

## Letter to the Editor

### Ochronosis and Osteoporosis: A Case Report<sup>☆</sup>

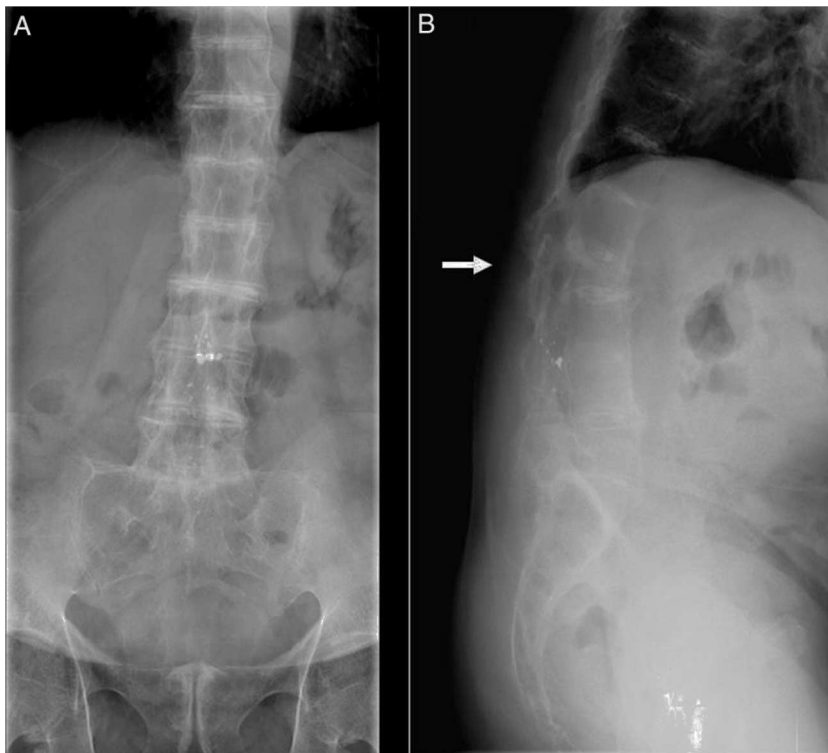


### Ocronosis y osteoporosis: a propósito de un caso

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 spondyloarthritis. 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.<sup>1–4</sup> Prolapsed discs are rare<sup>5</sup> and vertebral fracture is an exceptional complication, with only one case reported in the literature.<sup>6</sup>

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,  $-3.0$  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).

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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 teriparatide. 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.<sup>2</sup> 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.<sup>7</sup> The same authors showed the ineffectiveness of alendronate for reverting the process of bone mass loss in a considerable number of patients with ochronosis and osteoporosis. This suggests that the existence of a specific physiopathological mechanism (microlesions of the matrix, viability of the osteocytes and deterioration of the collagen network), not involved in the pharmacodynamics of bisphosphonates, could be responsible.<sup>8</sup> Although our patient had advanced-stage disease (stage IV, osseous ankylosis<sup>9</sup>) 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 fracture 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.

## References

1. Ranganath LR, Jarvis JC, Gallagher JA. Recent advances in management of alkaptonuria (invited review; best practice article). *J Clin Pathol.* 2013;66:367–73.
2. Babanagare SV, Deshmukh SD, Khadilkar MS, Patil AA. Ochronosis: a report of 3 cases and review of the literature. *Indian J Pathol Microbiol.* 2011;54:626–8.
3. Çapkin E, Karkucak M, Yayli S, Serdaroglu M, Tosun M. Ochronosis in differential diagnosis of patients with chronic backache: a review of the literature. *Rheumatol Int.* 2007;28:61–4.
4. Phornphutkul C, Introne WJ, Perry MB, Bernardini I, Murphey MD, Fitzpatrick DL, et al. Natural history of alkaptonuria. *N Engl J Med.* 2002;347:2111–21.
5. Kalevs.ki SK, Haritonov DG, Peev NA. Alkaptonuria with lumbar disc prolapse: case study and review of the literature. *Spine J.* 2007;7:495–8.
6. Millea TP, Segal LS, Liss RG, Stauffer ES. Spine fracture in ochronosis. Report of a case. *Clin Orthop Relat Res.* 1992;281:208–11.
7. Aliberti G, Pulignano I, Schiappoi A, Minisola S, Romagnoli E, Proietta M. Bone metabolism in ochronotic patients. *J Intern Med.* 2003;254:296–300.
8. Aliberti G, Pulignano I, Pisani D, March MR, del Porto F, Proietta M. Bisphosphonate treatment in ochronotic osteoporotic patients. *Clin Rheumatol.* 2007;26:729–35.
9. Jebaraj I, Chacko BR, Chiramel GK, Matthai T, Parameswaran A. A simplified staging system based on the radiological findings in different stages of ochronotic spondyloarthropathy. *Indian J Radiol Imaging.* 2013;23:101–5.

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