BACKGROUND

Pseudohypoparathyroidism type Ib (PHP-Ib) due to a maternal loss of GNAS exon A/B methylation leads to decreased expression of stimulatory G protein (Gsα) in specific tissues.

Evidence suggests an increased incidence of imprinting disorders in children conceived by Assisted Reproductive Technologies (ART).

Nevertheless, no associations between ART and PHP – Ib have been found to date.

CLINICAL CASE

7.4-years-old male with history of mild motor delay. Conceived by ART, born at 37 weeks appropriate for gestational age. At 4 yrs of age, an increased creatine kinase (CK) was detected.

At 6 yrs after ruling out miopathy, an elevated PTH was detected with normal calcium, and alkaline phosphatase, normal high phosphorus and a low 25(OH) Vitamin D (Table). He was asymptomatic for Ca-P abnormalities, and diagnostic work-up excluded systemic, thyroid and adrenal diseases, inborn errors of metabolism, skeletal and chromosomal abnormalities.

Physical exam was unremarkable except for a narrow forehead, nasal bridge hypoplasia and micropenis.

Vitamin D supplementation increased 25(OH)D, but PTH remained high.

Molecular studies confirmed an almost complete loss of methylation at GNAS exons A/B and AS, and a gain of methylation at exon NESP (Fig).

After 1 year of 0.5 ug QD of calcitriol treatment he remains asymptomatic, but mild developmental delay persists. Currently on learning supportive therapy.

He presents biochemical improvement (Table). DEXA scan at age 8 years had normal areal and volumetric BMD. L2-L4 (+1.4, +2.0 SDS) and at the right and left hip (-1.1 SDS both).

CONCLUSIONS

We present a patient with PHP – Ib due to impaired methylation at GNAS exons A/B, AS and NESP most likely associated to ART.

References
