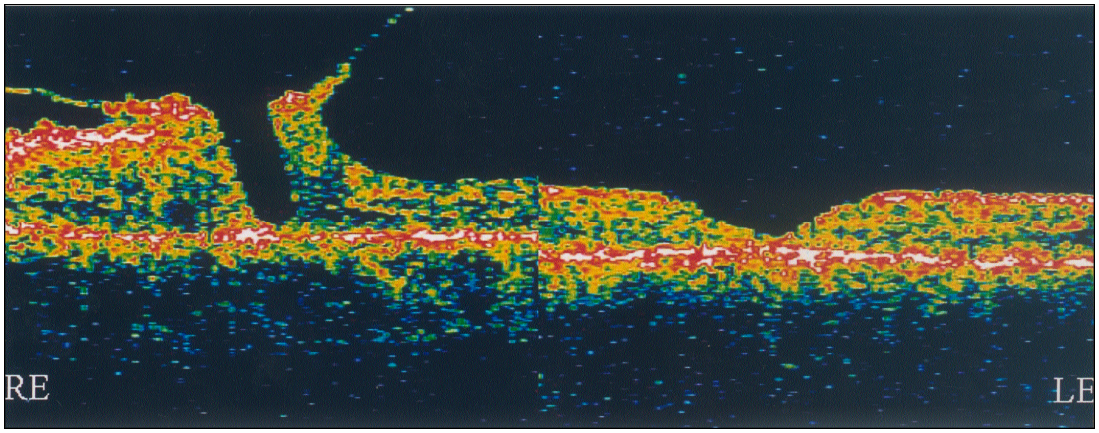

Fig. 4 - *Optical coherence tomography (April 2003) showing a full-thickness macular hole in the right eye and a dramatic decrease of foveal thickness in the left eye.*

DISCUSSION

In our patient, the diagnosis of Stargardt macular dystrophy was verified both by the molecular genetic results (ABCR mutation) and the clinical findings (age at onset, severity of central visual loss, fundus manifestation, and silent choroid at fluorescein angiography).

The development of a macular hole in the right eye is clearly demonstrated by the comparison of previous fundus pictures with the posterior pole manifested during the last examination. The OCT scan showed a full-thickness macular defect with vitreofoveal attachment at its edges.

The association of macular hole with Stargardt disease has never been reported and might be incidental. On the other hand, a pathogenetic relation between retinal degeneration and vitreoretinal traction can be speculated on the basis of previously made reports of a macular hole in other inherited retinal degenerations. In fact, a macular hole has been observed in retinitis pigmentosa (1), Best disease (2), and Bietti crystalline retinopathy (3).

The pathogenesis of a macular hole in Stargardt disease gives rise to many possibilities. The most reliable hypothesis lies on the evidence that in Stargardt disease there is a widespread alteration of the RPE with an accumulation of lipofuscin granules; the impairment of RPE functions might reduce its pumping effect, lowering the adherence of the neurosensory retina to the underlying RPE. Moreover, the macular area usually shows severe RPE and photoreceptors atrophy with a reduced retinal thickness, which might facilitate the hole formation in association with vitreoretinal interface abnormalities.

Furthermore, in retinal degenerative disorders inflammatory mechanisms might play a role. The development of a macular hole could be caused by an increase in the perimacular vessels' permeability. An inflammatory process has been theorized in some patients with retinitis pigmentosa and cystoid macular edema. In these cases an activation of cellular and circulating immunoreactivity has been evidenced (1).

Finally, previous reports have suggested that minor trauma might cause subretinal fibrosis in patients with Stargardt disease (4).

The management of a patient with a macular hole associated with Stargardt maculopathy is puzzling. Some authors report a favorable outcome with vitrectomy and membrane peeling operation performed on a patient with Stargardt disease (5). Surgical procedures were not performed on our patient for several reasons: the severe visual loss (existing before the macular hole formation), the gradual decrease of visual acuity (suggesting an impairment mainly related to macular dystrophy), and the low visual acuity in the fellow eye.

The authors have no proprietary interest in any aspect of this study.

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REFERENCES

1. Heckenlively JR, Jordan BL, Aptsiauri N. Association of antiretinal antibodies and cystoid macular edema in patients with retinitis pigmentosa. Am J Ophthalmol 1999; 127: 565-73.
2. Mehta M, Katsumi O, Tetsuka S, Hirose T, Tolentino FI. Best's macular dystrophy with a macular hole. Acta Ophthalmol 1991; 69: 131-4.
3. Saatci AO, Yaman A, Berk AT, Soylev MF. Macular hole formation in Bietti's crystalline retinopathy. Ophthalmic Genet 1997; 18: 139-41.
4. Ober RR, Limstrom SA, Simon RM. Traumatic retinopathy in Stargardt's disease. Retina 1997; 17: 251-4.
5. Potter MJ, Lee AS, Moshaver A. Improvement in macular function after epiretinal membrane removal in a patient with Stargardt disease. Retina 2000; 20: 560-1.