Diagnostic and Therapeutic Challenges

Mohamed Genead, MD, Gerald Fishman, MD, Martin Lindeman, COMT

Institute affiliation

Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, USA

Address for correspondence

Gerald A. Fishman

Department of Ophthalmology and Visual Sciences (MC 648), Room 3.85, Eye and Ear Infirmary, 1855 W Taylor Street, Chicago, Illinois 60612-7234.

Tel: +1- 312-996-8939; Fax: +1-312-996-1950; email: gerafish@uic.edu

The authors have no proprietary interests in this report.

Supported by funds from the Foundation Fighting Blindness, Owings Mills, Maryland; Grant Healthcare Foundation, Lake Forest, Illinois; NIH core grant EYO1792; and an unrestricted departmental grant from Research to Prevent Blindness.

Clinical Case

A 46-year old white male of Polish and Russian ancestry was initially seen in the Ophthalmology Department of the University of Illinois at Chicago in September 1990. He had been followed-up by one of the authors (GAF) since then.

At his first examination in our clinic, he had no subjective visual complaints until two months prior to his visit when he received an Amsler grid in the mail and noticed a waviness in the left portion of the grid in his left eye and blurred areas in the upper right and lower right quadrants of his right eye. These patterns on the grid had not changed for a duration of two months. He did not complain of photoaversion, poor color vision, nyctalopia or poor central acuity. A general review of systems indicated a past history for a high-frequency hearing loss which he indicated was secondary to noise from jet engines. The patient was an air force pilot for 22 years and subsequently a commercial airline pilot.

A review of his prior ocular records stated that the patient's father had a history of impaired central vision associated with perifoveal pigmentary degenerative changes. His paternal grandparents were first cousins.

Vision was correctable to 20/15-3 OD with a -1.25+0.50x5 and 20/15 OS with a -1.50+0.75x160. External examination showed both eyes were orthophoric and there was full range of ocular motion in all directions of gaze.

The pupils were round and reacted normally. Ocular pressures measured by applanation tonometry were 17mmHg OD and 15mmHg OS. The left cornea showed a small scar from a presumed previous foreign body. The lenses and vitreous were clear. There was a Mittendorf dot OS.

Dilated fundus examination showed yellowish-white fleck-like lesions within the posterior pole of each eye. The lesions spared the foveola. The peripheral retina, optic discs, and retinal vessels were normal in each eye.

Visual field examination was performed by Goldmann kinetic perimetry 940 (Haag-Streit AG, Switzerland), using II-2-e and II-4-e test targets. The testing showed no evidence of peripheral field restriction or central/paracentral scotomas in either eye.

A review of a previously obtained fluorescein angiogram (FA) showed no evidence for a dark choroid or apparent fluorescein leakage. There were regions of both hyper and hypofluorescence associated with the fundus flecks.

On subsequent visits, the patient did not have any subjective visual complaints. Specifically, he did not complain of any difficulty with either central or peripheral vision, color vision or night vision. Previously he underwent dark adaptation testing with a Goldmann-Weekers dark adaptometer. The testing showed no abnormalities in the bleach recovery time or the final rod thresholds.

Nine years after the initial visit, the patient continued to maintain excellent central acuity with no abnormalities of his peripheral or mid-peripheral fields. Vision was still correctable to 20/15 in each eye. Dilated fundus examination showed moderately extensive fleck-like lesions throughout the posterior pole and mid-peripheral retina which continued to spare the foveola. The flecks were more extensive than those noted on prior exams.

At his most recent visit, which was 29 years after the initial visit, subjectively the patient still did not notice any changes in his central or peripheral vision, night vision or color vision.

Visual acuity was correctable to 20/20-1 OD with a -0.25+0.75x180 and 20/20 OS with a -0.50+1.25x165. He read J1 for near at 14 inches with a +2.25 add.

The corneas and anterior chambers were clear while the lenses showed trace nuclear sclerosis in each eye. Ocular pressures were 13mmHg OD and 14 mmHg OS.

Dilated fundus examination showed diffuse flecks throughout the posterior pole and mid-peripheral retina with a relative sparing of the foveola. The peripheral retina, optic discs, and retinal vessels were normal (Figure 1A-B).

Fundus autofluorescence (AF) testing was performed. The AF and Infrared (IR) images were obtained with a confocal scanning laser ophthalmoscope (cSLO) (Heidelberg Retina Angiograph (HRA), Heidelberg Engineering, Heidelberg, Germany). AF images showed diffuse foci of hyper-autofluorescence scattered throughout the posterior pole and mid-peripheral retina associated with the fundus flecks. There were also scattered foci of hypo-autofluorescence within the posterior pole (Figure 1C-F).

The most recent visual field testing by Goldmann kinetic perimetry showed small paracentral scotomas to a II-2-e target which were not apparent on his prior visual field tests.

Spectral-domain OCT (SD-OCT) was performed by imaging with Spectralis HRA+OCT technology (Heidelberg Retina Angiograph (HRA), Heidelberg Engineering, Heidelberg, Germany). The OCT scans showed several rounded-oval elevated lesions at the level of retinal pigment epithelium (RPE), which extended into the inner segment/outer segment junction of the photoreceptors, external limiting membrane and the outer nuclear layer as well. Additionally, the OCT scans showed focal areas of the photoreceptor layer disruption within the posterior pole of the fundus (Figure 2A-F).

Questions for Discussants

1. What would be the differential diagnosis of the ocular disease in this patient?

2. What findings on history, clinical fundus features, fundus imaging, and/or genetic testing would be most useful in leading to the correct diagnosis?

3. What is the most likely diagnosis in this patient?

Follow up:

A blood sample was drawn and sent for genetic molecular analysis. The patient's DNA contained a mutation within the peripherin/RDS gene (CAG to TAG nucleotide substitution) in the coding sequence of exon 3 of the peripherin/RDS gene resulting in an amino acid change from glutamine to a stop codon at codon 331- compatible with the diagnosis of pattern dystrophy.

The genetic results, absence of a dark choroid on FA, absence of relative peripapillary sparing of pigmentary changes (as noted in Stargardt disease), and the positive family history of a paternal central retinal pigmentary degeneration (the latter suggestive of autosomal dominant disease), are collectively most consistent with the diagnosis of pattern dystrophy.

Figure Legends

Fig.1 Color fundus photographs (top panel) of the right (A) and left (B) eyes show fundus flecks within the posterior pole and anterior to the vascular arcade. Infrared (IR) images (middle panel) highlighting the pigmentary degenerative changes of the right (C) and left (D) eyes. Autofluorescence (AF) images (bottom panel) show diffuse foci of hyper and hypo-autofluorescence scattered throughout the posterior pole associated with the fundus flecks of the right (E) and left (F) eyes.

Fig. 2 Spectral-domain OCT (SD-OCT) in the right (A, C, E) and left (B, D, F) eyes allow for visualization of focal disruption in distal retinal structures and in regions which correspond to dome-shaped deposits located in the inner part of the retinal pigment epithelial cell (RPE) layer.