A new mutation associated with pseudohypoparathyroidism? 2 case reports.

INTRODUCTION

Pseudohypoparathyroidism is a metabolic disorder characterized by peripheral resistance to the action of parathyroid hormone (PTH) which can associate other hormonal disturbances. Their molecular basis is a defect in adenylate cyclase Gs system encoded by the GNAS gene receptor.

CASE REPORTS

We describe the clinical case of 2 childbearing age women with thyroid dysfunction, hypocalcemia, hyperphosphatemia, and high levels of PTH.

Both patients are asymptomatic and remain safe levels of calcium under treatment with calcium and vitamin D.

Clinical and analytical variables

<table>
<thead>
<tr>
<th>Type</th>
<th>Heredity</th>
<th>Albright hereditary osteodystrophy</th>
<th>Ca/P</th>
<th>PTH</th>
<th>Hormone resistance</th>
<th>Gs mutation</th>
<th>cAMP (urine)</th>
<th>Phosphorus (urine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Autosomal dominant</td>
<td>Yes</td>
<td>1/1</td>
<td>↑</td>
<td>Thryotropin, glucagon, gonadotropine</td>
<td>GNAS1 mutation</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ib</td>
<td>Sporadic/ autosomal dominant</td>
<td>No</td>
<td>1/1</td>
<td>↑</td>
<td>Occasional PTH renal and/or thyrotopin resistance</td>
<td>No GNAS1 mutation</td>
<td>Mutations 2013.3 exon 1</td>
<td>No</td>
</tr>
<tr>
<td>Ic</td>
<td>No Acquired vs. intercurrent abnormalities?</td>
<td>Yes</td>
<td>1/1</td>
<td>↑</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Autosomal dominant</td>
<td>Yes</td>
<td>N/N</td>
<td>N</td>
<td>No</td>
<td>GNAS1 mutation</td>
<td>Yes (N)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Note: Reference values: calcium 8.5-10.10 mg/dl, phosphorus 2.70-4.5 mg/dl, PTH 7-74 pg/ml and vitamin D > 30 ng/ml.

TREATMENT

- Treatment with vitamin D or analogues is necessary to normalize serum calcium. Fixed preparations of calcium and vitamin D are not recommended. Treatment must get low-normal range of serum calcium.
- Use thiazides if there is significant hypercalcuria. In this cases, an ophthalmologic examination and renal ultrasound should be done to exclude cataracts and nephrolithiasis/nephrocalcinosis, respectively.
- Teriparatide or synthetic PTH 1-34 could be an option in patients with evidence or risk of nephrocalcinosis, because it normalizes serum calcium without increasing calcuria.

CONCLUSION

We describe two suspected cases of pseudohypoparathyroidism type 1a or 1c with negative genetic test for mutations in the GNAS gene but with a common polymorphism in heterozygosis.
No GNAS gene mutations are detected in 30-40% of pseudohypoparathyroidism so many of their molecular mechanisms are not known.
We think that polymorphism c.393C>T(p.Ile131Ile) could be a new mutation related to pseudohypoparathyroidism.