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HYPERINSULINEMIC HYPOGLYCEMIA DUE TO BIALLELIC MUTATIONS IN THE *DNAJC3* GENE

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INTRODUCTION

- **DNAJC3,**

  Endoplasmic reticulum (ER) co-chaperone involved in folding/processing of secretory and transmembrane proteins

  The defect impairs adaptive ER responses and leads to apoptosis, impairment of organ function with multisystemic involvement

- **Biallelic mutations in the *DNAJC3* Biallelic mutations in the *DNAJC3*, described in a limited number of cases cause multiple endocrine dysfunction and neurodegeneration of nervous system.**
- Herein, we report a new patient with severe growth retardation, microcephaly, early-onset hypothyroidism, hyperinsulinemic hypoglycemia and neuromotor retardation due to a novel homozygous mutation

CASE REPORT

- ✓ A 6.5 month-old boy was presented with growth retardation and hypothyroidism
- ✓ The parents were first degree cousins
- ✓ He was born at 27^{+3} gestational weeks because of preeclampsia
- ✓ Birth weight was 610 g (-1.8 SDS)
- ✓ He had been hospitalized for 5 months in a neonatal care unit
- ✓ At presentation, his height, weight and head circumference was 51 cm **(-4.4 SDS)**, 3120 g **(-4.3 SDS)** and 33.5 cm **(-6 SDS),** respectively
- ✓ Biochemistry, echocardiography and abdominal ultrasonography were normal
- ✓ Anterior pituitary hormones were normal
- ✓ Neurodevelopmental milestones were significantly delayed for age

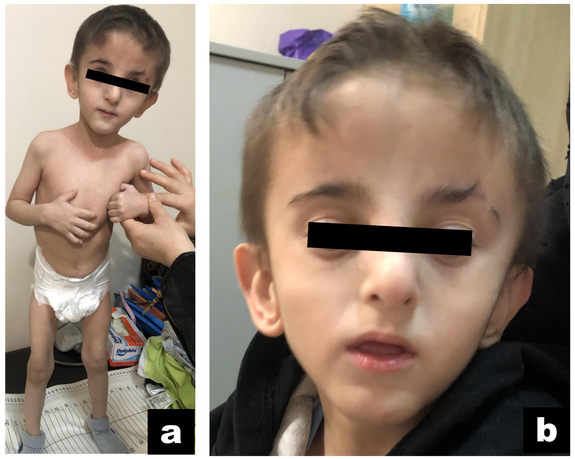

Figure 1. Body stature **(a)** and facial view **(b)** of the patient.

He had a triangular face, antevert prominent ears, prognathism, clinodactyly, pectus carinatum and upturned eyebrows

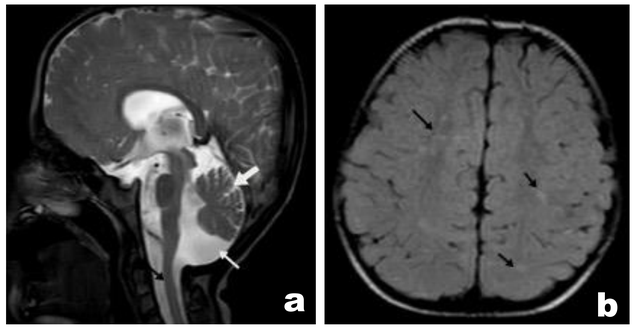

Figure 2. Brain magnetic resonance imaging of the patient at 4.5 years.

MRI showed cerebellar and brainstem atrophy **(a)** and in axial FLAIR examination, there were hyperintensities in frontoparietal,subcortical areas **(b)**.

- ✓ Whole exome sequencing revealed a novel homozygous frameshift variant (c.1314dupG; p.F439Vfs*3) in *DNAJC3*
- ✓ An OGTT was performed after the molecular diagnosis revealed previously undiagnosed and clinically asymptomatic hyperinsulinemic hypoglycemia by a glucose level of 34 mg/dl and insulin 2.5 mIU/L at 180 minutes of the test
- ✓ Blood glucose remained stable on frequent feeding and corn starch at night time without any other intervention

CONCLUSIONS

- ✓ Hyperinsulinemic hypoglycemia is associated with increased morbidity and poor neurodevelopmental outcomes in patients with *DNAJC3* gene mutations
- ✓ Impaired glucose metabolism should be considered and investigated in patients with molecular defects affecting endoplasmic reticulum