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CORRESPONDENCE

Novel Variations in *MYO5B* Presenting as Isolated Intrahepatic Cholestasis: Long-Term Outcome after Partial Internal Biliary Diversion

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To the Editor: Mutations in myosin-5B (*MYO5B*) have recently been reported to present as isolated intrahepatic cholestasis without intestinal involvement; closely mimicking progressive familial intrahepatic cholestasis (PFIC) types 1 or 2 with similar age of onset, clinical features, presence of low gamma-glutamyl transferase (GGT) cholestasis, elevated serum bile acids (BA), and histological findings in children [1–3]. We report 2 siblings with novel compound heterozygous variations in *MYO5B* presenting as isolated cholestasis with excellent long-term response after partial internal biliary diversion (PIBD).

A 15-y-old girl presented in 2015 with intractable pruritus since 9 mo of age refractory to medical therapy and growth failure. She had low-GGT cholestasis, elevated BA (362 µmol/L) and marked cholestasis with portal fibrosis on liver biopsy. Treating unit's provisional diagnosis was PFIC1/2. Genetic confirmation could not be done at that time. Child underwent PIBD (cholecysto-jejuno-colonic anastomosis) with significant relief in pruritus and marked decrease in BA (362 --> 62µmol/L). Six years after PIBD, she remains pruritus free, with good catch-up growth (weight *z* score: −3.6 --> −0.48; height *z* score: −3.7 --> −1.4) and without fibrosis progression. Recently, her younger brother presented with infantile cholestasis at 7 mo of age and his genetic sequencing showed compound heterozygous variations in *MYO5B* gene. Following this, patient 1 also underwent genetic sequencing which revealed same compound heterozygous mutations in the *MYO5B* gene (chr18:47462664T>C; p.Tyr654Cys) and (chr18:47480695G>C; p.His552Gln). Both the observed variations are novel mutations, lie in motor domain (myosin head) of MYO5B protein and are disease causing as per various in silico prediction tools.

MYO5B in combination with RAB11 is involved in normal trafficking of ABC transporter proteins to the canalicular membrane [3, 4]. *MYO5B* mutations impair MYO5B/RAB11A interaction leading to impaired BSEP transport to canalicular membrane causing decreased canalicular bile secretion [3, 4]. Biliary diversion surgery dramatically improves pruritus, reduces serum bile acids, and improves growth in those refractory to medical therapy.

Declarations

Conflict of Interest None

References

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