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.

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.

<table>
<thead>
<tr>
<th>Involvement</th>
<th>Prevalence in 50-years adults</th>
<th>Exploration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parathyroid</td>
<td>90 %</td>
<td>Hyperplasia, adenoma</td>
</tr>
<tr>
<td>Pancreas</td>
<td>75 – 90 %</td>
<td>Insulinoma, Gastrinoma, Glucagonoma, Vipoma, Somatostatinoma, pancreatic polypeptide tumor, SSR tumor</td>
</tr>
<tr>
<td>Pituitary</td>
<td>50 – 60 %</td>
<td>Prolactinoma, GH-secreting adenoma, Non-functioning pituitary adenoma, ACTH or TSH secreting adenoma</td>
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<tr>
<td>Adrenocortical</td>
<td>36 %</td>
<td>Multiple adenoma, Hyperplasia</td>
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<td>Thyroid</td>
<td>25 %</td>
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<td>Carcinoid or anaplastic tumor</td>
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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 18.2 μU/mL (N<1). Hyperinsulinism was diagnosed. Pancreatic MRI showed a cephalic nodular lesion of 15 mm. 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 2.84 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 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.

CONCLUSION

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 hyperparathyroidism, 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.

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