HUPPKE-BRENDEL SYNDROME: IS IT TREATABLE LIKE MENKES DISEASE?

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Background:
Huppke-Brendel syndrome (HBS) is a very rare disease inherited as an autosomal recessive. It is characterized by bilateral congenital cataracts, sensorineural hearing loss, severe developmental delay and very low serum copper and ceruloplasmin levels. We report two Tunisian siblings from consanguineous parents with the syndrome.

Case Presentation:
Case 1: A 1 year old baby boy (Fig.1), with cutis marmorata, who developed by the age of 1 month recurrent pneumopathies, sepsis-like syndrome and neurological regression, by the age of 7 months seizures. PEA –TC : no responses, Brain MRI with spectroscopy: cerebral atrophy, megacistern and suspected Leigh syndrome. We explored this Leigh-like syndrome by genetic analysis. We found a homozygous pathogenic variant in the SLC33A1 gene: c.1267-1G>A. Copper in plasma: 12.3 µmol/l (NV: 3.00-11.0) and ceruloplasmin in plasma: <0.20 g/l (NV: 0.15-0.30). He died by the age of 16 months.

Case 2: A 5 months old boy (Fig.2), who was followed carefully since birth to look for Huppke-Brendel syndrome like his older brother. His parents refused prenatal diagnosis. The infant developed a mild hypotony and he had horizontal nystagmus and no visual contact related to bilateral cataracts. Copper in plasma: 1.0 µmol/l (NV: 3.00-11.0) and ceruloplasmin in plasma: <0.03 g/l (NV:0.15-0.30), ASAT: 47 UI/l , ALAT: 22 UI/l GGT: 14 UI/l , magnesimea: 20.70 mg/l.

He had cutis marmorata and neurodevelopmental regression with recurrent aspirated pneumonia. He had treatment with enteral copper without biological and clinical improvement. What about treatment by Copper-Histidine (ctx-101) injections?

Conclusions:
This rare syndrome seems to be relatively frequent in Tunisia, with a founder effect. The same mutation c.1267-1G>A was described by Huppke and Brendel in their first description of the syndrome in two Tunisian siblings. Should we propose a treatment with Copper-Histidine injections to this disease, without known curative treatment and with dramatic outcome?