From Retinitis Pigmentosa to Joubert Syndrome: The Impact of Genomic Testing in Retinal Dystrophy Diagnosis

Dr Ahlam-Nourelhouda Boussaid Othmani, Clinical Teaching Fellow University of Leicester, Mr Sebastian Mathew, Ophthalmology Consultant[1], Mr Paul Tesha, Ophthalmology Consultant[1], 1- United Lincolnshire Hospitals NHS Trust

Introduction

Inherited retinal dystrophies (IRDs) are a heterogeneous group of progressive disorders with variable onset and systemic associations[1]. Retinitis pigmentosa (RP) is the most common phenotype[2], but syndromic ciliopathies such as Joubert syndrome (JS) may present with similar retinal findings[3,4]. JS is characterised by cerebellar and brainstem malformations, developmental delay, hypotonia, and oculomotor abnormalities[3,4]. Variants in AHI1 are strongly associated with JS type 3 and retinal degeneration[5–7].

History

A patient presented with progressive visual field constriction and long-standing visual impairment, initially suspected as RP. Congenital oculomotor apraxia raised suspicion of a syndromic ciliopathy[3,4]

Examination

Reduced visual acuity, concentric peripheral field loss, bone-spicule pigmentation, vascular attenuation, optic disc pallor, and relative macular preservation.

Investigations

OCT demonstrated preserved macular structure, while electrodiagnostic testing confirmed advanced rod–cone dysfunction in keeping with ISCEV standards[8].
Genomic testing (gene panel and whole-genome sequencing) identified biallelic pathogenic AHI1 variants, confirming JS type 3 [5–7].
Further investigations included brain MRI for the “molar tooth sign” and renal assessment for nephronophthisis risk[3,6]. Multidisciplinary management and family cascade testing were initiated.

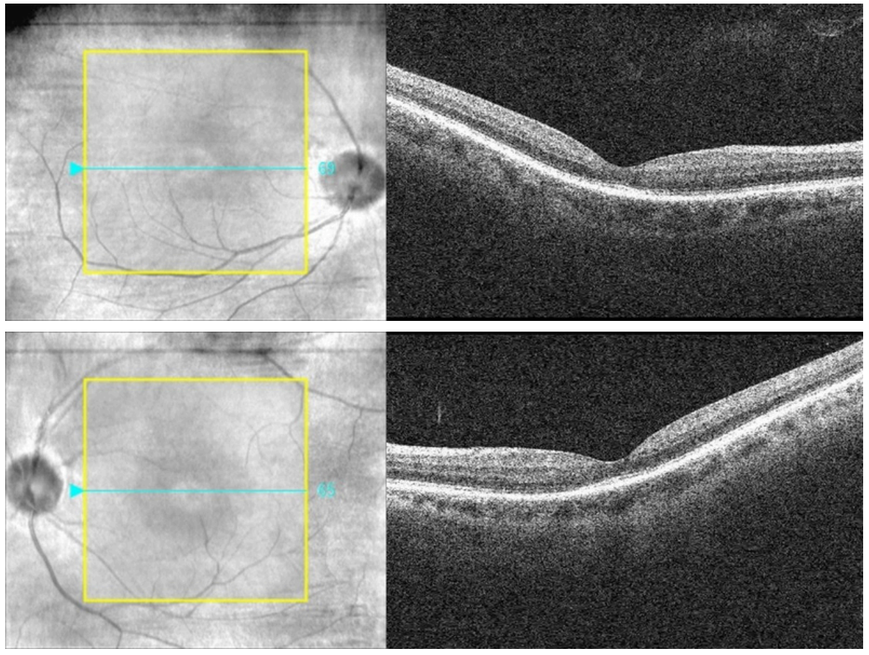

Fig. 1 RE and LE OCT images

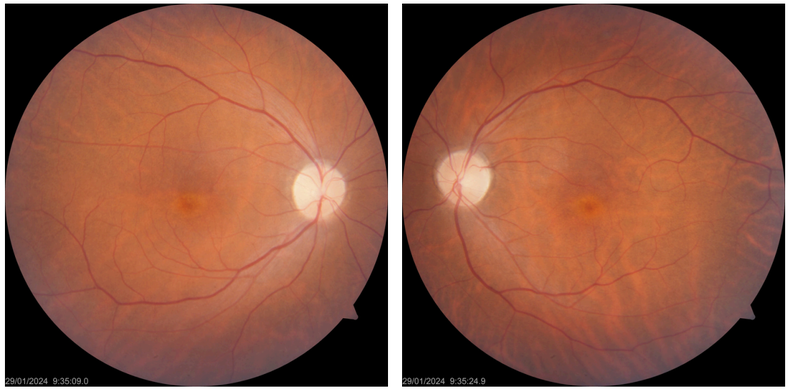

Fig. 2. RE and LE fundus images

Discussion

This case highlights the overlap between RP and syndromic ciliopathies. Although retinal findings were typical of RP[2], oculomotor apraxia and macular preservation suggested an alternative diagnosis[3,4].

AHI1-associated disease demonstrates marked phenotypic variability, limiting clinical differentiation alone[6,7].

Genetic diagnosis is critical for systemic surveillance, prognostication, and family counselling[3,6], and facilitates access to emerging therapies and registries[9].

Conclusion

Genomic testing is essential in atypical retinal dystrophy. In this case, it enabled reclassification from RP to AHI1-associated JS, significantly altering multi-system clinical management and follow-up.

References

1. Tsang SH et al. Springer; 2018.
2. Hamel CP. Orphanet J Rare Dis. 2006.
3. Parisi MA. Am J Med Genet C. 2009.
4. Louie CM et al. Hum Mol Genet. 2005.
5. Ferland RJ et al. Nat Genet. 2004.
6. Bachmann-Gagescu R et al. J Med Genet. 2015.
7. Huber C et al. Hum Mutat. 2017.
8. Robson AG et al. Doc Ophthalmol. 2018.
9. Cideciyan AV et al. Br J Ophthalmol. 2019.
10. Westerfield L et al. Ophthalmology. 2017.