In the Middle of the Macula

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Introduction:

A 52-year-old female presented to our clinic with gradually worsening central vision in both eyes. She was referred for macular degeneration in both eyes. She has a history of hearing loss requiring a hearing aid and diabetes on insulin. Her visual acuity was 20/50 in the right eye and 20/25 in the left eye. Intraocular pressures were normal in both eyes. There was no relative afferent pupillary defect. Anterior segment exam was unremarkable. Fundus exam and color photos revealed atrophy in the macula sparing the fovea in both eyes.

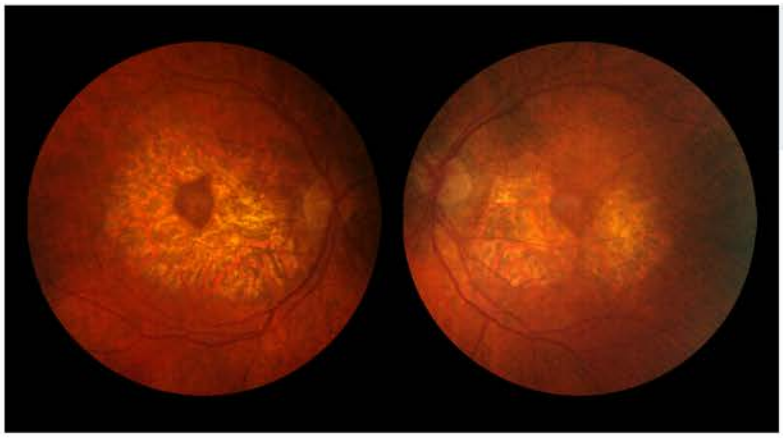


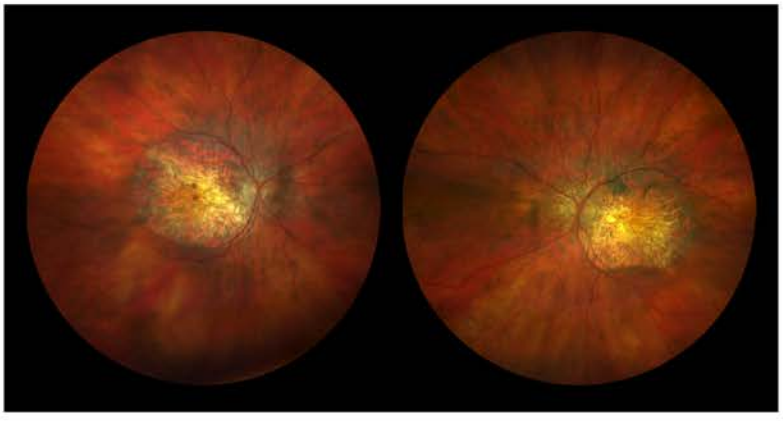
Figure 1: Fundus photos of both eyes showed atrophy in the macula sparing the fovea.

Ten years later her vision worsened to 20/400 in the right eye and 20/150 in the left eye. The geographic atrophy had progressed in both eyes. Color photos revealed expansion of the geographic atrophy towards the arcades and involving the fovea. OCT of the macula showed outer retinal and RPE atrophy. Fundus autofluorescence was significant for hypoautofluoresence in the areas of macular atrophy.

She eventually had genetic testing performed and was found to have heteroplasmic mosaicism for a mitochondrial mutation (mutant G) at position 3243. This was consistent with the diagnosis of Maternally Inherited Diabetes and Deafness (MIDD).

Discussion:

MIDD, first described in 1992, is a type of diabetes mellitus caused by a change in mitochondrial DNA and manifests as diabetes, sensorineural hearing loss, macular dystrophy, low BMI, and intestinal malabsorption.[1,2] Prevalence among patients with



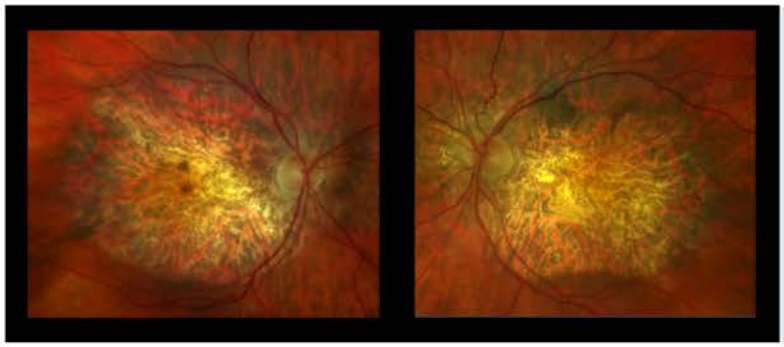


Figure 2 (top): Fundus photos of both eyes revealed expansion of the geographic atrophy to the arcades and involvement of the fovea

Figure 2 (bottom): Detailed photos of the posterior pole of both eyes.

diabetes is 2% or less.[3] Etiology is most commonly an A to G mutation in mitochondrial DNA at position 3243. This mutation impairs ATP production, thus affecting organs with high metabolic demand, and can also cause mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS).[4] The diabetes and hearing loss usually develop in the 2nd to 4th decades, and the hearing loss often develops before the diabetes.[1] 50-86% of patients develop a macular dystrophy.[5]

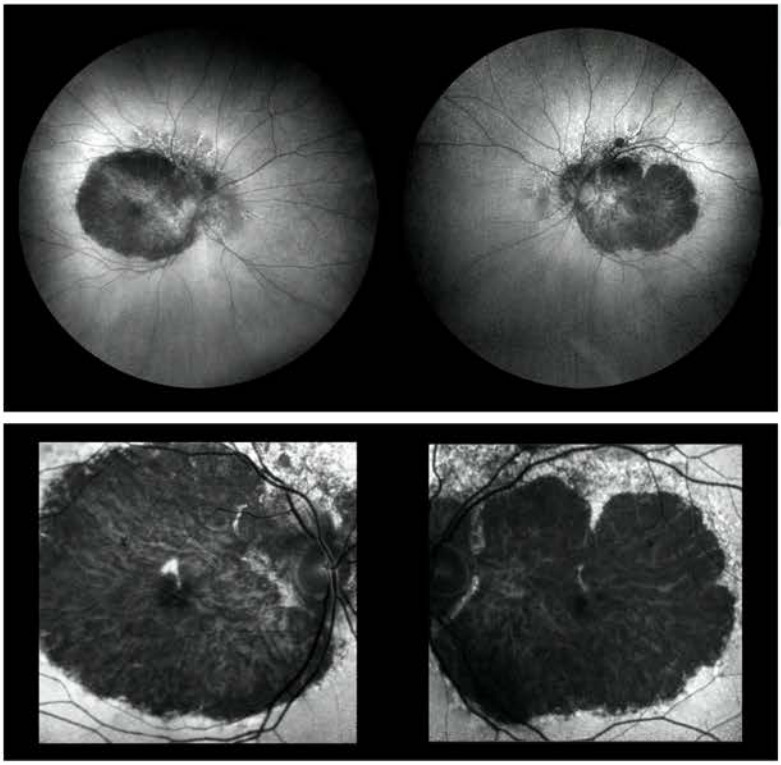


Figure 3: In the areas of macular atrophy, fundus autofluorescence showed significant hypo-autofluoresence.

Patients may present with decreased vision, nyctalopia, scotomas but often have absent or minimal visual symptoms. Vision at presentation is usually about 20/40 or better.[6] Visual symptoms usually happen around the fifth decade of life.[7] Fundus exam may show a pigmentary retinopathy, perifoveal atrophy that may progress to involve the fovea, or pattern dystrophy without significant atrophy.[8] Other ocular findings may also include ptosis, external ophthalmoplegia, and posterior subcapsular cataract.[9]

On ancillary imaging, optical coherence tomography early in the disease may show disorganized outer retinal layers or hyperreflective RPE deposits while later in the disease may reveal atrophy of the outer retina and RPE.[10] Fundus autofluorescence shows hypoautofluorescence in the areas of atrophy with a rim of mottled hyperautofluorescence.[6,11]

Differential diagnoses should include advanced age-related macular degeneration with geographic atrophy, cone rod dystrophy, late-onset Stargardt disease, pattern dystrophy, North Carolina Macular Dystrophy, Central Areolar Choroidal Dystrophy, Plaquenil toxicity, myopic degeneration, and atrophy due to laser scarring.

To confirm the diagnosis, genetic testing should be performed, and genetic counseling should be recommended. Children of affected mothers will inherit the mutation, but symptoms and phenotypes may vary.[7]

In diagnosing and managing MIDD, it is important recognize the macular findings and make a timely diagnosis using systemic features and maternal inheritance to aid in the diagnosis. Cardiomyopathy, renal failure, and gastrointestinal dysmotility have also been associated with the A3243G point mutation so systemic evaluation is warranted. These patients should avoid metformin due to the increased risk of lactic acidosis.[12] MIDD is slowly progressive, and

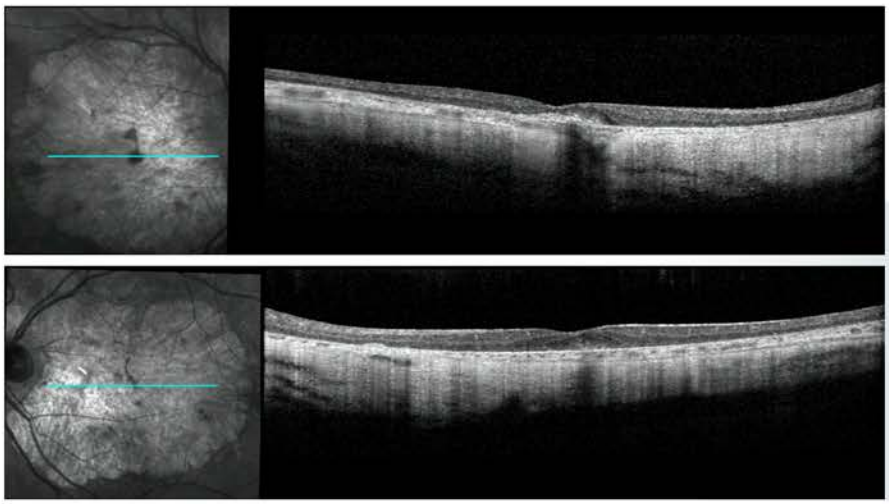


Figure 4: Ocular Coherence Tomography of the macula showed outer retinal and RPE atrophy in both eyes.

the macular dystrophy can range from mild RPE changes to severe atrophy.[13] The patient should be followed yearly.[12]

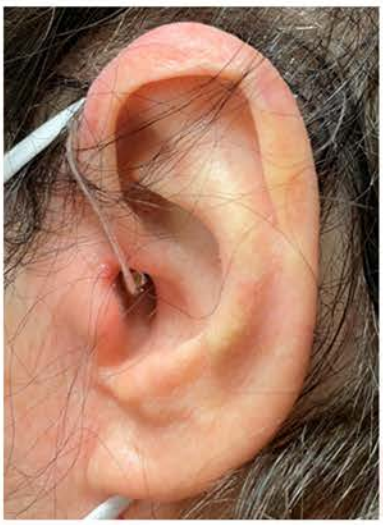


Figure 5 (left): A glucose monitoring patch.

Figure 5 (right): A hearing aid.

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