Multiple Endocrine Neoplasia Type 1: an underdiagnosed disorder

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INTRODUCTION

Multiple Endocrine Neoplasia type 1 is an underdiagnosed autosomal dominant disorder, with inter and intrafamilial variability without a genotype-phenotype correlation.

Case Report

- A young female (born in 1986) presented with galactorrhea and secondary amenorrhea in 2002, and a diagnosis of prolactinoma was made.
- Her brother (born in 1982) presenting gynecomastia and erectile dysfunction at age 21, was also diagnosed with prolactinoma. *Pancreatic tumors* were identified at age 30.
- The female patient was first referred to our appointment in 2013 due to pancreatic tumors, treated with cabergoline.

Laboratory: prolactin 44ng/mL [1,9-25], GH 25,8ng/mL [0,06-5], IGF1 1.208ng/mL [117-329], OGTT: GH basal/nadir 18,5/12,1ng/mL; calcium 11,3mg/dL [8,4-10,2], PTH 95pg/mL [10-70]. VIP, gastrin, glucagon, insulin, chromogranin-A: normal (Table 1).

Thoraco-abdominopelvic-CT: tumors on pancreatic tail with 40×27×36mm and 7mm; heterogeneous liver mass 48×49×51mm (Figure 1).

Octreoscan: two focus of hyperfixation in pancreas; "cold" liver lesion (Figure 2).

Endoscopic ultrasonography with biopsy of liver and pancreatic tumors: pancreatic neuroendocrine tumor with liver infiltration.

MRI revealed diffuse pituitary hyperplasia (Figure 3).

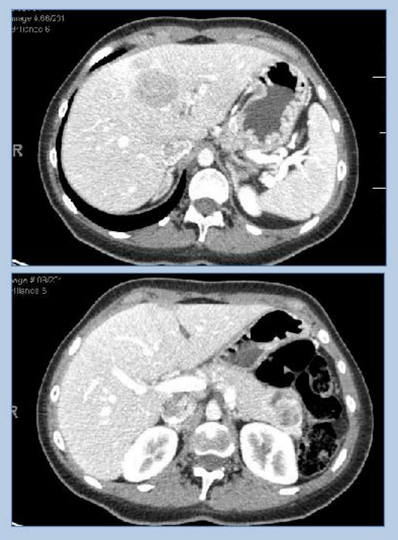

Figure 1 - **Thoraco-abdominopelvic-CT**

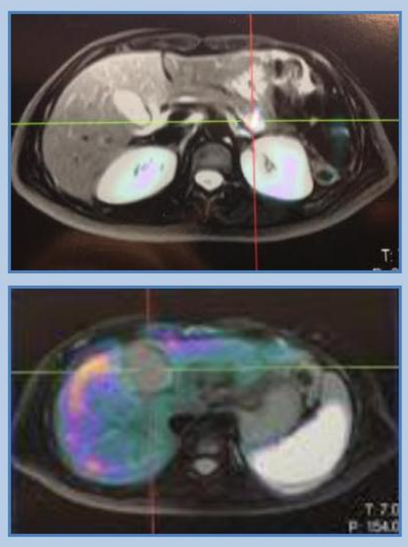

Figure 2 - **Octreoscan**

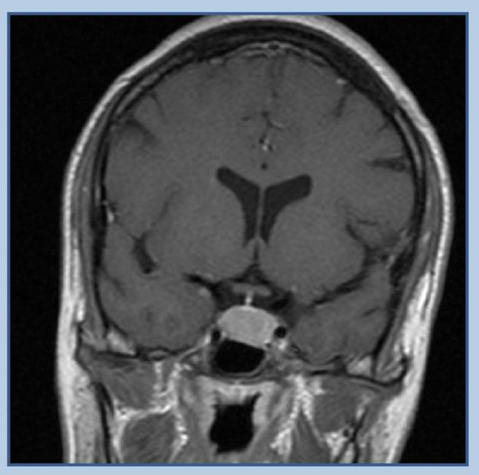

Figure 3 - **Pituitary Magnetic Ressonance:** diffuse pituitary hyperplasia

Prolactin [1.9-25 ng/mL]	**44**
GH [0,06-5 ng/mL]	**25.8**
IGF-1 [117-329 ng/mL]	**1208**
OGTT – GH basal/nadir	**18.5/12.1**
Calcium [8.4-10.2 mg/dL]	**11.3**

Table 1

Treatment and Follow-up

Subtotal parathyroidectomy, distal pancreatectomy and liver metastasectomy were performed in the same surgical time (12/2013).

Histopathology: pancreatic neuroendocrine tumors, Ki-67<2%; secondary infiltration of liver.

After surgery (01/2014): IGF1 424ng/mL, OGTT basal/nadir 0,6/0,25ng/mL, calcium 10,3mg/dL (Table 2).

Octreoscan and abdominal-CT were negative 4 months later.

MRI revealed regression of pituitary hyperplasia (09/2014) - Figure 4.

GHRH immunohistochemical study on pancreatic samples was negative.

IGF-1	**424**
OGTT – GH basal/nadir	**0.6/0.25**
Calcium	**10.3**

Table 2

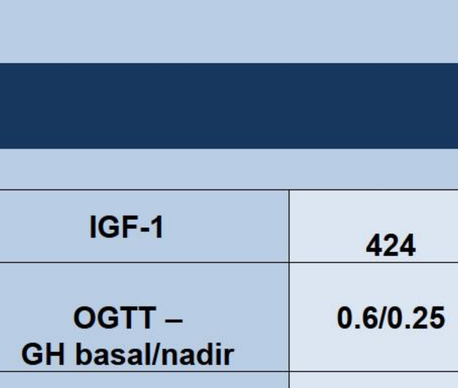

Figure 4 - **Pituitary MRI:** regression of pituitary hyperplasia

Family study was performed:

- Her brother underwent total pancreatectomy due to multiple non-functioning tumors on pancreatic head and tail (11/2014)
- Their 60-year-old father: evidence of bronchopulmonary carcinoid tumor, non-functioning pancreatic tumors, primary hyperparathyroidism.

DNA sequence analysis:

Family DNA sequence analysis of the MEN1 gene identified a germinal mutation on exon 2: deletion of 4bp involving codon 88, not yet described.

CONCLUSION

The occurrence of prolactinoma at a young age in two siblings should have prompted a thorough investigation, possibly implying a different prognosis in this family. The diagnosis of acromegaly in the female patient, it´s etiology and pituitary imaging need to be further elucidated.