BARAKAT SYNDROME: AN UNCOMMON CAUSE OF HYPOCALCEMIA

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INTRODUCTION

- ✓ **BARAKAT SYNDROME** is a very rare disease and an uncommon etiology of hypocalcemia. Also known as **HDR syndrome** it is an autosomal dominant disorder characterized by **hypoparathyroidism**, **sensorineural deafness** and **renal disease**.
- ✓ Mutations in **GATA3**, a gene localized in chromosome region 10p14-15, have been detected in families affected by the syndrome. GATA3 is a transcription factor that is involved in the embryonic development of parathyroid glands, kidneys, inner ears, thymus and central nervous findings.

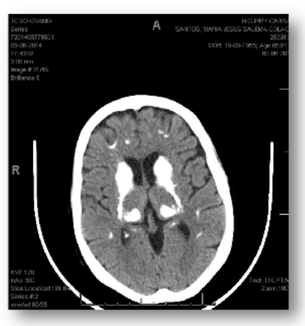
CLINICAL CASE

1990 – 35 years old

- Admitted in Emergency department with generalized seizures and signs and symptoms of cardiac failure.
- **Intracranial basal ganglia calcifications** were revealed at this time and a diagnosis of **HYPOCALCEMIC miocardiopathy** was established.
- Started calcium replacement.

January 2014

- Hospitalized due to **hypocalcemia** (6.9 mg/dL) and acute heart failure.



May 2014 – 59 years old

- Admitted in the Endocrinology ward due to hypocalcemia despite being medicated with oral calcium (**1 g**/day of calcium carbonate and calcitriol **0.75 ug**/day).
- She complained of tiredness, decreased muscle strength and unsteadiness when walking, for the last twelve months.

HOSPITALIZED

Initiated calcium carbonate **3 g**/day + calcitriol **0.75 ug**/dia

LABORATORY WORK-UP:

Ca2+	**7.7** mg/dL (8.4-10.2)	D Vit	9.8 ng/mL (4,8-52)
Pi	3.1 mg/dL (2.5-4.5)	Ca2+/24h urine	**68** mg/24h (100-300) ↓
Mg2+	1.9 mg/dL (1.6-2.3)	U	57 mg/dL (15-45)
PTH	**1.3** pg/mL (14-88)	Cr	**1.10** mg/dL (0.7-1.2)

ABDOMINAL CT SCAN

Right kidney **hypoplasia**

Progressive **HEARING LOSS** over the last **20 years** / Diagnosed with **BILATERAL NEUROSENSORY DEAFNESS**

HYPOPARATHYROIDISM | **NEUROSENSORIAL DEAFNESS** | **RENAL DISEASE**

BARAKAT / HDR SYNDROME SUSPECTED

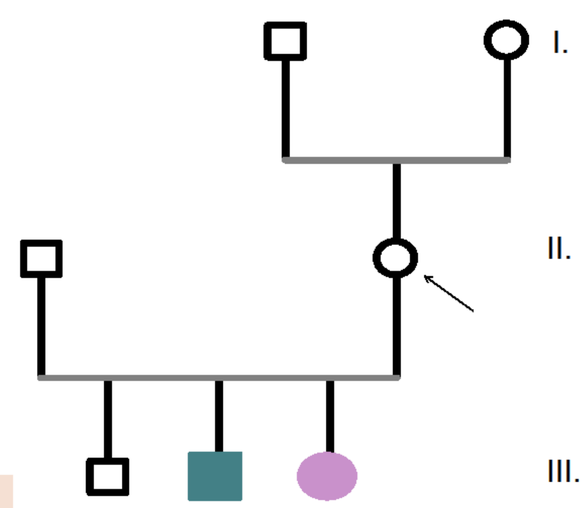
DNA sequence analysis revealed on exon 5 of **GATA 3** gene a **heterozygotic mutation** c.1043T>C (p.Leu348Pro), that CONFIRMED the diagnosis of **BARAKAT SYNDROME**.

FAMILY HISTORY

We observed one of the two adult sons and the adult daughter of this patient:

- **38** years old, paraplegic due to a work accident. B**ilateral deafness** since infancy.
- Ca2+ **7.4** mg/dL (8.4-10.2); PTH **11** pg/mL (11-80). Renal ecography: Normal.

- **21** years old, **bilateral deafness** diagnosed at 15 years old.
- Ca2+ 8.6 mg/dL (8.8-10.8); PTH 19 pg/mL (12-88)



The **same mutation was identified** in her children - c.1043T>C(p.Leu348Pro) on exon 5 of **GATA3**

COMMENTS

- ✓ Barakat syndrome may present a variable phenotype. **Renal manifestations** are the most **heterogeneous** and usually **determine disease prognosis**.
- ✓ This patient has the **classical triad**. The severity of hypocalcemia since young age and subsequent irreversible cardiac involvement were determinant for prognosis.
- ✓ Timely diagnosis and appropriate hypocalcemia treatment are paramount. **Genetic screening** of relatives takes **particular relevance** in this context.

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Calcium, vitamin D and bone

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