# RARE DISEASE MYSTERY CASES

## Can you diagnose these unusual cases based on the examination and imaging?

By Kenneth C. Fan, MD, MBA; Caroline C. Awh, MD; Nimesh A. Patel, MD; Marta Stevanovic, MD, MSc; Maria Emfietzoglou, MD; Demetrios Vavvas, MD, PhD; Mary V. Lang; Lisa A. Schimmenti, MD; and Brittni A. Scruggs, MD, PhD

*Patients are referred to retina specialists for myriad reasons, many of which are easy to diagnose. However, when a patient's symptoms, examination, and/or imaging don't add up, it's the retina specialist's job to unravel the mystery, regardless of the winding path to diagnosis. These challenging cases are designed to test your diagnostic skills and help improve your rare and inherited disease (IRD) know-how.*

**- Rebecca Hepp, MA, Editor-in-Chief**

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## MYSTERY CASE NO. 1

By Kenneth C. Fan, MD, MBA

A 47-year-old woman presented with a history of central vision loss that began in her 30s. She described central vision distortion that had gradually worsened, now coalescing into blind spots. Her vision was 20/40 OU with normal IOP OU. Family history revealed that her mother had been diagnosed with AMD in her 50s. Her sister and two children have no visual symptoms. There was no evidence of consanguinity. The physical examination did not reveal any other syndromic findings.

Fundus imaging showed symmetric subtle flecks in the macula and posterior pole and a beaten-bronze appearance of central atrophy in each eye (Figure 1). Fundus autofluorescence (FAF) revealed severe central decreased autofluorescence with macular and midperipheral flecks (Figure 2). OCT imaging demonstrated patchy multifocal atrophy of the ellipsoid zone (EZ) and retinal pigment epithelium (RPE) in each eye (Figure 3).

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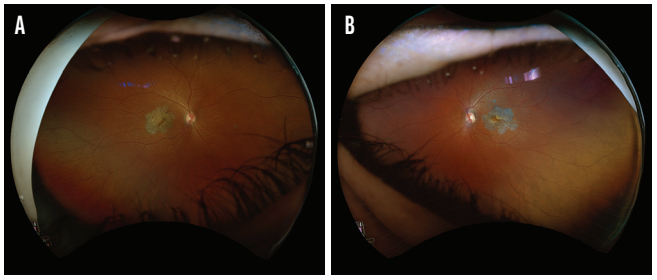


Figure 1. Fundus photography of the right (A) and left (B) eye demonstrates subtle flecks in the macula and posterior pole and a beaten-bronze appearance of central atrophy.

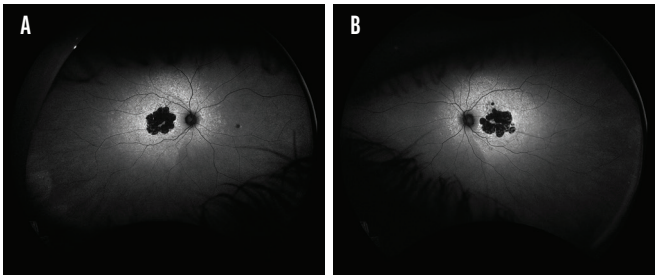


Figure 2. FAF of the right (A) and left (B) eye demonstrates severely decreased central autofluorescence with macular and midperipheral flecks.

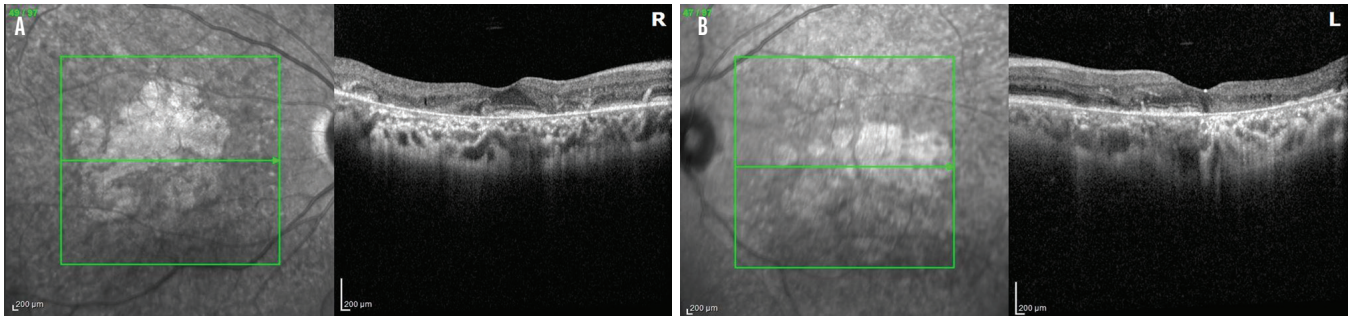


Figure 3. OCT imaging of the right (A) and left (B) eye demonstrates patchy multifocal atrophy of the EZ and RPE.

## MYSTERY CASE NO. 2

By Caroline C. Awh, MD, and Nimesh A. Patel, MD

A 6-year-old healthy girl was referred for bilateral retinal pigmentary changes. She was asymptomatic with a VA of 20/25 OU. The dilated fundus examination demonstrated 360° peripheral retinal hyperpigmentation (Figure 4) with normal FAF imaging (Figure 5). OCT imaging revealed subtle outer plexiform deposits in the macula (Figure 6).

The referring ophthalmologist had ordered an autoimmune workup, an infectious and inflammatory workup, and a retinal dystrophy panel, all of which were negative. Her review of systems and family history for IRD were negative.

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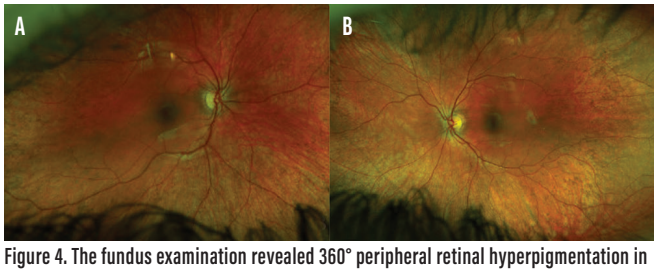


Figure 4. The fundus examination revealed 360° peripheral retinal hyperpigmentation in the right (A) and left (B) eye.

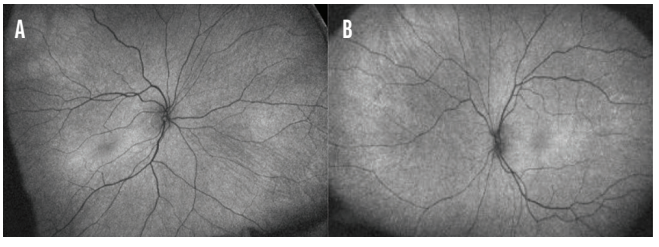


Figure 5. FAF showed a normal fluorescence pattern in the right (A) and left (B) eye.

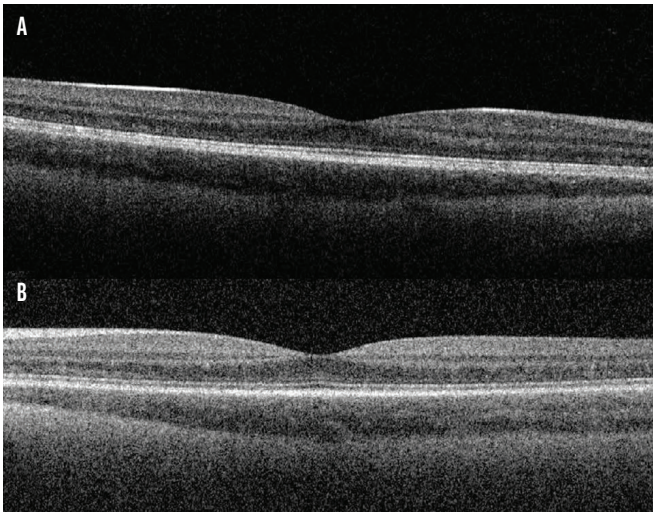


Figure 6. OCT imaging was remarkable for subtle outer plexiform deposits in the macula of the right (A) and left (B) eye.

# Rare and Inherited Retinal Disease

## MYSTERY CASE NO. 3

By Marta Stevanovic, MD, MSc; Maria Emfietzoglou, MD; and Demetrios Vavvas, MD, PhD

A 63-year-old man presented with a VA of counting fingers OU (Figure 7). He reported no personal medical history, and family history included an uncle and cousin (in his 40s) who also had decreased visual acuity. Dilated fundus examination revealed large areas of central atrophy with surrounding drusen. FAF showed central areas of hypoautofluorescence, and OCT demonstrated significant retinal thinning and EZ loss.

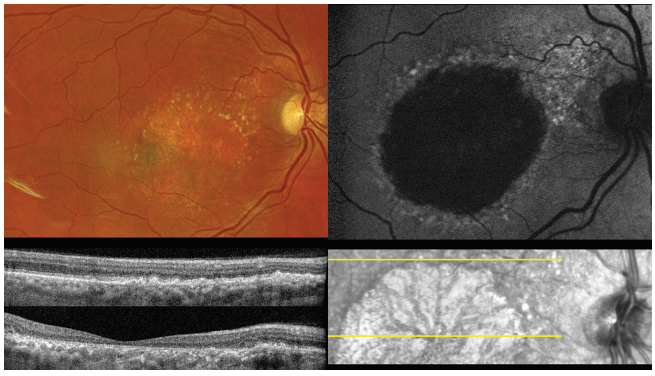

Figure 7. Fundus photography shows central retinal atrophy with surrounding drusen. There is a corresponding area of hypoautofluorescence. OCT shows significant central retinal atrophy and drusen surrounding the atrophic region.

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## MYSTERY CASE NO. 4

By Mary V. Lang; Lisa A. Schimmenti, MD; and Brittni A. Scruggs, MD, PhD

A 78-year-old man presented for a second opinion regarding progressive geographic atrophy (GA). He had a 7-year diagnosis of wet AMD managed with aflibercept (Eylea, Regeneron) every 6 weeks due to recurrent subretinal fluid accumulation with injection spacing. A review of systems revealed long-standing leg claudication. BCVA was 20/200 OD and 20/125 OS, and Ishihara color plates were 3/14 in each eye. Fundus examination and FAF were remarkable for profound GA, peripapillary atrophy, and subtle angioid streaks (Figure 8). ■

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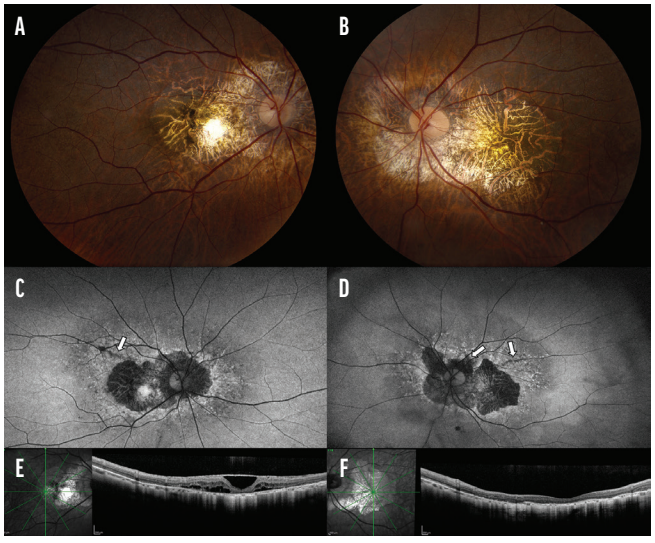


Figure 8. Fundus photography shows bilateral parafoveal and peripapillary atrophy (A, B). FAF imaging demonstrates angioid streaks (arrows) with peripapillary and parafoveal atrophy surrounded by perifoveal hyperautofluorescence (C, D). OCT demonstrates bilateral GA with a diffuse epiretinal membrane in the right eye (E) and disorganization of the inner retinal layers in the left eye (F).

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# MYSTERY CASE MASQUERADE

## By Yicheng Bao, MD, and Hossein Ameri, MD, PhD, FRCSI, MRCOphth

A 35-year-old man presented with a 2-year history of progressive nyctalopia. He reported difficulty adjusting from bright light to dark environments but noted no significant deficits in central or color vision. The patient lacked a family history of vision loss, and review of systems was negative.

BCVA was 20/40 OD and 20/25 OS. IOP was 9 mm Hg OD and 12 mm Hg OS. Dilated fundus examination revealed bilateral, symmetric fine granular pigmentary changes across the midperiphery (Figure 1), supported by fundus autofluorescence imaging (Figure 2). Spectral-domain OCT showed parafoveal inner retinal atrophy. Functional testing provided evidence of severe photoreceptor dysfunction. Electroretinography demonstrated a profound loss of rod function and significantly reduced cone responses (Figure 3). The clinical picture was complicated by a significant systemic history, including ANCA-positive vasculitis, focal segmental glomerulosclerosis, and chronic pancreatitis.

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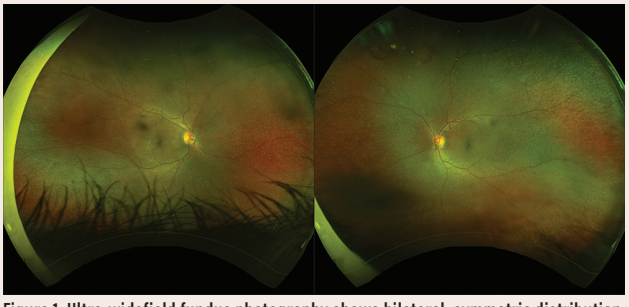

Figure 1. Ultra-widefield fundus photography shows bilateral, symmetric distribution of fine granular pigmentary changes across the midperiphery.

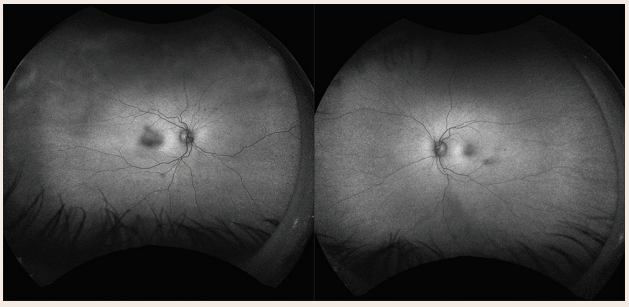

Figure 2. Fundus autofluorescence shows bilateral stippled hypoautofluorescence in the midperiphery.

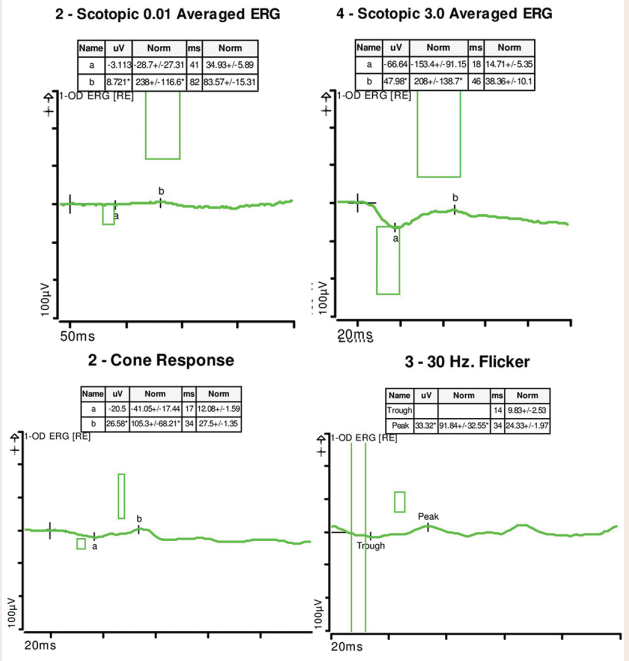


Figure 3. Electroretinography demonstrates severely reduced rod and cone function in each eye.