A Homozygous INPP5E Mutation Associated Joubert Syndrome with Retinitis Pigmentosa- A Case Report

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Introduction

Joubert syndrome (JS) is a ciliopathy that caused by over 34 heterogenous genes that affect the function of primary cilia. It manifest as a neurodevelopmental disorder with related retinal or renal dystrophies and other organs, depending on the genes involved. It is inherited in an autosomal recessive pattern. INPP5E mutations have been recognized as a rare cause of ciliopathy and contribute to JS with associated diseases. Retinitis pigmentosa (RP) has been rarely reported in patients with JS. We would like to present a case with a novel homozygous mutation of INPP5E in a patient with JS combined with RP.

Methods

Case Report: A 11-year-old girl presented with progressive vision loss, lack of coordination, and muscular weakness. Vision acuity was 20/60 bilaterally. Dilated fundus exam revealed temporal disc pallor, retinal pigmentary epithelial mottling and atrophy, and diffuse white specks throughout the retina bilaterally (Fig. 1) . Given her systemic presentation, further diagnostic work up including genetic testing, neurologic imaging, pediatric and neurologic consults were pursued.

Results

Genetic testing revealed a homozygous mutation at INPP5E c.1073C>T (p.Pro358Leu). Further diagnostic testing results including fundus autofluorescence (Fig 2), optical coherence tomography (Fig.3), Humphry visual field (Fig. 4) and electroretinography (Fig. 5) were consistent with RP. Magnetic resonance imaging of the brain demonstrated the molar tooth sign (Fig. 6) that is known to be associated with JS.

Results

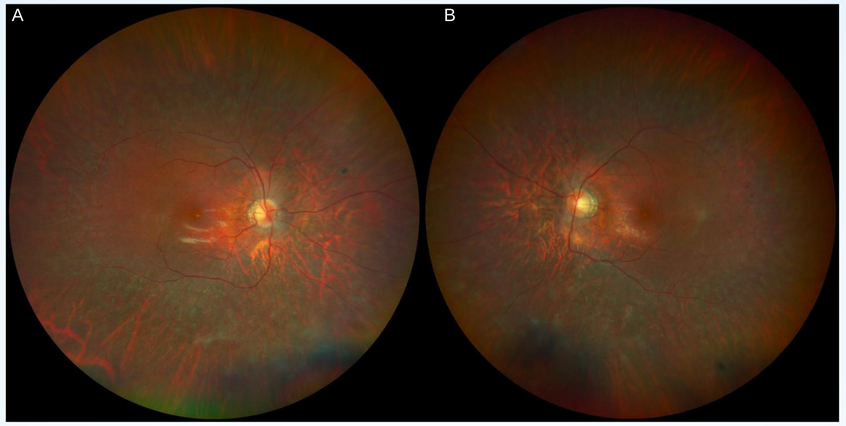

Figure 1. Color Fundus photography of the right eye (A) and left eye (B), both demonstrated peripheral RPE mottling.

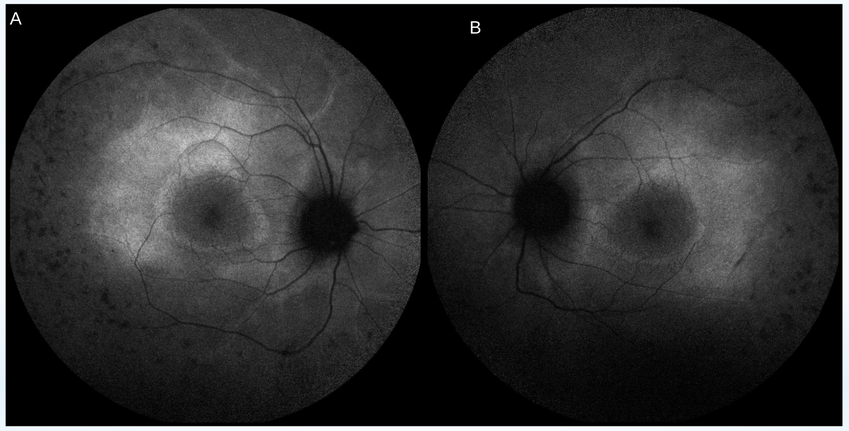

Figure 2. Fundus autofluorescence of the right eye (A) and left eye (B) showed bone-spicule hypoautofluorescence.

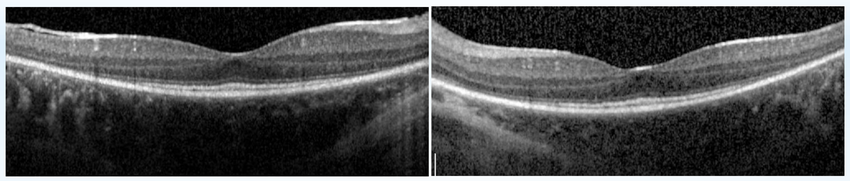

Figure 3. Optical coherence tomography of the right eye (A) and left eye (B), revealed outer retinal atrophy with perifoveal ellipsoid zone loss.

Results

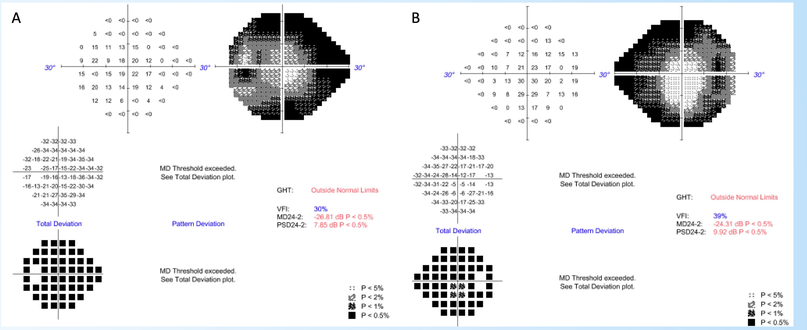

Figure 4. Humphry visual field demonstrated peripheral visual field restrictions in the right eye (A) and the left eye (B).

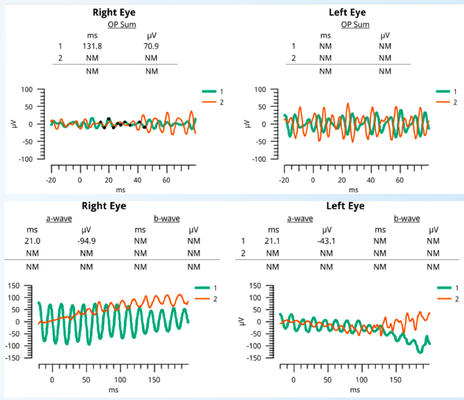

Figure 5. Electroretinography. Top panel: Flash 3.0 at 0.1Hz; lower panel: Flash 10.0 at 0.05Hz, consistent with decreased cone and rod responses.

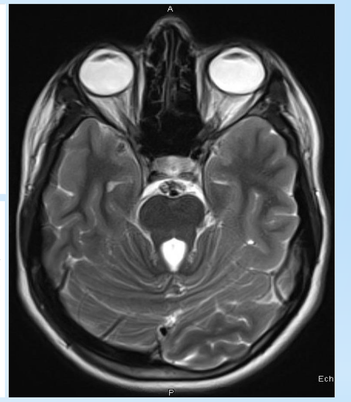

Figure 6. Magnetic resonance imaging of the brain demonstrated the molar tooth sign.

Conclusion

Although retinal dystrophies have been known to be associated with JS, a case with JS combined RP has not been reported in the literature. INPP5E is one of genes that contribute to JS. A novel homozygous mutation in INPP5E (c.1073C>T (p.Pro358Leu) can be associated with JS combined with RP.

References

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