Letter to the Editor

**Ochronosis and Osteoporosis: A Case Report**

**Ochronosis y osteoporosis: a propósito de un caso**

Dear Editor,

Alkaptonuria is a hereditary metabolic disorder caused by homogentisate 1,2-dioxygenase (HGD) deficiency. Oxidative conversion of HGD leads to the production of a melanin polymer, whose accumulation in the connective tissue causes a characteristic pigmentation known as ochronosis. The fusion of the ochronotic pigment to the conjunctive tissue causes a multisystem disorder characterized by premature spondyloarthitis. Other systemic characteristics include calculi (salivary, renal, biliary), renal failure, respiratory failure, hearing loss, aortic valve disease, osteoporosis and rupture of tendons, muscles and ligaments.1–4 Prolapsed discs are rare5 and vertebral fracture is an exceptional complication, with only one case reported in the literature.6

We present the case of a 55-year-old male patient who had been referred to our consultation to evaluate chronic thoracolumbar pain. Findings of the physical examination included an important reduction in spinal column mobility and grey-brown pigmentation of both sclerae. After the radiology study (Fig. 1), we decided to measure HGD levels in urine (4218.0 mg/L; normal < 10 mg/L), which confirmed the suspected diagnosis of ochronosis. The patient began with physical therapy sessions, and the improvement was noticeable. At that time (January 2004), dual-energy X-ray absorptiometry was used to determine the bone mineral density (BMD) of the lumbar spine (LS), which showed a T-score of −3.0 SD. The patient initiated treatment with risedronate (75 mg weekly). In March 2005, BMD was evaluated once again, with a T-score of −2.4 SD in the LS, −30 SD in the femoral neck (FN) and −2.7 SD in the total hip (TH). Treatment was continued with bisphosphonates, and then changed to alendronate (70 mg weekly). In June 2007, BMD showed improved T-scores in the LS (−1.7 SD) and TH (−2.3 SD) and stabilization in the FN (−3.0 SD). In January 2013,

![Fig. 1. (A) Calcification of intervertebral discs, fusion of vertebrae, diffuse vertebral sclerosis, bony bridge in pubic symphysis; (B) calcification of intervertebral discs, fusion of vertebral bodies with diffuse sclerosis, vertebral fracture of the third lumbar vertebra (arrow).](image)

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the patient came to our emergency department with acute back
pain, but reported having had no trauma. Lateral LS radiography
revealed a fracture of the third lumbar vertebra (Fig. 1). After that
incident, we opted to begin treatment with subcutaneous teri-
paratide. To date (November 2014), no new vertebral fractures have
appeared.

There are several hypotheses that attempt to explain how the
accumulation of HGD leads to ochronosis and arthropathy. These
include the interference of HGD with the intertwining of collagen
fibres and inflammatory response triggered by free radicals formed
by the oxidation of HGD. As for the development of osteoporosis,
Aliberti et al. indicated that ochronosis can be associated with a
higher rate of bone resorption, which would involve accelerated
bone mass loss. The same authors showed the ineffectiveness of
alendronate for reverting the process of bone mass loss in a con-
siderable number of patients with ochronosis and osteoporosis.
This suggests that the existence of a specific physiopathological
mechanism (microlesions of the matrix, viability of the osteo-
cytes and deterioration of the collagen network), not involved in
the pharmacodynamics of bisphosphonates, could be responsible.
Although our patient had advanced-stage disease (stage IV, osseous
ankylosis) and in spite of the reported general tendency, his BMD
progressively increased thanks to treatment with bisphosphonates.
It did not, however, prevent the appearance of a vertebral frac-
ture due to fragility. Given that treatment with bisphosphonates is
well tolerated and can improve BMD in some cases, this treatment
could be useful in patients with ochronosis and osteoporosis. Its
indication should be individualized until new scientific evidence is
reported.

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