A Case of Declining Night Vision

Tony Stork* is a 55-year-old software sales representative who, over the course of two years, was having a harder time stargazing at night with his wife. He also had difficulty visually adapting to different light conditions when he moved from an outdoor to an indoor environment. He had never had vision problems before, so he decided to see an eye specialist.

He initially consulted a general ophthalmologist who—based on an initial examination and the above symptoms—concluded that Mr. Stork had degenerative retinal drusen consistent with age-related macular degeneration (AMD) in both eyes. He was referred to our retina clinic.

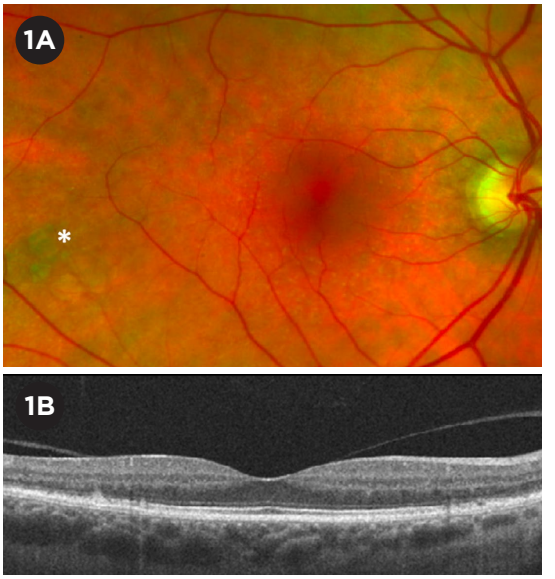
We Get a Look

History. Mr. Stork had no relevant medical or surgical history. He had not experienced any peripheral visual field loss, photopsias, or eye pain. Notably, he told us that his paternal grandmother, his father, an aunt, and a cousin all had a history of presumed retinitis pigmentosa (RP), but he did not know whether they had undergone confirmatory genetic testing.

Exam. Mr. Stork's best-corrected VA was 20/20 in both eyes, and his IOPs were normal. The anterior segment exam was normal, apart from 1+ nuclear sclerotic cataracts in both eyes.

The posterior segment exam of both eyes demonstrated symmetric, fine yellow-white drusen-like deposits in the temporal macula and midperiphery, with patchy areas of retinal pigment epithelium (RPE) atrophy in the temporal midperiphery (Fig. 1A).

Imaging. Mr. Stork's age, which was on the younger side for AMD, along with the clinical findings prompted us to pursue further investigations. OCT showed parafoveal ellipsoid zone and RPE disruption with subretinal deposits (Fig. 1B). Fundus autofluorescence (FAF) demonstrated well-defined scalloped areas of RPE atrophy consistent with the clinical exam, which had revealed symmetric hypopigmented deposits along the temporal midperiphery (Fig. 2).



WE GET A LOOK. *(1A) Magnified widefield fundus image, right eye, demonstrates fine yellow-white drusen-like deposits in the temporal macula and midperiphery, with patchy areas of RPE atrophy in the temporal midperiphery (asterisk). (1B) OCT of the right eye demonstrates parafoveal ellipsoid zone and RPE disruption with subretinal deposits. The left eye, not pictured, had symmetric findings.*

Differential Diagnosis

When examining a middle-aged patient with new-onset nyctalopia and hypopigmented midperipheral RPE changes in the absence of intraocular inflammation, the clinician should consider the following:

- paraneoplastic- or nonparaneoplastic-associated autoimmune retinopathy,
- vitamin A deficiency,
- outer retinal inflammatory conditions such as acute zonal occult outer retinopathy, or
- inherited retinal diseases, including late-onset retinal degeneration (L-ORD), RP, and fleck-related retinal dystrophies (e.g., Stargardt disease, fundus albipunctatus, or retinitis punctata albescens).

Mr. Stork had not experienced photopsias and had no history of malignancy. Although cancer-associated retinopathies can affect both eyes, the symmetry and the strong dominant family history of nyctalopia pointed

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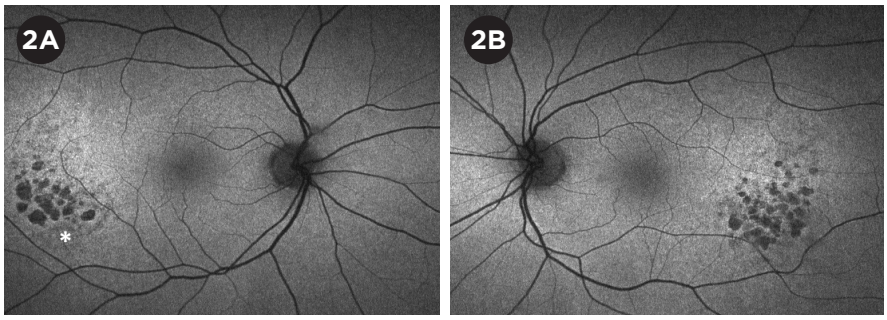

FAF. *Fundus autofluorescence of the right (2A) and left (2B) eyes demonstrates temporal hyperautofluorescence with scalloped areas of patchy hypoautofluorescence (asterisk) corresponding to the RPE atrophy seen on the exam.*

toward an inherited retinal disease. In addition, the appearance of the fundus on FAF was not suggestive of an autoimmune retinopathy, which can present with a parafoveal hyperautofluorescent ring.[1] The patient was younger than is usual for advanced AMD. Vitamin A deficiency seemed unlikely, given that he had no history of bowel surgery, had normal conjunctivae, and said that he ate a diet of meat and vegetables.

Our Diagnosis and Confirmatory Testing

The characteristic symmetric, temporal macular findings and nyctalopia led us to strongly suspect a diagnosis of L-ORD. Electroretinogram testing demonstrated significantly attenuated scotopic responses with prolonged implicit times and slightly reduced photopic responses. Confirmatory genetic testing was positive for a common mutation in the *C1QTNF5* gene, p.S163R, which is consistent with a diagnosis of L-ORD.[2]

Discussion

Pathogenesis. The exact pathogenesis of L-ORD is unknown. The *C1QTNF5* gene on chromosome 11 encodes complement component 1q and tumor necrosis factor–related protein 5 and is expressed in the RPE, ciliary processes, and lens epithelium.[3] Postmortem exams demonstrate thick, lipid-rich deposits between the RPE and the Bruch membrane; these deposits may act as a barrier to nutrients.[4,5] Increased deposit thickness and loss of photoreceptors have been correlated.[5] Electrophysiology shows that rod-specific functions are the first to be compromised, with subsequent cone dysfunction.[4]

Typical presentations. L-ORD patients begin to report ophthalmic symptoms, such as progressive nyctalopia, at approximately 50 to 60 years of age.[2] Clinical exams may initially appear normal; as the disease progresses, fine yellow-white drusen-like deposits appear in the midperiphery. These deposits form atrophic areas that spread throughout the retina, eventually leading to loss of central and peripheral vision, choroidal neovascularization (CNV), and pigmentary retinopathy.[2,6] Long anterior zonule insertions, early cataracts, and peripupillary iris transillumination deficits may also be present.[7]

The early midperipheral changes may often be missed on clinical exam, and this case highlights the importance of FAF in demonstrating the characteristic pattern in the beginning stages of L-ORD.

Management. No specific treatment is available; reports of vitamin A supplementation to slow progression are scant.[3] Affected patients should be monitored for the development of secondary CNV, which would then warrant treatment.[2] Because of the autosomal dominant inheritance pattern of L-ORD, genetic counseling and, when appropriate, family planning counseling should be provided.

Our Patient

Mr. Stork continues follow-up to monitor for CNV. He was counseled to discuss his diagnosis with those of his relatives who had a history of presumed RP, and they were offered exams to determine whether their diagnoses were more consistent with L-ORD.

* Patient name is fictitious.

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Relevant financial disclosures: None.
For full disclosures, view this article at aao.org/eyenet.

FURTHER READING. Agerwal et al. Late-Onset Retinal Macular Degeneration: An Entity Not to Be Overlooked. *Retina Cases Brief Rep.* 2010;4(3):257-261.