The response to teriparatide of a patient with beta-thalassemia major and multiple endocrine complications

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Introduction
Osteoporosis osteoporosis in young adults with beta thalassemia major (BTM) is a prominent cause of morbidity despite adequate transfusion and iron chelation therapy. The reported frequency of osteoporosis, even in well treated BTM patients varies from 13.6% to 50%, with an additional 45% affected by osteopenia. There are gender differences not only in the prevalence but also in the severity of the osteoporosis, as males are more frequently and more severely affected than females.

The pathogenesis of osteoporosis in BTM is multifactorial and is related to endocrine complications (delayed puberty, hypogonadotropic hypogonadism, growth hormone and insulin-like growth factor I deficiency, hypothyroidism, parathyroid gland dysfunction, secondary diabetes), ineffective hematopoiesis with progressive marrow hyperplasia, iron toxicity on osteoblasts, direct toxic effect of deferoxamine on bone growth, calcium, vitamin D and zinc deficiency, decreased physical activity and genetic factors.

Early identification and management of endocrine complications with adequate hormone replacement therapy and induction of puberty at a proper age are key points in the prevention of bone disease in patients with BTM. Because of the proven increase of bone resorption markers in BTM, bisphosphonates have been used in the management of thalassemia-induced osteoporosis. Agents that stimulate bone formation, such as teriparatide (a recombinant peptide fragment of PTH), might be useful in the management of thalassemia-induced osteoporosis, but there are few data regarding teriparatide efficiency in the literature.

Case report
November 2011

The patient was submitted in our endocrine department, for follow-up after one year therapy with teriparatide for severe osteoporosis.

Medical history
- at 6 months of age - diagnosed with BTM and he was treated with chronic blood transfusions since that moment;
  - Mean pretransfusional Hb=8.8 g/dl;
  - Mean post transfusional Hb=11 g/dl;
- 3 ys- splenectomy;
- 3 ys- iron chelation therapy was initiated with desferrioxamine; because the treatment was performed intermittently due to limited availability and lack of compliance of the patient the serum ferritin level was very high (6000 ng/dl);
- 30 ys- therapy with deferoxamine was started and his serum ferritin level decreased progressively from 2000 ng/dl (at initiation) to 800 ng/dl in the present time;
- Liver disease related to iron overload and chronic hepatitis C;
- Cardiomegaly from hemosiderosis;
- Femoral diaphysis fracture (1982);
- Hypothyroidism (2008);
- Secondary diabetes mellitus (2008) treated with insulin;
- Hypogonadotropic hypogonadism (2008) treated with testosterone undecanoate;
- Severe osteoporosis (2009) treated with Insulin;
- Vertebraplasty performed at T11 and T12;
- Began treatment with alendronate until Nov 2013;
- Nov 2013- vertebral fracture occurred at L5;
- therapy with rPTH was initiated.

Physical exam
- Hemoglobinosis skin and jaundiced soles;
- BP=100/80 mmHg, 76 bpm;
- Hypotension;
- Tanner P502, penis 11 cm.

Laboratory tests
- Hb= 9.2 g/dl

<table>
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<th>7</th>
<th>12.30</th>
<th>18.30</th>
<th>21.30</th>
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<tr>
<td>Serum glucose (mg/dl)</td>
<td>121</td>
<td>120</td>
<td>150</td>
<td>147</td>
</tr>
<tr>
<td>ALT</td>
<td>13 U/L</td>
<td>AST = 15 U/L</td>
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<tr>
<td>Serum calcium = 8.6 mg/dl</td>
<td>(8.1-10.2 mg/dl)</td>
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<tr>
<td>TSH</td>
<td>3.56 microUI/ml</td>
<td>(0.4-4.4 microUI/ml)</td>
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<tr>
<td>PTH</td>
<td>13.4 pg/ml</td>
<td>(10-69 pg/ml)</td>
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| Testosterone | 758 ng/dl | (300-1000 ng/dl) |}

DNA Measurements

<table>
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<tr>
<th>Year</th>
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<td>T score (T)</td>
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<td>-3.5</td>
<td>-3.4</td>
<td>-2.1</td>
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<tr>
<td>T score (T)</td>
<td>-1.6</td>
<td>-3.3</td>
<td>-3.3</td>
<td>-3.1</td>
</tr>
</tbody>
</table>

Fracture Pathology

1. Diagnosis of osteoporosis
2. Vertebral compression fracture
3. Alendronate treatment

Discussion
In spite of the fact our patient received substitutive therapy with testosterone for hypogonadotropic hypogonadism and calcium and vitamin D for hypothyroidism and the diabetes was treated with insulin with appropriate doses, he presented a severe bone disease at a young age (31ys) with 2 vertebral fractures (T11, T12).

During treatment with bisphosphonates, a new vertebral fracture occurred (L5); therefore, therapy with rPTH was initiated.

DXA measured lumbar spine BMD significantly improved (8.9% increment) after 1 year of treatment with teriparatide, the lumbar spine radiography showed no signs of a new fracture.

Conclusions
Despite improvement of treatment, the sequelae of osteoporosis are a major cause of morbidity in BTM patients. A better understanding of the pathogenic mechanisms are of paramount importance for the management of these patients.

The osteoporosis in BTM has a complex mechanism, both increased bone resorption and decreased formation being involved. Probably the extent of contribution of the two mechanisms varies in each patient.

Although the bisphosphonates are the most used treatment for osteoporosis in BTM, our case report suggests that, at least in some patients, decreased bone formation is the predominant mechanism and teriparatide could be the most appropriate therapy.

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References