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 involvment
- 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

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

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

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

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).

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