Hypoglycaemia in adolescence as the presenting sign of familial MEN1 syndrome

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INTRODUCTION

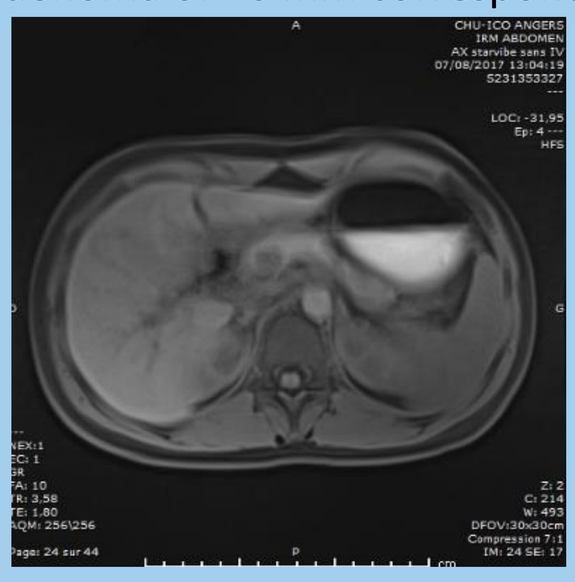
Multiple Endocrine Neoplasia Type 1 (MEN1) is an inherited autosomal dominant syndrome due to mutations in the MEN1 tumor suppressor gene. The prevalence is about 2/100 000 and penetrance increases with age. Pediatric diagnosis is therefore rare out of familial screening following the identification of an adult index case.

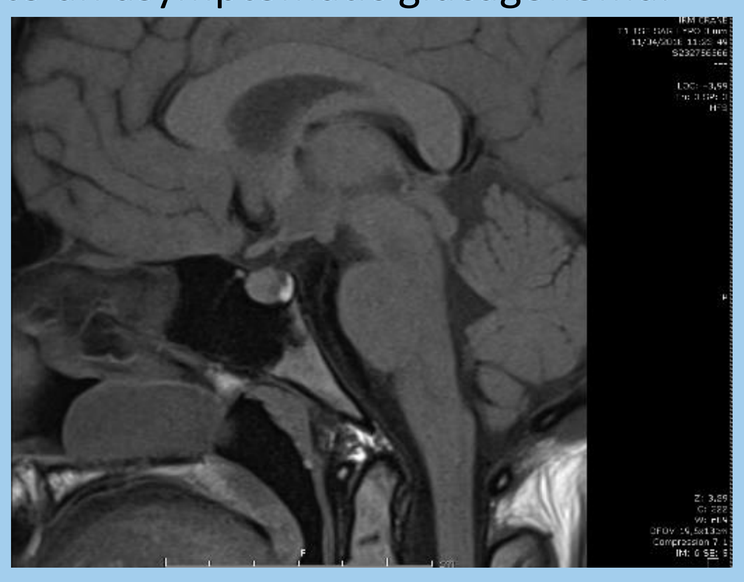
Involvement	Prevalence in 50-years adults		Exploration
Parathyroid	90 %	Hyperplasia, adenoma	Serum total and ionized calcium, phosphate, intact PTH 1-84, urinary Ca, scintigraphy
Pancreas	75 – 90 %	Insulinoma, Gastrinoma, Glucagonoma, Vipoma, Somatostatinoma, pancreatic polypeptide tumor, GRF tumor	Glycaemia, insulinemia, C peptide, gastrin, glucagonemia, somatostatin, VIP, PP (± meal stimulatory test) Ultrasound, MRI, CT
Pituitary	50 – 60 %	Prolactinoma GH-secreting adenoma Non functioning pituitary adenoma ACTH or TSH secreting adenoma	Prolactinaemia, GH, IGF1 T3-T4-TSH, 8 am cortisol, UFC, FSH, LH, estradiol/testosterone Pituitary RMI
Adrenocortical	36 %	Multiple adenoma, hyperplasia	Abdominal CT, dexamethasone suppression test
Thyroid	25 %	Goiter, adenoma	
Carcinoid or anaplastic tumor	5 %	Bronchial, thymic, gastric, small intestin, appendix	
Lipoma	6 %		
Ovarian or testicular tumor	Rare		

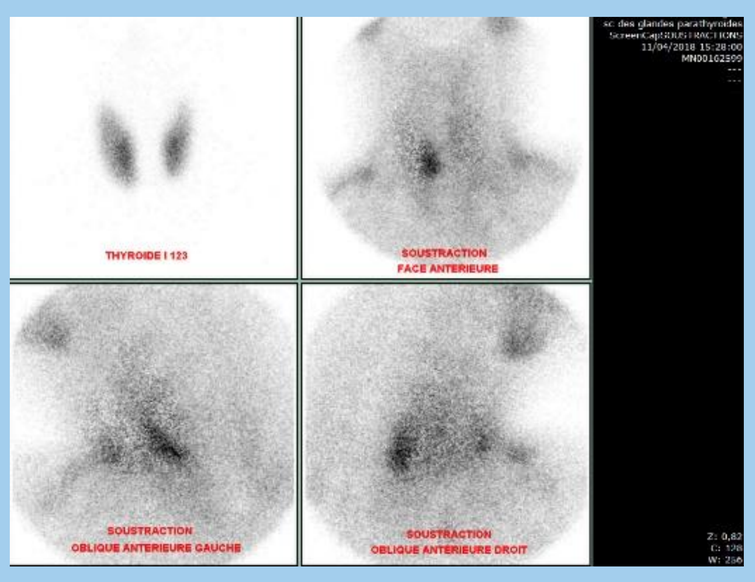
The clinical expression is extremely variable, and mainly associates hyperparathyroidism (often revealing the syndrome), pancreatic adenomas, (mainly gastrinoma or insulinoma), and anterior pituitary adenomas (GH or PRL secreting adenomas, or silent adenomas). Clinically latent forms are common. We report the diagnosis of a familial MEN1 syndrome diagnosed because of hypoglycaemia in a 13-year-old girl.

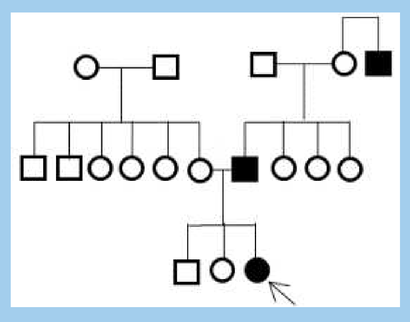
CLINICAL CASE

The index case was a 13-year-old girl who had a episode of coma associated with tonic-clonic seizure. Glycemia was 21 mg/100 mL, and insulinemia 18.2µU/mL (N<1). Hyperinsulinism was diagnosed. Pancreatic MRI showed a cephalic nodular lesion of 15 mm. A systematic search for other MEN1 involvement showed asymptomatic primary hyperparathyroidism (Ca 2.84 mmol/L, PTH = 44.6 pg/mL). The patient had no associated pituitary, adrenal, thyroid, bronchial or thymic lesions. Surgical management allowed the removal of the insulinoma and found a second adenoma of 10 mm corresponding to an asymptomatic glucagonoma.









The familial survey showed a history of renal lithiasis responsible for several renal colic episodes in the father in the previous 10 years. Given the specific history of his daughter, primary hyperparathyroidism was suspected, and confirmed: Ca 2.75 mmol/L, PTH 108 pg/mL. The familial hyperparathyroïdism, and the pancreatic adenomas in the girl prompted the search for MEN1 gene mutation. A mutation of MEN1 (c.136del) was identified in the girl and her father. The extended family survey is underway.

CONCLUSION

The diagnosis of familial MEN1 syndrome can sometimes be made from a pediatric case. In children, cases of pancreatic adenomas, pituitary adenomas, or primary hyperparathyroidism should lead to a familial survey and to the molecular analysis of the MEN1 gene.