Cholestasis with ductal paucity related to Alper's syndrome

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**Introduction**

Mitochondrial DNA (mDNA) Depletion Syndrome (MDS): heterogeneous group of mitochondrial diseases caused by mutations in nuclear genes.

**Clinically classification:** 4 forms
- Hepato-cerebral
- Myopathic
- Encephalomyopathic
- Neurogastrointestinal
Case report (1)

- A 4 months old girl
- Consanguineous marriage
- Family history of cholestasis diagnosed as:
  - biliary atresia (in her brother died at the age of 8 months)
  - cystic fibrosis (in 2 cousins).
- Perinatal period without incident
- Presented at the age of 2 months with an elevated GGT cholestasis.

Clinical examination:
- No facial dysmorphism
- Jaundice
- Hepatomegaly (9 cm)
- Neurological features +++
  - Developmental delay
  - Generalized hypotonia and muscle weakness
  - Areflexia
  - Choreiform movements
Case report (2)

Biology at presentation:
- Elevated GGT cholestasis
- Liver failure (low prothrombine time, hypoalbuminemia, hypocholesterolemia)
- Increased Creatine phosphokinase
- Recurrent hypoglycemia
- Hyperlactatemia

Differential diagnosis:
Biliary atresia, Alagille syndrome, alpha1 antitrypsin deficiency, cystic fibrosis and type 1 tyrosinemia were ruled out by:
- Liver ultrasound and MRI: no signs of a biliary atresia.
- Echocardiography: normal
- Radiography of the entire spine: no butterfly vertebra
- Ophthalmological examination: no posterior embryotoxon
- Protein electrophoresis: normal
- Sweat test: normal
- Succinyl acetone in blood and urine: negative
- Liver biopsy: cholestasis with ductal paucity.
Diagnosis and evolution

- **Diagnosis:**

  Whole exome sequencing: c.375+5G>A mutation in MPV17 gene (which encodes for mitochondrial inner membrane protein)

  ➔ *Infantile* onset of *hepatocerebral MDS*

- **Evolution:**

  severe liver failure + ascitis, oedema, recurrent hypoglycemia + gastrointestinal haemorrhage

  ➔ *death at the age of 7 months*

**Conclusion**

In this case, an accurate neurologic assessment in the context of cholestasis was the clue of the diagnosis of MDS.

MDS are:

- Severe hereditary disorders with poor prognosis
- Risk of diagnostic wandering and recurrence in the same family
- Genetic counselling is warranted.