

Clinical features of *PRPS1*-associated retinopathy in female patients

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INTRODUCTION

Background: *PRPS1* (phosphoribosyl pyrophosphate synthetase 1) catalyzes the formation of phosphoribosyl pyrophosphate, a key metabolite in DNA synthesis. Variants in the X-linked *PRPS1* gene are associated with severe syndromic disease in males, but can give milder disease, including a variable retinal degeneration, in female carriers. Improved phenotypic characterization may help prevent diagnostic delay and guide appropriate systemic management.

Objective: To characterize the clinical phenotype of retinopathy in a cohort of patients with molecularly-proven *PRPS1*-associated disease.

METHODS

Study design: Retrospective case series

Setting: Large inherited retinal disease service (Moorfields Eye Hospital)

Inclusion: Patients with genetically confirmed *PRPS1*-associated retinopathy identified via electronic records search

Data collected:

- Genotype and variant classification
- Visual acuities (converted to logMAR equivalents)
- Retinal imaging including ultra-widefield autofluorescence
- Electroretinogram (ERG) features

Analysis: Descriptive statistics reported as mean (SD) and median with range. Interocular visual acuity asymmetry quantified for all patients.

RESULTS

9

Female patients identified

100%

Missense variants

5 / 5

De novo variants (of tested)

Genotype

All 9 patients had **missense variants**. The p.Arg214Trp variant was the most recurrent, occurring in **3 patients**. Among those with parental genetic data available (n=5), all variants were confirmed to be ***de novo***.

Visual Acuity

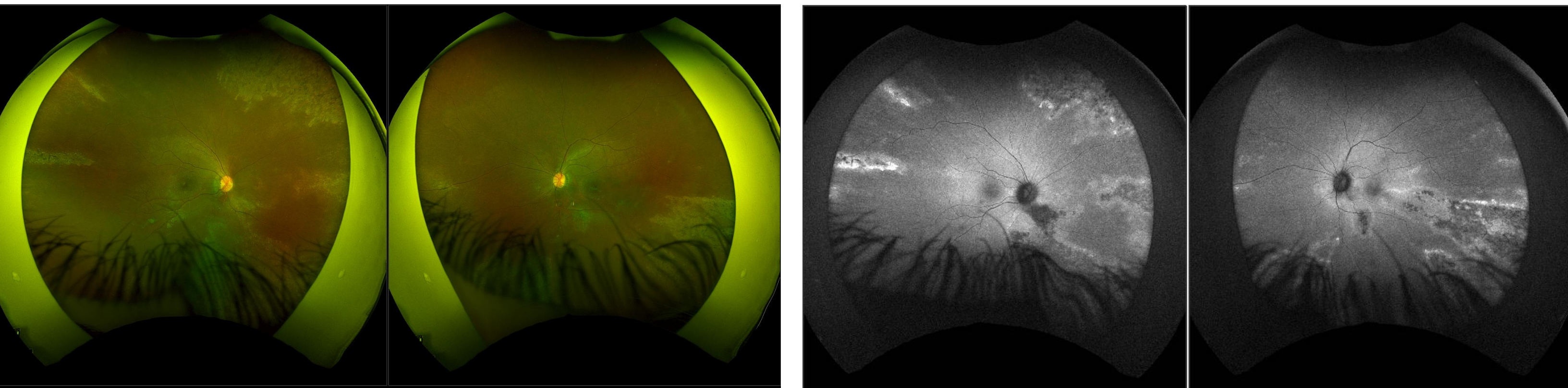
Parameter	Right Eye (n= 9)	Left Eye (n= 9)	Interocular Difference
Mean VA at first visit (logMAR)	0.48 (0.55)	0.44 (0.63)	0.40 (0.50)
Median VA at first visit (logMAR)	0.3 (0 to 1.78)	0.18 (0 to 1.9)	0.2 (0 to 1.42)

Parameter	Right Eye (n= 6)	Left Eye (n= 6)	Patients with follow up at least one year later
Mean VA at first visit (logMAR)	0.51 (0.74)	0.51 (0.58)	
Mean VA at second visit (logMAR)	0.65 (0.68)	0.55 (0.67)	

Mean (SD) age at first reliable acuity: **31.8 (24.6) years** (median 23; range 4.5–69.6 years). For patients with follow up, mean (SD) age was **38.1 (27.5)** and **45.4 (28.4)** years at first and last visit respectively.

Retinal Imaging & ERG

Ultra-widefield autofluorescence (righthand panels below): patchy retinal involvement with asymmetry between eyes. **ERGs (n=5):** Generalised retinal involvement; some responses showed interocular asymmetry.



KEY FINDINGS

Asymmetric Disease

Patchy, asymmetric retinal involvement is a frequent and distinctive feature — unlike most inherited retinal diseases which show bilateral symmetry.

Misdiagnosis Risk

The asymmetric, patchy pattern can mimic inflammatory retinopathy, leading to diagnostic delay if genetic testing is not pursued.

De Novo Variants

High incidence of de novo variants observed (confirmed in 5/5 patients with parental data) — important for genetic counselling and family screening.

Wide Age Range

Disease manifests across a broad age range (4.5–69.6 years), highlighting variable expressivity and the importance of monitoring across the lifespan.

CONCLUSIONS

- *PRPS1*-associated retinopathy in females shows **patchy, often asymmetric** retinal involvement, distinguishing it from most inherited retinal diseases.

- High incidence of ***de novo variants*** is notable for genetic counselling.

- Given syndromic associations, **genetic confirmation** should guide systemic referral and management.

- Consider *PRPS1* in females with asymmetric retinopathy to avoid misdiagnosis as inflammatory disease.

Take-home message: *PRPS1*-associated retinopathy in females is characterized by asymmetric, patchy retinal involvement and a high incidence of de novo variants. Genetic diagnosis guides both retinal management and systemic screening.