Insulinoma as initial presentation of Multiple Endocrine Neoplasia type 1

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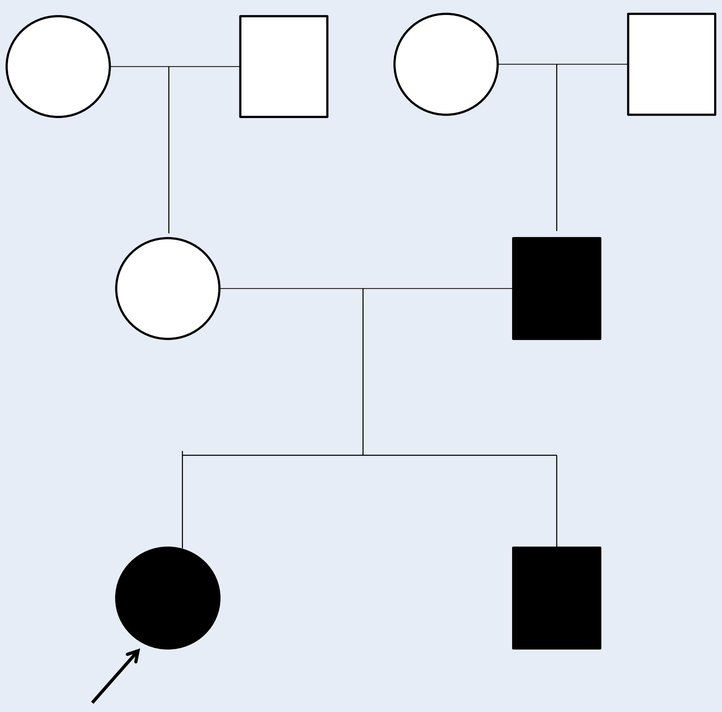
Background:
Multiple Endocrine Neoplasia type 1 (MEN1) is a disorder with autosomal dominant inheritance pattern. It is characterized by the occurence of parathyroid, pituitary and pancreatic tumors. MEN1 presented by insulinoma as a first presentation in children is very rare. On the other hand insulinoma affects 10% patients with MEN1 and occurs usually in young patients.

Case:
Eleven years and eight months old girl was admitted, after a syncopal episode due to neuroglycopenia. For the previous 2 months she had experienced headaches, subsiding after a meal. Her fasting tolerance was limited to 2 hours. Her father was diagnosed with MEN1 manifested with insulinoma at the age of 20 and subsequently with hyperparathyroidism.
Laboratory results (Table 1) revealed hyperinsulinemic hypoglycemia. Abdominal MRI scan showed pancreatic lesion 11x8,5x3,5 mm localized in uncinate process. 68Ga-DOTATATE PET/CT scan confirmed pancreatic nodule with high SSTR expression (Graph 1). No other MEN1 –like lesions were found. Serum calcium level and PTH level were normal.
She was referred for pancreatic surgery. Before surgery she was treated with diazoxide (4mg/kg/d) with a good response. After pancreatic tumour enucleation, hypoglycemia resolved. The diagnosis of insulinoma was confirmed by histopathological examination.
In 7 months of follow up the patient remained euglycemic and without symptoms of other pathologies connected with MEN1 syndrome. Genetic molecular tests indentified mutation p.Glu478STP in 10 exon of MEN1 gene, the same mutation was found in her father and younger brother. (Figure 1)

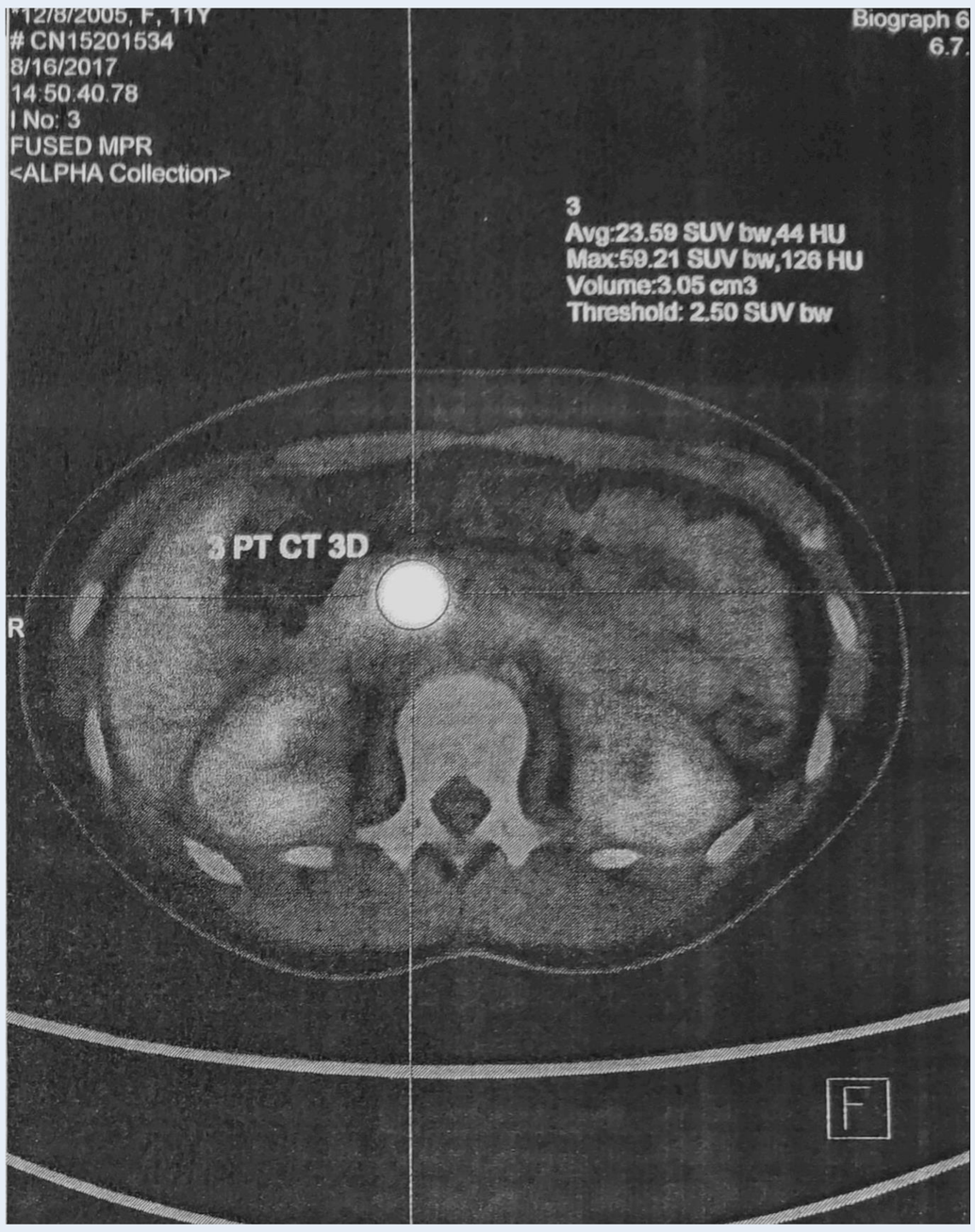
Table 1. Laboratory tests results on admission

Parameter	Value (normal range)
Glucose	**43 mg/dL**
Insulin	**10.3 µIU/mL (6-27)**
ACTH	87.7 pg/mL (7.2-63.3)
Cortisol profile	06:00 11 µg/dL (1.2-14.7) 08:00 13.4 µg/dL 20:00 1.2 µg/dL 24:00 0.8 µg/dL
IGF-1	228 ng/ml (120-559)
PRL	3.9 ng/mL (3.2-15.0)
Ca	10.5 mg/dL (8.8-10.6)
P	4.4 mg/dL (3.3-5.4)
PTH	41.5 pg/mL (12-95)
25(OH)D	21.7 ng/mL (20-50)
TSH	2.37 µIU/mL (0.6-4.84)
fT4	1.15 ng/dL (0.97-1.67)
Gastrin	40 ng/L (13-115)
C-peptide	1.41 ng/mL (1.1-4.4)

Figure 1. Familial pedigree



Graph 1. 68Ga-DOTATATE PET/CT scan.



Conclusions:
Insulinoma is a rare initial manifestation of MEN1, especially in children. In presented case positive family history of MEN1 helped to establish diagnosis and begin proper treatment.
Genetic examination in offsprings should be the mandatory element of medical care of adult patients with potentially life threatening inherited diseases.

References
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