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CASE STUDY

Brain phenolip to MPV1 variant s.106C> T

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Abstract

MPV17-related mitochondrial DNA (mtDNA) maintenance defect presents in the vast majority of affected individuals as an early-onset encephalohepatopathic (hepatocerebral) disease that is typically associated with mtDNA depletion, particularly in the liver. A later-onset neuromyopathic disease characterized by myopathy and neuropathy, and associated with multiple mtDNA deletions in muscle, has also rarely been described. MPV17-related mtDNA maintenance defect, encephalohepatopathic form is characterized by: ● Hepatic manifestations (liver dysfunction that typically progresses to liver failure, cholestasis, hepatomegaly, and steatosis); ● Neurologic involvement (developmental delay, hypotonia, microcephaly, and motor and sensory peripheral neuropathy); ● Gastrointestinal manifestations (gastrointestinal dysmotility, feeding difficulties, and failure to thrive); and ● Metabolic derangements (lactic acidosis and hypoglycemia).

Keywords: MPV17, mtDNA, liver, Hepatic, hypoglycemia

1 | INTRODUCTION

In a recent article Meldau et al. reported about 2 black South African pediatric patients with neuro-hepatopathy due to the variant c.106C>T in the *MPV17* gene[1]. We have the following comments and concerns.

The authors claim that hypotonia was “central”. However, patient-2 had reduced tendon reflexes and both patients had proximal muscle weakness[1] , suggesting “peripheral” hypotonia. “Central” hypotonia implies that there was cerebral involvement in the two patients. Thus, it would be interesting to know if cerebral imaging was carried out in any of the 24 homozygous carriers of the *MPV17* variant. Clinical cerebral abnormalities have been previously reported in carriers of *MPV17* variants and include microcephaly [2] , dystonia[2] , nystagmus[2] , or failure-to-thrive [2] . Abnormalities on imaging include leucoencephalopathy[3] , subdural hemorrhaghes[2] , or peri-ventricular leucomalacia[2] , T1W hyperintensities, representing delayed myelination, in the anterior limb of the internal capsule

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and the corpus callosum splenium [4] , and T2W hyperintensities in the reticular formation of the lower dorsal brain stem and the reticulospinal tracts of the cervico- medullary junction [4] .

Since both patients had marked liver involvement and since hepatopathy in *MPV17* carriers may go along with hyper-ammonemia, it essential to report serum ammonia levels. Assuming that there was hyper- ammonemia, it is conceivable that cerebral involvement was rather secondary (hepatic encephalopathy) than primary (leucoencephalpathy).

MPV17 variants may also cause mtDNA depletion [5] . Were the 24 patients investigated for mtDNA depletion and did the authors find mtDNA depletion or multiple mtDNA deletions in any of these patients? Myopathy has been particulary reported in *MPV17*-assocaited mtDNA depletion.

In conclusion, this case study could be more meaningful if cerebral imaging studies would have been provided, if the effect of the *MPV17* variant on the amount of mtDNA would have been investigated, and if hepatic encephalopathy would have been excluded.

2 | MATERIALS AND METHODS

Treatment of manifestations: Ideally management is by a multidisciplinary team including specialists in hepatology, neurology, nutrition, clinical genetics, and child development. Nutritional support should be provided by a dietitian experienced in managing children with liver diseases; prevention of hypoglycemia requires frequent feeds and uncooked cornstarch (1-2 g/kg/dose). Although liver transplantation remains the only treatment option for liver failure, it is controversial because of the multisystem involvement in this disorder. Prevention of secondary complications: Prevent nutritional deficiencies (e.g., of fat-soluble vitamins) by ensuring adequate intake. Surveillance: Monitor: ● Liver function to assess progression of liver disease; ● Serum alpha fetoprotein (AFP) concentration and hepatic ultrasound examination for evidence of hepatocellular carcinoma; ● Development, neurologic status, and nutritional status. Agents/circumstances to avoid: Prolonged fasting.

3 | RESULTS:

Genetic counseling is the process of providing individuals and families with information on the nature, inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members. This section is not meant to address all personal, cultural, or ethical issues that individuals may face or to substitute for consultation with a genetics professional. —ED. (1–7)

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