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Video

Neovascular Glaucoma in MELAS syndrome

Saira Khanna , Bradley T. Smith *

The Retina Institute, 2201 S. Brentwood Blvd, St. Louis, MO, 63144, USA

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ABSTRACT

Purpose: To describe examination and findings in a case of mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) with particular focus on the ocular sequelae from diabetes.
Observations: Neovascular glaucoma is not a common manifestation of MELAS.
Conclusions and Importance: We present a rare case of neovascular glaucoma in a patient with MELAS with a history of diabetes, hearing loss, and macular dystrophy. MELAS should be suspected in patients with this constellation of symptoms.

1. Introduction

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) is a rare mitochondrial disorder with multiple systemic manifestations. This disease follows maternal inheritance and is frequently caused by the m.3243A > G variant in *MT-TL1*.[1,2] This variant prevalence has ranged from 7.6/100,000 to 236/100,000.[3] Common ocular presentations of this specific variant include ocular myopathy, myogenic ptosis, and fovea-sparing retinal dystrophy. Up to 86 % of patients with that mutation demonstrates had retinal dystrophy upon fundus examination.[4]

2. Case report

A 48-year-old female initially referred to a retina practice for possible proliferative diabetic retinopathy and age-related macular degeneration in both eyes. The patient presented to the practice 5 years prior for possible diabetic macular edema but was lost to follow-up. Past medical history per the patient was significant for Type 1 Diabetes (diagnosed ~30 years old), deafness, hypertension, and hyperlipidemia. The patient had no prior past ocular history and past surgical history is non-contributory. Family history was notable for diabetes in multiple family members. At that time, the visual acuity was 20/25 OU with mild diabetic retinopathy without macular edema.

Upon initial examination at re-presentation, the patient had noted some vision loss in both eyes. Her uncorrected visual acuity was 20/200 OD and 20/50 OS with no improvement with pinhole. Her intraocular pressure was 21 mm Hg OD and 11 OS. Her slit lamp examination was notable for florid neovascularization of the iris in both eyes (OD > OS) and mild nuclear sclerotic cataracts (Fig. 1). Dilated fundus examination revealed a clear vitreous, neovascularization of the disc OS, macular atrophy OU, arteriolar attenuation, and dot blot hemorrhages OU (Fig. 2). Optical coherence tomography revealed complete retinal pigment epithelium and outer retinal atrophy (Fig. 3). Fundus autofluorescence demonstrated hypoautofluorescence corresponding to the area of atrophy in both eyes (Fig. 4). Unfortunately, fluorescein angiography was not performed at this visit. However, CT Angiography was performed to rule out ocular ischemic syndrome which revealed mild carotid artery stenosis.

The patient was injected with aflibercept in the right eye with plans to perform panretinal photocoagulation (PRP) in the right eye and inject aflibercept and perform PRP in the left eye at subsequent visits. In addition, the plan included completion of genetic testing given the presence of macular atrophy in both eyes.

Initial genetic testing via buccal swab was done with Invitae Inherited Retinal Disease Panel (San Francisco, CA) which revealed a nondiagnostic test result. Testing showed a missense change in the *FSCN2* gene that was of uncertain significance. Importantly, the genes included on this assay did not include mitochondrial genes. Subsequent genetic testing was performed using the Blueprint Genetics Mitochondrial Genome Test (Seattle, WA) Panel. Testing revealed the pathogenic m.3243A > G variant in *MT-TL1* with 39.7 % heteroplasmy. Upon further questioning, the patient revealed that her mother and one sister have a history of diabetes. In addition, one of her sisters passed away at a young age with all of her children testing positive for MELAS.

She was referred to a glaucoma specialist who confirmed

* Corresponding author. 2201 S. Brentwood Blvd, St. Louis, MO, 63144, USA.
E-mail address: smithbradleythomas@msn.com (B.T. Smith).

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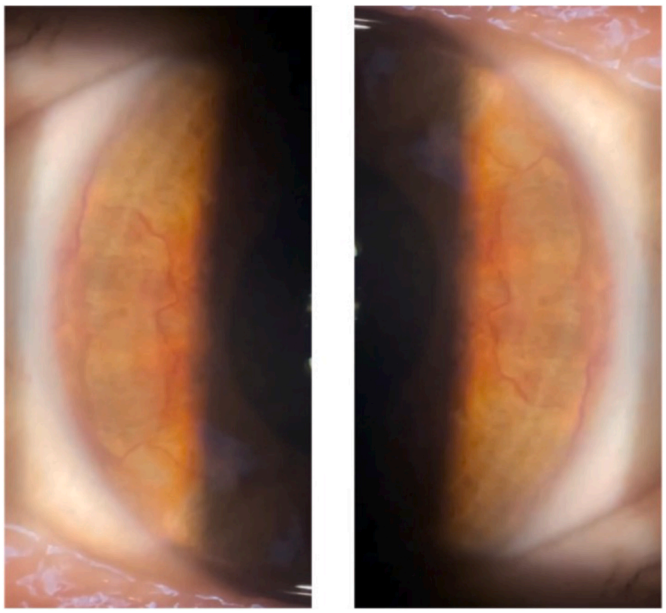

Fig. 1. Neovascularization of the iris in both eyes.

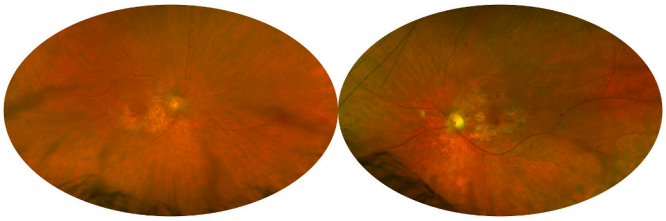

Fig. 2. Fundus photos of both eyes demonstrating a macular atrophy and diabetic retinopathy.

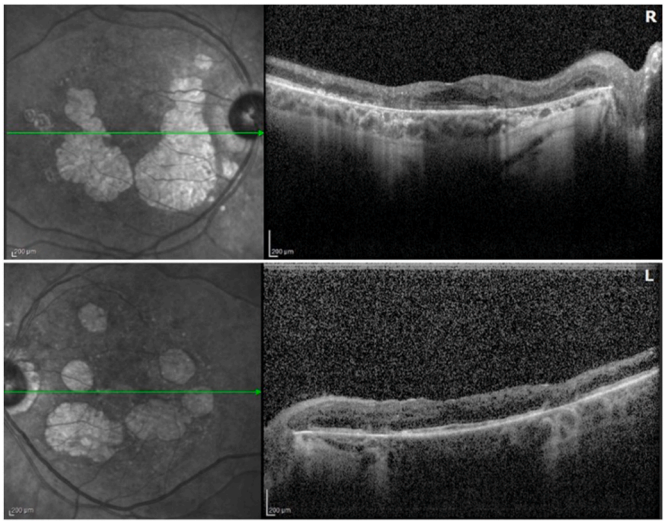

Fig. 3. Optical coherence tomography demonstrates complete RPE and outer retinal atrophy of both eyes sparing the fovea. The near infrared photo demonstrates hyperautofluorescence corresponding to areas of atrophy.

neovascularization on gonioscopy of the right anterior chamber angle. The IOP remain elevated despite maximum medical therapy. A glaucoma tube shunt was placed to help control IOP in the right eye. Despite these efforts, the optic nerve in the right eye developed pallor.

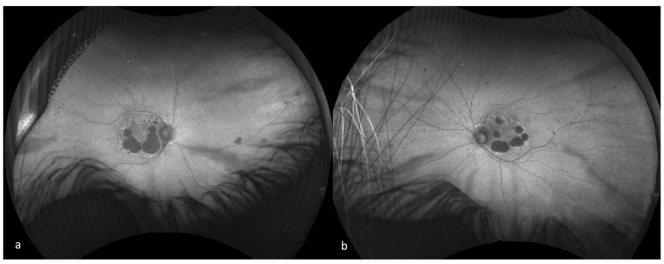

Fig. 4. Fundus autofluorescence demonstrates hypoautofluorescence corresponding to areas of atrophy sparing the fovea in both eyes.

3. Discussion

Our patient with hearing loss and presumed diagnosis of type 1 diabetes re-presented after five years with florid neovascularization of the iris in both eyes and macular atrophy. The diagnosis of MELAS complicated by neovascular glaucoma was made given the results of the genetic testing and family history of MELAS. Though the patient stated she had type 1 diabetes, given the results of the genetic testing, her diagnosis of diabetes is more likely to be related to MELAS. It has previously been reported that the prevalence of m.3243A > G carriers increases to over 5 % in patients with diabetes who have deafness of a family history of deafness.[5,6] However, a previous case-control study reported that prevalence of diabetic retinopathy in these patients was low, suggesting possible protective factors against diabetic retinopathy in patients with maternally inherited diabetes.[7]

Maternally inherited diabetes and deafness (MIDD) is another diagnosis that should be considered, especially considering the most common variant (seen in this patient) is commonly associated with MIDD as well.[8] It is hypothesized that these two entities are on the same disease spectrum, with MELAS often representing a more severe manifestation of this disease. Previous reports have hypothesized a possible evolution of MIDD to MELAS.[8] Another study examined the correlation between heteroplasmy levels and severity of macular dystrophy, finding no correlation.[9] In this patient, given the family history of MELAS, she was given the diagnosis of MELAS instead of MIDD.

Neovascular glaucoma in the setting of MELAS or other mitochondrially-inherited retinal dystrophies is an extremely rare diagnosis. Though prevalence of diabetic retinopathy in these patients is low, there should be a high index of suspicion of inherited retinal disease given the constellation of symptoms. It is important to keep this diagnosis on the differential due to the severity of other systemic manifestations of these diseases. Finally, genetic testing is useful in making the diagnosis, but ensuring the assays include mitochondrial genome testing is critical as not all inherited retinal disease panels have this.

Patient consent

Consent to publish the case report was not obtained. This report does not contain personal information that can lead to the patient's identification.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

CRediT authorship contribution statement

Saira Khanna: Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Bradley T. Smith:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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None.

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