Results Of 22 Weeks Of Burosumab Therapy In A Patient With Severe Bone Deformities Due To XLH

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INTRODUCTION AND OBJECTIVES:

X-linked hypophosphatemic rickets (XLH) is the most common form of hereditary rickets. It is caused by inactivating mutations in the PHEX gene (phosphate-regulating-endopeptidase-analog, X-linked), leading to increased fibroblastic growth (FGF-23) levels, responsible for the renal phosphate wasting. This results in hyperphosphaturia and hypophosphatemia, and altered bone mineralization, in the absence of vitamin D deficiency.

Classical treatment consists on oral supplementation of phosphate and bioactive forms of vitamin D. Recently, the European Medicines Agency approved the use of Burosumab, an anti-FGF-23 monoclonal antibody, in patients older than one year with radiographic signs of bone disease.

CLINICAL OBSERVATION:

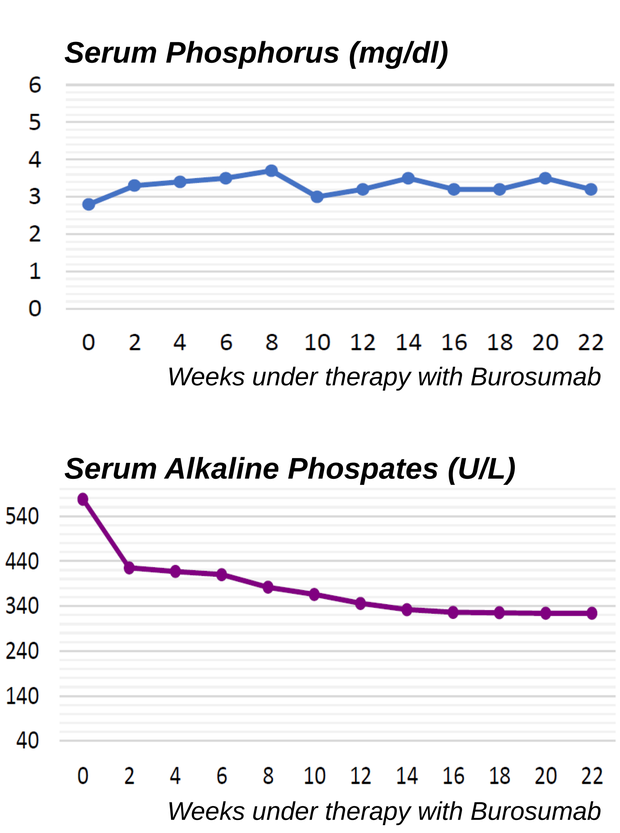
We present the case of a 6-year-old male patient, attended initially at the age of 21 months, for severe genu varum and radiographic signs of rickets. Along with the characteristic analytical alterations (see table), plasma FGF-23 levels were markedly increased **(>427 RU/ml; NV<145)**, and genetic testing confirmed the clinical diagnosis, showing a **mutation in exon 6 of the PHEX gene in hemicigosis**.

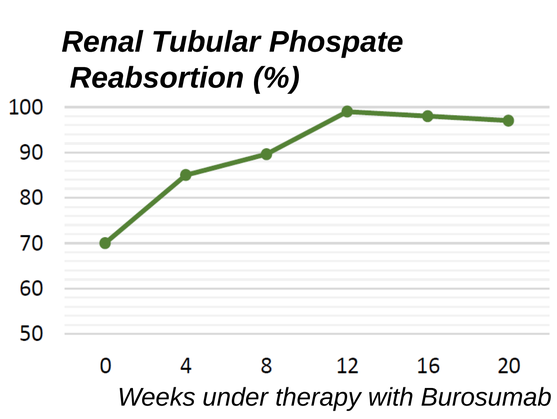
He received conventional therapy for 4 years, with adequate adherence, with no clinical or biochemical response, and even required hemiepiphysiodesis of the distal femur and bilateral proximal tibia due to significant deformity, which rendered no positive results and were eventually removed.

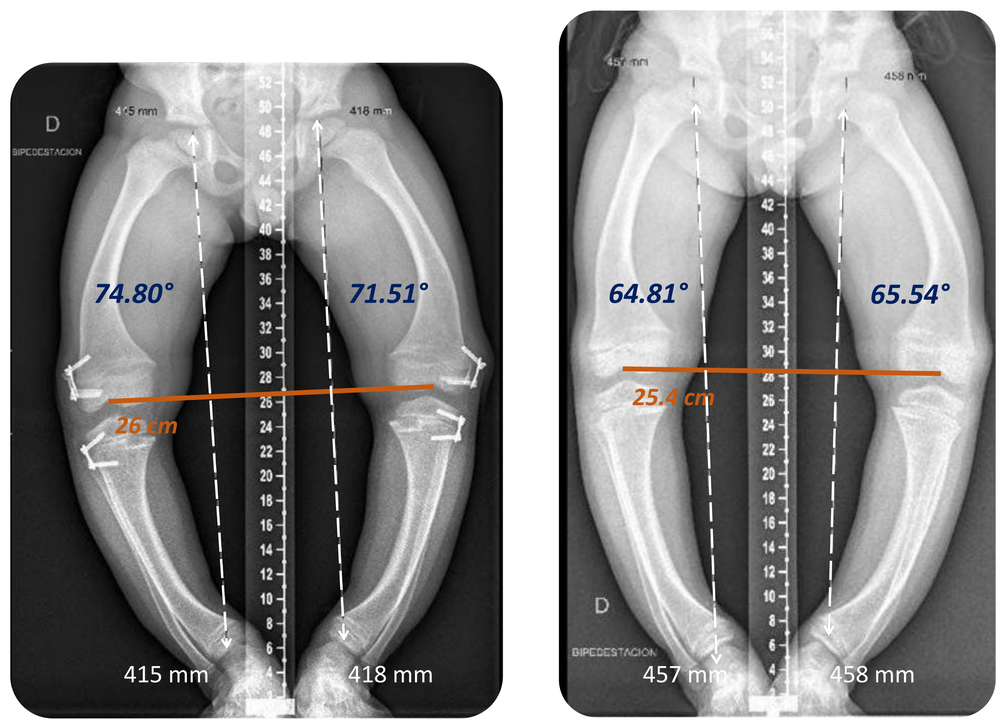
He started burosumab therapy at 0.8 mg/kg every 15 days via an early access program. No local or systemic adverse events appeared. He has now completed **22 weeks** of therapy with evident improvement of different analytical and radiological parameters..

In addition, the family refers improvement in quality of life, with greater mobility and less effort to perform physical exercise**.**

	Serum Calcium (mg/dl)	*Serum Phosphorus (mg/dl)*	*Serum Alkaline Phosphatase (U/L)*	*Renal Tubular Phospate Reabsortion (%)*	*PTH (pg/ml)*	*1,25 dyhidroxy -vitamin D (pg/ml)*	*Height (SDS)*	*Height Velocity (SDS)*	*Bone Mineral Density (SDS)*
Normal Values	8.5-11	3,8-7,5	40-462	85-95	15-65	16-56	(-2 to +2)		
Baseline at diagnosis	9.7	**2.2**	**539**	**70**	**77**	**106**	**-2.32**	**-3.64**	-0.1
Oral phosphate salts (40 mg/kg/day) + Calcitriol 0.25 mg/day	10.2	2.5	426	60	39.2		-2.12		
Oral phosphate salts (60 mg/kg/day) + Calcitriol 0.50 mg/day (4 years of treatment)	9.2	2.5	274	63	15.8	44			
Burosumab 30 mg	9.9	**3.4**	**326**	**97**	34.7	32	**-1.58**	**+1.92**	+1.8







Radiological evolution under therapy with Burosumab
(intercondylar distance, length of lower extremities and angulations)

CONCLUSIONS:

In our case, burosumab therapy has been effective clinically and biochemically, with no adverse events up to date.
In our case, the follow-up is still too short to evaluate long term benefits and clinical outcome.

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Bone, growth plate and mineral metabolism

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