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Abstract Nº 669

Hypophosphatemic Hypercalciuric Ricket: 3 brothers with Dent´s Disease

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Introduction

The objective of this poster is to demonstrate the importance of performing the study of bone deformations, especially those asymmetric ones.

Rickets should be ruled out, with physical examination, radiographs, and measurement of plasmatic Calcium and Phosphatum.

Most rickets are hypocalcemic. The hypophosphatemics are mostly by alteration of FGF-23 that generates phosphaturia. But those that are not related to FGF-23 alterations, can be associated with losses of other electrolytes by the kidney. The molecular study can help in these cases to find the specific ethology

Clinical cases

Brother 1: 7 years old boy, with right genu valgum and short stature (-2,1 DS), mild muscular weakness; X ray shows rickets features. He was operated.

Brother 2: 4 y.o boy with frequent respiratory diseases in infant period. Genu valgum from 3 years old. Short stature (-3,08 DS) and BMI p16. Rachitic rosary and wide metaphysis.

Brother 3: Healthy boy until 10 y.o when he started genu valgum. He was operated.

They receive phosphate, citrate salts and thiazide diuretics; plasma Phosphate increased. Genu valgum partially improved. They still had normal renal function.

The molecular study* identified mutation in CLCN5 gen: c.731C>T (p.S244L) in the 3 brothers. The mother is a carrier, and the father has no mutation.

(*Done in Spain by RenalTube Project, e Instituto Salud Carlos III and Fondo Europeo Desarrollo Regional “Una manera de hacer Europa” y Asdent)

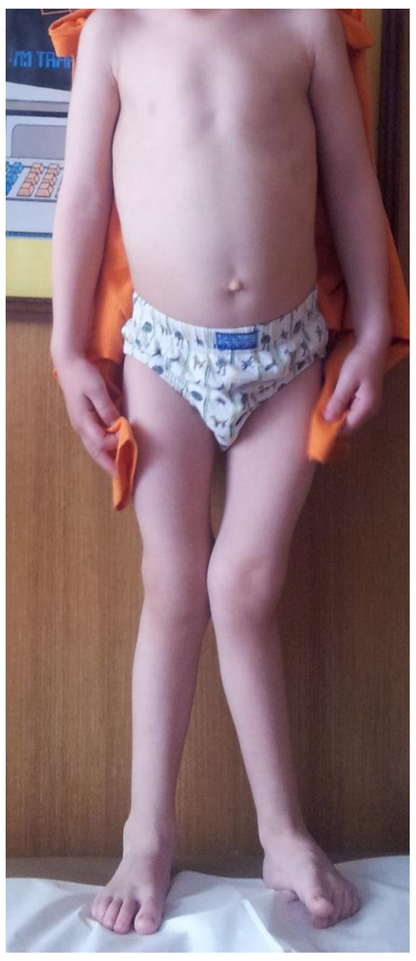
	Brother 1	Brother 2	Brother 3	Nprmal value
Calcium	9,0	9,6	10.4	8,8 – 10,1 mg/dl
Phosphate	2,5	3,1	2.8	3,0 – 6,0 mg/dl
Alkaline Phosphatases	529	660	942	156 – 386 U/L
Parathyroid Hormone	83	46	59	12 -55 pg/ml
25 OH Vitamin D	16,6	14,8	14.5	20 – 60 ng/ml
Creatinine	0,5	0,4	0.9	0,4 – 0,9 mg/dl
Urinary Phosphate 24 h per K	870 43	670 51	1410 35	mg/día 15 -25 mg/K/día
TmP/GFR	2,6	1,9	3,1	3,8 – 5,0
Urinary Calcium 24 h per K	284 14	210 18	342 8,5	mg/día < 4 mg/K/día
Uca/Ucr	0,67	1,23	0,5	<0,21
Urinary protein	100	100	32	(-) mg/dl
Hematuria	no	(+) 6 -8 xc	no	(-)
Renal ultrasound	Normal	Nefro calcinosis	Normal	normal

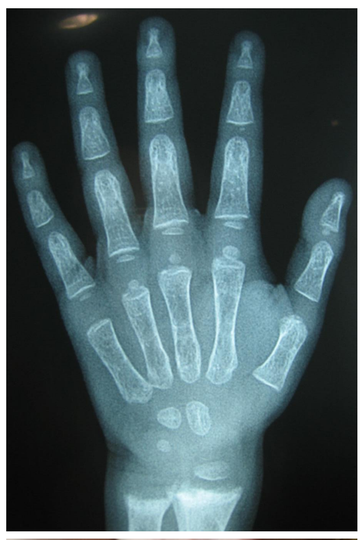
Bibliography:

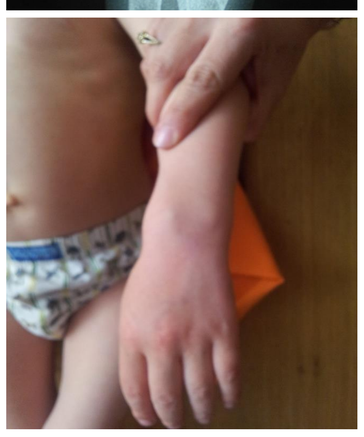
Pediatr Nephrol 2017;32(10)1851-59 Proteinuria in Dent Disease: a review of the literature.

Mutation update of the CLCN5 Gene responsible for Dent Disease. Hum Mutat 2015;36(8):743-52

Brother 2.







Dent´s Syndrome Characteristics	%
Nepholithiasis	21
Renal Failure	29
Hypophosphatemia	53
Rickets	33

DISCUSSION

Dent´s Disease is a X-linked inherited renal tubular disorder characterized by manifestation of proximal tubular dysfunction, including proteinuria, hypercalciuria, nephrolitiasis, nephrocalcinosis and progressive renal failure. Rickets occur in a minority of patients. The disease is found in males, generally in early childhood. Female carriers are asyntomatic or show a very mild phenotype.

It´s caused by mutations in either CLCN5 (Dent´s Disease1) or OCRL1 (Dent´s Disease2) genes located on chromosome Xp11.22 and XQ25 respectively. CLCN5 encodes the electronic CL-/H+ CIC-5 and it´s inactivation is associated with severe trafficking defect in tubular cells.

Treatment is supportive, with focus on prevention of nephrolithiasis. Thyazides diuretics are used to treat hypercalciuria. In case of rickets must use phosphate suplements; Vitamin D must be used with caution since it may increase hypercalciuria. High citrate diets seem to delay progresión of renal disease.