Progression of Macular Atrophy and Phenotypic Variability in Autosomal Dominant Stargardt-like Macular Dystrophy due to PROM1 mutation

Aaron Ricca, MD
Iowa City
Ian C Han, MD, Jeremy Hoffman, Edwin M Stone, MD, PhD, Elliott H. Sohn, MD

Purpose:

Macular dystrophy due to a PROM1 mutation can result in atrophy similar to Stargardt disease and age-related macular degeneration but occurs at an early age with little known about its phenotypic spectrum and rate of disease progression. Our purpose was to describe the phenotypic variability and rates of progression of atrophy using multimodal imaging in patients with PROM1-associated macular dystrophy.

Methods:

A retrospective, longitudinal case series was compiled from a single, tertiary referral center. Fifteen affected patients from 6 separate pedigrees with a p.R373C mutation in the PROM1 gene seen at the University of Iowa were included in the study. Clinical records were reviewed, and multimodal imaging data were analyzed. Manual delineation of atrophic areas on confocal scanning laser ophthalmoscope (SLO) images and optical coherence tomography volume scans was performed by two independent graders and rates of atrophy progression were estimated for those with longitudinal imaging ≥12 months duration. The main outcome measures were measuring areas of retinal pigment epithelium and ellipsoid zone loss over time.

Results:

The average age of participants was 39 years (range 8-82), and most were female (12/15, 80%). Mean Snellen best-corrected visual acuity (BCVA) was 20/40 (range 20/15 – 20/320) at presentation and 20/57 (range 20/15 - 20/1400) at last follow up (average duration 5.1 years). Three distinct macular phenotypes were observed: 1) central geographic atrophy (GA) (13%, 2/15 patients), 2) multifocal GA (20%, 3/15), and 3) bull’s eye maculopathy (BEM) (67%, 10/15). Six patients (12 eyes) had at least two OCTs separated by >12 months. Overall rate of atrophy progression was 0.36 mm²/year (SD=0.32). Average rate of atrophy progression was 1.08 mm²/year (SD=0.29); 0.53 mm²/year (SD=0.31); 0.23 mm²/year (SD=0.14), for central GA, multifocal GA, and BEM, respectively.

Conclusions:

Patients with PROM1-associated autosomal dominant Stargardt-like macular dystrophy demonstrate several distinct phenotypes, with BEM being the most common. The rate of atrophy progression is similar to reported rates for ABCA4-related Stargardt disease and less than age-related macular degeneration. These findings are important for future gene and stem-cell based retinal therapies and contribute to our understanding of mechanisms of geographic atrophy in various disease states.