Idiopathic infantile hypercalcemia: presenting in childhood, diagnosed in adulthood – case report

Catarina Silvestre[1], Raquel Paixão[1], José Maria Aragüés[1], Sílvia Guerra[1], Mário Mascarenhas[1]
1-Endocrinology, Diabetes and Metabolism Department, Hospital de Santa Maria, Lisbon, Portugal

Introduction

- Hypercalcemia is known to be caused by a variety of pathologies or factors;
- Vitamin D plays a central role in calcium homeostasis, where a tight control of its metabolism is necessary;
- Inadequate 24-hydroxylase-enzime (CYP24A1) activity leads to failure of 25-hydroxyvitamin and 1,25-dihydroxy-vitamin D3 inactivation, resulting in hypercalcemia.

Case report

An asymptomatic, 22-year-old woman was admitted in an Endocrinology appointment for evaluation of **persisting hypercalcemia: 10,5-13,6 mg/dL** (reference range: 8,6-10,2 mg/dL).

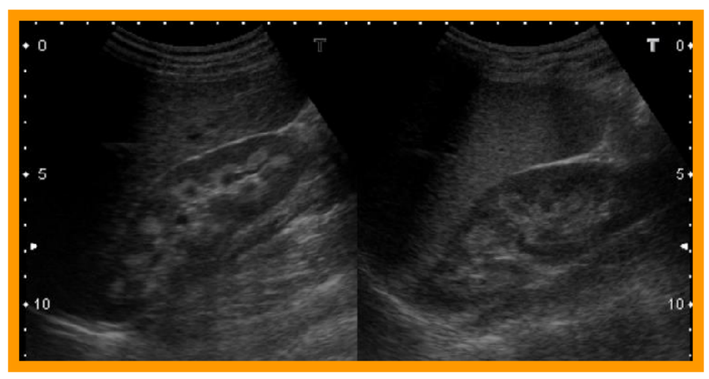
Medical history:

- The patient had suffered a transient period of polyuria in childhood (4-5-years-old) with calcium oxalate crystals in urine, diagnosed by her pediatrician as recurrent cystitis;
- Normal global development;
- Currently without any known disease or medication;
- No arterial hypertension;
- Born to nonconsaguineous parents; no other known familial cases.

Laboratory evaluation

Parathyroid hormone	**< 2,5 pg/mL (↓)**	7-65 pg/mL
25-hydroxy-vitamin D3	**22,4 ng/mL (insufficiency)**	30-100 ng/mL
1,25-dihydroxy-vitamin D3	**85 pg/mL (↑)**	18-78 pg/mL
Serum creatinine	0,6 mg/dL	0,5-1,1 mg/dL
Serum phosphorus	3,6 mg/dL	2,4-5,1 mg/dL
Angiotensin converting enzyme	25 U/L	8-52 U/L
Calciuria	**324,9 mg/24 h (↑)**	100-320 mg/24 h

Imagiologic evaluation



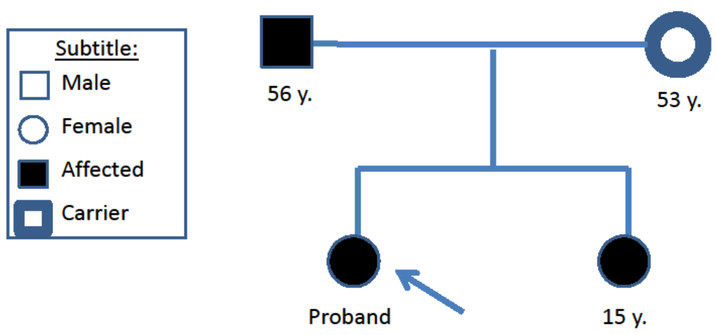
Renal ultrasound demonstrates medullary nephrocalcinosis

Genetic study and familial evaluation

- Sequence analysis of the CYP24A1 gene was performed, revealing that the patient has <u>two mutations in heterozygosity</u>:
  - **c.1186C>T(p.Arg396Trp) and**
  - **c.1226T>C(p.Leu409Ser)**

→ **Idiopathic infantile hypercalcemia**

- Analytic and genetic study of first-degree relatives was mandatory (parents and 15-year-old sister):



- **<u>Father:</u>** has the **c.1186C>T(p.Arg396Trp)** mutation in **homozygosity**, with normocalcemia, but decreased level of PTH (8,7pg/mL); no signs of nephrocalcinosis.
- **<u>Mother:</u>** is a carrier of the **c.1226T>C (p.Leu409Ser)** familial mutation, in heterozygosity; with normal analytic evaluation.
- **<u>Sister:</u>** has two mutations in **heterozygosity**: **c.1186C>T (p.Arg396Trp)** and **c.1226T>C(p.Leu409Ser)**. Analytic evaluation revealed **hypercalcemia** (10,5 mg/dL) and decreased parathyroid hormone (6,4pg/mL); **medullary nephrocalcinosis** observed on renal ultrasound.

- A low-calcium diet, avoidance of vitamin D supplements and sun protection were recommended.

Conclusion

Idiopathic infantile hypercalcemia is an autosomal recessively inherited disease, with an unknown real prevalence. This particular case emphasizes two main issues:

1. The diagnosis of the underlying cause of hypercalcemia in Endocrinology turns out to be more complex, as the vitamin D has an important role, besides PTH.
2. The identification of patients with this disease as an at-risk group brings a new aspect to the debate concerning vitamin D supplementation. More studies are necessary to understand the severity of this disease over time.

References / Bibliography: **1-** ***A Lifetime of Hypercalcemia and Hypercalciuria, Finally Explanined***, Thomas P. Jacobs *et al.* , J Clin Endocrinol Metab, March 2014, 99(3): 708-712; ***2- Mutations in CYP24A1 and Idiopathic Infantile Hypercalcemia***, Karl P. Schlingmann *et al.*, N Engl J Med 2011; 365: 410-21; **3 –** ***Medullary nephrocalcinosis in na adult patient with idiopathic infantile hypercalcaemia and novel CYP24A1 mutation,*** Edgar Meusburger *et al.*, Clin Kidney J 2013; 6: 211-215.

E-mail contact: catarina.silvestre@gmail.com