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

Pablo Ruiz-Ocaña (1,2), Virginia Roldán-Cano(3), Ana Castellano-Martínez (3), Patricia Salazar-Oliva(1), Alfonso Lechuga-Sancho(1,2,4)

1. Endocrinology Unit. Department of Pediatrics, Puerta del Mar University Hospital, Cádiz, Spain
2. Department of Mother and Child Health and Radiology, School of Medicine, Cádiz University, Cádiz, Spain.
3. Nephrology unit, Department of Pediatrics, Puerta del Mar University Hospital, Cádiz, Spain
4. Research Unit, Puerta del Mar University Hospital, Cadiz, Spain

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 hemizygosis.

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

He started brosumab 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.

<table>
<thead>
<tr>
<th>Serum</th>
<th>Serum</th>
<th>Renal</th>
<th>PTH</th>
<th>1,25 dyhidroxyvitamin D</th>
<th>Height</th>
<th>Height</th>
<th>Bone Mineral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dl)</td>
<td>Phosphorus (mg/dl)</td>
<td>Alkaline Phosphatase (U/L)</td>
<td>Tubular Phosphate Reabsorption (%)</td>
<td>(pg/ml)</td>
<td>(ng/ml)</td>
<td>(SDS)</td>
<td>Velocity (SDS)</td>
</tr>
<tr>
<td>Normal Values</td>
<td>8.5-11</td>
<td>3.8-7.5</td>
<td>40-462</td>
<td>85-95</td>
<td>15-65</td>
<td>16-56</td>
<td>(&lt;2 to +2)</td>
</tr>
<tr>
<td>Baseline at diagnosis</td>
<td>9.7</td>
<td>2.2</td>
<td>539</td>
<td>70</td>
<td>77</td>
<td>106</td>
<td>-2.32</td>
</tr>
<tr>
<td>Oral phosphate salts (40 mg/kg/day) + Calcitriol 0.25 mg/day</td>
<td>10.2</td>
<td>2.5</td>
<td>426</td>
<td>60</td>
<td>39.2</td>
<td>-2.12</td>
<td></td>
</tr>
<tr>
<td>Oral phosphate salts (60 mg/kg/day) + Calcitriol 0.50 mg/day (4 years of treatment)</td>
<td>9.2</td>
<td>2.5</td>
<td>274</td>
<td>63</td>
<td>15.8</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Burosumab 30 mg</td>
<td>9.9</td>
<td>3.4</td>
<td>326</td>
<td>97</td>
<td>34.7</td>
<td>32</td>
<td>-1.58</td>
</tr>
</tbody>
</table>

CONCLUSIONS:

In our case, brosumab 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.