**MPV17: FATAL HEPATOCEREBRAL PRESENTATION**

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**Introduction**

The hepatocerebral forms of mtDNA depletion syndromes typically manifest soon after birth and cause premature death in childhood [1]. Presentation is usually with early liver failure, followed by development delay and muscle weakness during the first year of life, as well as lactic acidosis and hypoglycemia [2]. These conditions are associated with mutations in at least six genes [3] though further heterogeneity is expected. An ample array of MPV17 mutations (Figure 1) has been described in about 30 patients from different ethnicities.

![Figure 1 - Described mutations in the MPV17 gene. ○ Missense mutation; ● Nonsense mutation; ▲ Small deletion; ▲ Gross deletion; ◊ Small insertion; ◼ Splicing mutation; ■ c.186+2T>C.](image)

**Results**

The patient presented severe mtDNA depletion (residual mtDNA levels were 2% in liver and 23% in muscle) and molecular studies detected a homozygous mutation c.186+2T>C in MPV17, a variant already reported in a heterozygous state with poor prognosis in a singleton [4]. This mutation is located at the invariant splice donor site and is predicted to abolish the splicing donor site of exon 3 (http://www.cbs.dtu.dk/services/NetGene2 and http://www.fruitfly.org). The c.186+2T>C was also detected in the proband’s elder sister who had presented at birth with neonatal hypoglycemia, failure to thrive and hepatic insufficiency, later developed seizures and hypotonia, and died at 10 months. The mutation was heterozygous in the parents who were from nearby villages in south Brazil.

**Discussion/Conclusion**

To date a total of 32 patients have been reported with MPV17 mutations. Our study expands the ethnic background of MPV17-mutated patients and will be important for an accurate genetic counseling and a prenatal diagnosis to the affected family. MtDNA depletion should be looked for in neonates with progressive cholestasis and neurological deterioration.

**References**


