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Cerebral phenotype of the MPV17 variant c.106C>T

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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* gene¹. 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 weakness¹, 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 microcephaly², dystonia², nystagmus², or failure-to-thrive². Abnormalities on imaging include leucoencephalopathy³, subdural hemorrhages², or peri-ventricular leucomalacia², T1W hyperintensities, representing delayed myelination, in the anterior limb of the internal capsule and the corpus callosum splenium⁴, and T2W hyperintensities in the reticular formation of the lower dorsal brain stem and the reticulospinal tracts of the cervico-medullary junction⁴.

Since both patients had marked liver involvement and since hepatopathy in *MPV17* carriers may go along with hyper-ammonemia, it is 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 (leucoencephalopathy).

MPV17 variants may also cause mtDNA depletion⁵. 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 particularly reported in *MPV17*-associated 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.

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