HYPOPHOSPHATEMIC RICKETS: A NEW MUTATION

Patrícia Maio[1], Sara Rocha[2], Lia Mano[3], Telma Francisco[3], Helena Sousa[4], João Freixo[5], Margarida Abranches[3]

1 – Hospital do Espírito Santo, Évora, Portugal; 2 – Hospital de Santarém, Portugal; 3 – Paediatric Nephrology Unit, Department of Paediatrics Hospital de Dona Estefânia, CHLC – EPE, Lisbon, Portugal; 4 – Hospital de Vila Franca de Xira, Portugal; 5 – Medical Genetics Department, Hospital Dona Estefânia, CHLC – Lisbon, Portugal
Correspondence: patriciaspmaio@gmail.com

INTRODUCTION

Phosphopenic rickets is characterized by hypophosphatemia with hyperphosphaturia, normal calcemia and normal or mildly elevated PTH. This pathology may be caused by mutations in *PHEX* gene (phosphate regulating endopeptidase homolog X-linked), which results in excess circulating FGF-23 (fibroblast growth factor 23). FGF-23 impairs renal phosphate reabsorption on proximal tubule cells via FGFR1 (fibroblast growth receptor 1) and its co-receptor KLOTHO.
We present a clinical report of a girl with phosphopenic rickets, as a consequence of a new mutation of gene PHEX.

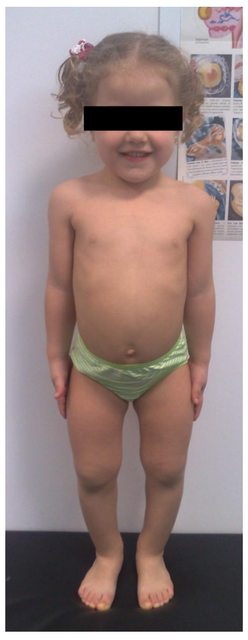
CASE DESCRIPTION

Patient: four-year-old female

Family history: unremarkable

Personal history: failure to thrive since the first year of life (height at the 5th centile until 2-years old, and with the age of four below 5th centile).
Bowing of legs noted at 18-months old.

Physical examination: frontal bossing; hyperlordosis; bowing of legs; bilateral genu varum; thickened wrists. Without bone pain. Normal teeth and hair.



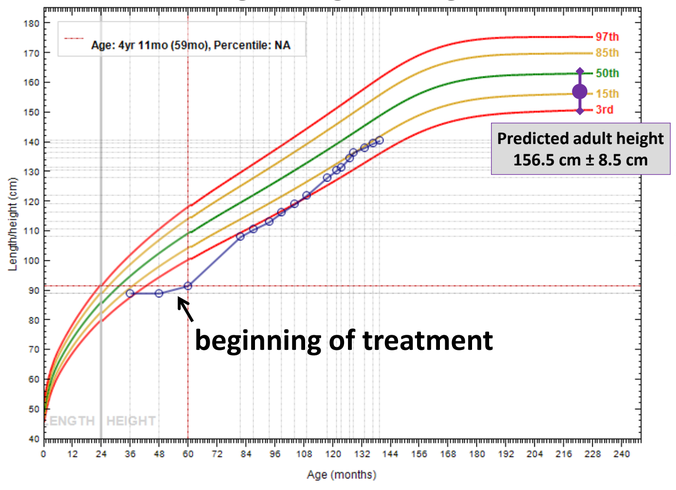
Blood tests:
- Hypophosphatemia – 2.4 mg/dL
- Normal calcemia
- Elevated alkaline phosphatase - 495 U/L
- Mildly elevated PTH - 97.2 pg/mL; RR <68.3
- Normal levels of 25(OH)D and 1.25(OH)D vitamins

Radiological study: bone deformity of the radius and femur.

Diagnosis: **Phosphopenic rickets**

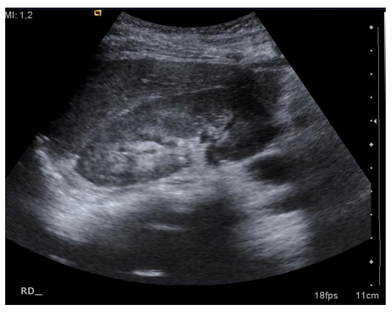
Medicated with phosphate 2000 mg/day (45 mg/kg/day) and calcitriol 1,25 mcg/day (29 ng/kg/day)

Lenght/height-for-age



Present day (11- years-old):
- Without clinical or radiographic signs of rickets
- Osseous age according to real age
- Considerable increase in growth rate (15th centile)
- Renal ultrasound shows incipient signs of nephrocalcinosis since the age of nine

- Blood tests: PTH 53.20 pg/mL, alkaline phosphatase 291 U/L, phosphatemia 3.0 mg/dL and calcemia 10.2 mg/dL



Renal ultrasound with nephrocalcinosis

Genetic study: heterozygous likely pathogenic variant of the PHEX gene: variant c.767_768del (p.Thr256Serfs*7)
This variant is not described in literature or databases. However, since it introduces a premature stop codon that can produce a truncated protein, this is very likely to be a pathogenic variant.
Parents' genetic study: in progress.

CONCLUSION

Presently more than 200 pathogenic variants in the *PHEX* gene have been found to cause hypophosphatemic rickets. We describe a new pathogenic variant of this gene. It is important to know the genetic diagnosis, because in some diseases this can affect treatment decisions. Knowledge about new pathogenic variants can improve patient's outcome.

REFERENCES: 1) Overview of rickets in children, available at Uptodate, accessed March 3, 2018; 2) Acar S, Demir K, Shi Y- Genetic Causes of Rickets, J Clin Res Pediatr Endocrinol, 2017, 9 (Suppl 2):88-105; 3) Pavone V *et al* - Hypophosphatemic rickets: etiology, clinical features and treatment, Eur J Orthop Surg Traumatol, 2015, 25(2):221-6.; 4) Shan-Shan LI, *et al* - Seven novel and six de novo PHEX gene mutations in patients with hypophosphatemic rickets, International Journal of Molecular Medicine 2016, 38:1703-1714; 5) Durmaz E, *et al* - Novel and de novo PHEX mutations in patients with hypophosphatemic rickets, Bone, 2013, 52(1):286-91