Infantile Hypercalcemia –
Still A Diagnostic And Therapeutic Enigma

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INTRODUCTION:
- A female born from uneventful pregnancy
- Normal delivery, on term
- Weight 3600 gr, Length 52 cm.

2nd month:
- blood in stools (Cow’s milk allergy?)
- irritable, decreased appetite,
- slow weight gain (300 g/month)

3rd month:
- erythrocyturia + leucocyturia (UTI?)

ABDOMINAL ULTRASOUND:
Bilateral Nephrocalcinosis

INITIAL INVESTIGATIONS:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Value</th>
<th>Abnormal Value</th>
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</thead>
<tbody>
<tr>
<td>Ca/Creatinine ratio</td>
<td>1.37 (N=0.26)</td>
<td>Hypercalciuria</td>
</tr>
<tr>
<td>total Calcium</td>
<td>3.62 mmol/l (2.08-2.65)</td>
<td>Hypercalcaemia</td>
</tr>
<tr>
<td>ionized Ca++</td>
<td>1.59 mmol/l (1.13-1.32)</td>
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</tr>
<tr>
<td>PTH intact</td>
<td>&lt; 3.00 pg/ml (11-67)</td>
<td>PTH-dependent</td>
</tr>
<tr>
<td>PTH-independent</td>
<td></td>
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</tbody>
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HIGH PTH
- Primary Hyperparathyroidism
  - Parathyroid adenomas/carcinomas
  - Familial Isolated Hyperparathyroidism
  - Multiple Endocrine Neoplasia
  - HYP-JT
- Neonatal Severe Hyperparathyroidism (homozygous inactivating CaSR mutations)

LOW PTH
- Williams-Beuren Syndrome
- Jansen’s Metaphyseal Chondro dysplasia
- Malignancy: PTHrP
- Hypervitaminosis D
- Vit D intoxication
- Subcutaneous Fat Necrosis
- Idiopathic Hypercalcemia of Infancy

TERTIARY HYPERPARATHYROIDISM
- Chronic Renal Failure
- Maternal Hypocalcaemia

IDIOPATHIC INFANTILE HYPERCALCEMIA

There was no history of familial hypercalcemia, subcutaneous fat necrosis or vitamin D intoxication.
No syndromic or dysmorphic features were found.
In the context of the new etiological causes a defect in 25-hydroxylase activity was suspected. A molecular genetic testing for mutation in the CYP24A1 gene was done in a referent center but showed negative results. At presentation, lower phosphate serum levels of 1.0 mmol/l were noticed to be present too. During the follow-up the phosphate levels slowly increased up to the lower limits of 1.6 mmol/l with TmP/GFR of 1.32, calcium levels are still on the upper limits and there is no significant progression of the nephrocalcinosis and no impairment of the renal function.

Initial treatment: 10 days on i.v. infusions + urbason + furantril
- total Calcium: 3.62 → 2.68 mmol/l (2.08-2.65)
- ionized Ca++: 1.59 → 1.37 mmol/l (1.13-1.32)

PAMIDRONATE: 2 days with doses of 1 mg/kg i.v.:
- total Calcium: 3.62 → 2.68 mmol/l (2.08-2.65)
- ionized Ca++: 1.59 → 1.37 → 1.51 → 1.29 mmol/l (1.13-1.32)

CONCLUSIONS:
The case is an example of the still uncovered mysteries of calcium and vitamin D metabolism. In many cases infantile hypercalcemia is still a diagnostic and therapeutic enigma.

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