A Family with Macular Scars

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Introduction:

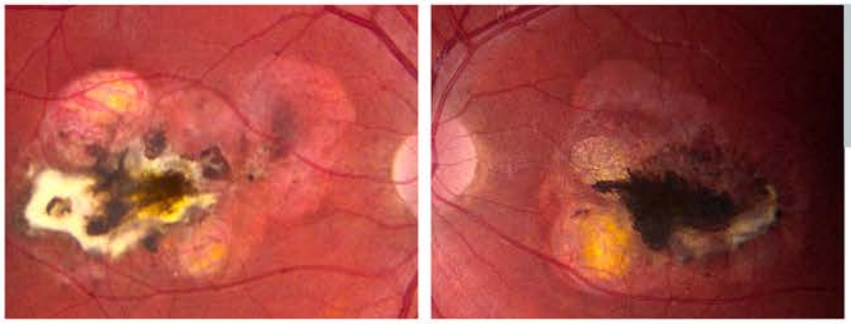

Figure 1: Fundus photos show the bilateral macular scars of the 29-year-old female.

A 29-year-old female presented to our clinic with gradually worsening central vision in both eyes. She had previously been diagnosed with bilateral macular scars from possible toxoplasmosis. She had a history of poor vision since childhood with the left eye worse than the right eye. Past medical history was significant for hypothyroidism and anemia. She has a family history of macular degeneration in her father, paternal aunt, and paternal grandfather.

Her visual acuity was 20/100 in the right eye and count fingers 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 revealed bilateral macular scars with atrophy involving the fovea. OCT of the macula exhibited geographic atrophy, a pigmented epithelial detachment, and subretinal hyperreflective material in both eyes. Fundus autofluorescence was significant for central hypoautofluorescence with a rim of hyperautofluorescence in both eyes. Fluorescein angiogram revealed macular hyperfluorescence consistent with staining and window defect as well as macular hypofluorescence consistent with blockage in both eyes.

Genetic testing revealed a pathogenic variant in PRDM13, which is associated with autosomal dominant

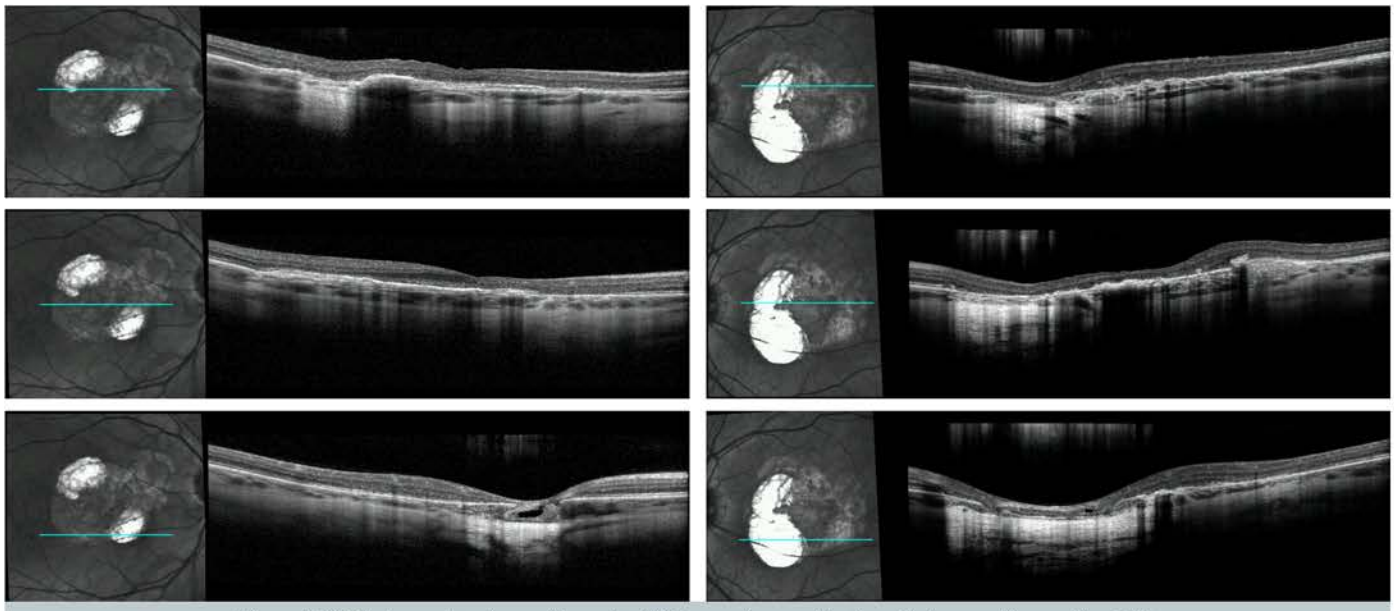

Figure 2: OCT shows atrophy and irregular RPE in each eye with choroidal excavation on the right.

North Carolina Macular Dystrophy.

Her 6-year-old son failed his vision test at school and was seen for examination at our clinic. His visual acuity was 20/200 in the right eye and 20/50 in the left eye. Fundus examination showed bilateral macular scars and atrophy. Genetic testing revealed the same mutation in PRDM13. OCT showed geographic atrophy, pigmented epithelial detachment, and subretinal hyperreflective material in both eyes.

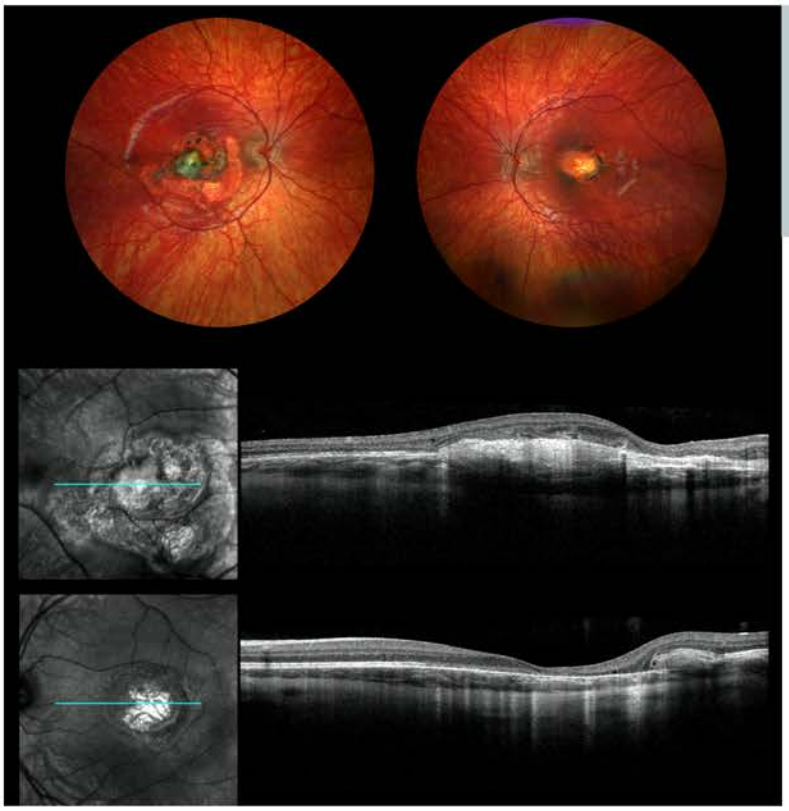

Figure 3: Fundus photos of the 6-year-old son show bilateral macular scarring and atrophy. OCTs show atrophy, PED, and RPE abnormalities.

Her 4-year-old and 3-year-old daughters were then brought in for examination. The 4-year-old's visual acuity was 20/90 in the right eye and 20/150 in the left eye. The 3-year-old was found to have 20/90 visual acuity in both eyes. Both daughters had bilateral macular scars on examination and fundus photos. Their OCTs showed bilateral outer retinal atrophy at the fovea without a choroidal neovascular membrane on OCTA.

Discussion:

North Carolina Macular Dystrophy, first described in 1971, was identified in a North Carolina family, descended from an Irish family who had settled in the U.S. in 1790 [1]. This rare inherited macular dystrophy has since been found around the world in unrelated families. North Carolina Macular dystrophy may cause severe bilateral vision loss, usually in infancy. Inheritance is autosomal dominant with complete penetrance and variable expressivity [2]. Onset is infantile or congenital [3,4]. Visual acuity usually ranges from 20/20 to 20/200. Clinical presentation ranges from central drusen to disciform, atrophic scars, to lesions that resemble a staphyloma or coloboma. The term "macular caldera" has been used to describe the deep chorioretinal excavations. There are 3 grades of severity with grade 1 characterized by small drusen, grade 2 by confluent drusen, and grade 3 by a large excavating atrophic lesions often with fibrosis [5]. Peripheral drusen may be present. The lesions are usually nonprogressive but complications may include geographic atrophy or development of a choroidal neovascular membrane, which could lead to progressive vision loss [4,6]. Patients may be asymptomatic until this occurs and may retain good vision despite severe macular lesions.

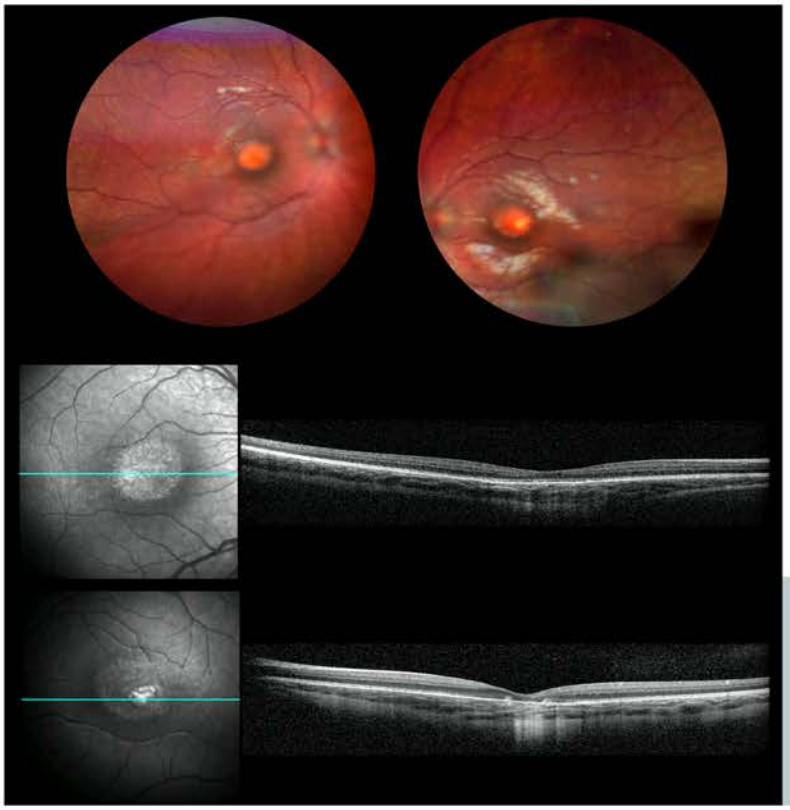

Figure 4: Fundus photos of the 3-year-old daughter show bilateral macular atrophy and scarring. OCTs show the bilateral outer retinal atrophy and irregular RPE.

Many patients are misdiagnosed as having

congenital toxoplasmosis. Differential diagnoses should also include Sorsby macular dystrophy, Doyne Honeycomb or Malattia Leventinese, Central areolar macular dystrophy, Stargardt disease, Best Disease, early onset age related macular degeneration, adult vitelliform macular dystrophy, pattern dystrophy, torpedo maculopathy, progressive bifocal chorioretinal atrophy, and cone dystrophy.

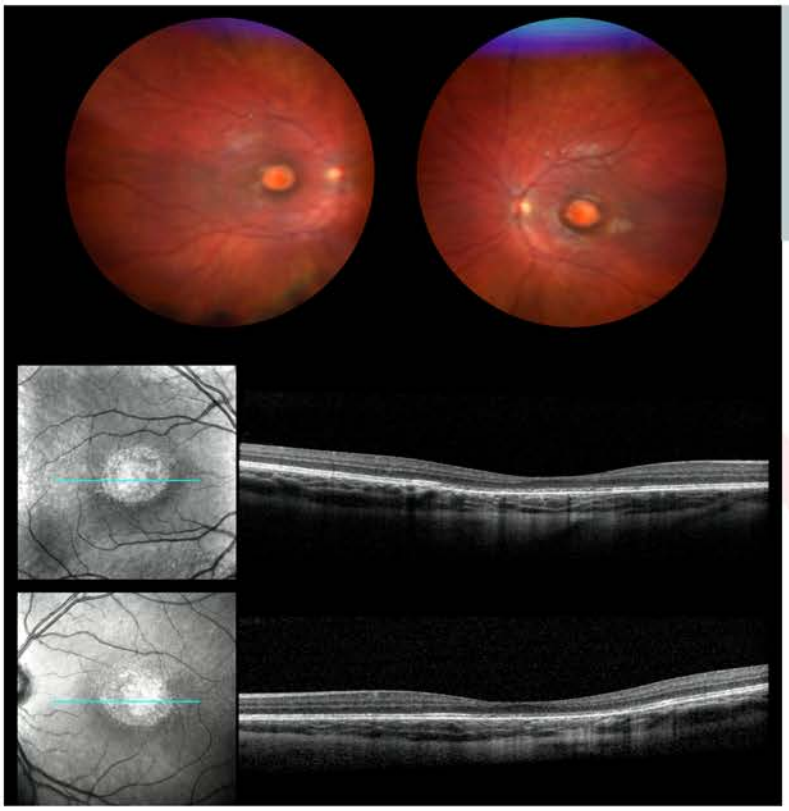

Figure 5: Fundus photos of the 4-year-old daughter show bilateral macular atrophy and scarring. OCTs show the bilateral outer retinal atrophy and irregular RPE.

On ancillary imaging, OCT findings may range from mild RPE abnormalities to large excavations, with atrophy affecting the RPE and choroid more than the neurosensory retina. Fluorescein angiogram may show window defects from atrophy, blockage from subretinal fibrosis, or leakage from a choroidal neovascular membrane. Fundus autofluorescence may show hypoautofluorescence in the areas of atrophy with a rim of hyperautofluorescence. On diagnostic testing and workup, color vision, full field ERG, and EOG are typically normal, but multifocal ERG may show reduced amplitudes [7]. To confirm the diagnosis, genetic testing should be performed and genetic counseling should be recommended. Genetic testing will show a mutation in PRDM13, a gene that encodes a retinal transcription factor, in the MCDR1 locus on chromosome 6q or a mutation within the MCDR3 locus on chromosome 5. The PRDM13 gene is involved in development of the macula during embryogenesis [8].

In managing North Carolina Macular Dystrophy, it is important to monitor for the development of a choroidal neovascular membrane as intravitreal anti-VEGF therapy may be beneficial for these patients [6]. Vision usually remains stable unless a choroidal neovascularization causes complications leading to further vision loss.

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