

Reply

Response to: Multiple fractures in Sjogrens syndrome

K.D. Stathopoulos, C. Kosmidis and G.P. Lyritis replied:

In the case of our patient with Sjogren's Syndrome and atypical fractures of the femur and ulna with complications of fracture healing, we assessed numerous etiopathogenic factors that could contribute to such a clinical presentation.

We agree that renal involvement is a well recognized extra glandular manifestation of primary Sjögren's syndrome. Common manifestations are related to tubular dysfunction, resulting from chronic interstitial nephritis, which can manifest as distal or proximal renal tubular acidosis (RTA)¹. Although the incidence of osteomalacia in Sjogren's patients with RTA has been reported to range from 25 to 45%, only 6 cases have been reported of metabolic bone disease as a primary manifestation in such patients to date².

The reported case, was referred to us for consultation in 2010. According to her attending rheumatologist, osteoporosis was diagnosed in 2001 not only on the basis of DXA T-score (-3.72 SD in the lumbar spine), but also of laboratory testing in order to exclude other bone metabolic disorders such as osteomalacia; nevertheless, bone biopsy was not performed. It should be noted that the patient did not present at that time with symptoms of diffuse musculoskeletal pain or muscle weakness, and there was no evidence of Looser's zones on x-rays. Unfortunately, values of relevant laboratory tests in 2001 are mostly missing, and we were able to retrieve only values of serum Calcium (9.4 mg/dl) and alkaline phosphatase (75 U/L with upper reference limit 120 U/L), that certainly do not suffice to exclude, but do not also support the diagnosis of osteomalacia. However, as most of the patients with rheumatologic diseases, she received nephrologic consultation as standard care, and urine analysis on numerous occasions revealed urine pH<5.5 without any evidence of hyperchloraemic metabolic acidosis. Therefore, the diagnosis of renal tubular acidosis was not confirmed. It is also of note, that the first fracture of the right femur occurred spontaneously in 2006 and displayed a radiologic pattern similar to "atypical" fractures in patients treated with bisphosphonates (thickening of the lateral cortex of the femur with a periosteal stress reaction) and did not resemble the radiological pattern one would expect in osteomalacia³. Evidence of extremely low levels of 25(OH) vitamin D with associated secondary hyperparathyroidism were only present in June 2010, and we consider this as a contributing factor both to skeletal fragility and fracture healing disorder in this particular patient at that time. As a result, she was then treated with high doses of vitamin D3. Since the causative association of bisphosphonates and atypical fractures is yet to be established⁴, we totally agree that the differential diagnosis in cases of "atypical" fragility should certainly include other bone metabolic disorders. However, in this particular patient we believe that the long term use of bisphosphonates and methotrexate were the major contributors in the pathogenesis of atypical fractures and delayed healing, although the actual mechanism is not clear to date.

Keywords: Atypical Fractures, Fracture Healing, Sjogren's syndrome, Bisphosphonates, Methotrexate

K.D. Stathopoulos

Bone Metabolic Unit, First Orthopaedic Department,
University of Athens, "Attikon" University General Hospital, Greece

C. Kosmidis

IKA, Athens, Greece

G.P. Lyritis

Post-graduate Course on Metabolic Bone Disease,
University of Athens, Greece

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