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Letter to the Editor

Cervical myelopathy revealing a unique case of retinoid hyperostosis

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We report a 38-year-old patient with a compressive cervical myelopathy revealing a severe case of Retinoid Hyperostosis (RH). He was treated since 7 years with isotretinoin (10 mg/day) for dissecting cellulitis of the scalp, when he reported neck pain and stiffness, associated with walking difficulties and joint pain. A cervical MRI (Fig. 1) identified a compressive C4-C5 cervical myelopathy caused by a hypertrophic ossification of the posterior longitudinal ligament. X-rays confirmed cervical (Fig. 1), dorsal and lumbar hyperostosis, and evidenced entheseal ossifications throughout the appendicular skeleton. These entheseal ossifications were moderately hyperfixating on bone-scan imaging (Fig. 2). Retinoid treatment was discontinued and our patient underwent urgent spinal canal decompression with a C3-C4-C5 laminarthrectomy enabling rapid resolution of neurological symptoms.

First described in 1983 [1], retinoid hyperostosis (RH) is an adverse effect reported after synthetic retinoid treatment [2,3]. Retinoids are widely prescribed since the 1970's, mostly for acne or psoriasis. RH is an ossification disorder affecting all entheses, where it causes abnormal bone growth. RH is often asymptomatic, but systematic X-rays evidence RH in up to 12% of patients after only 4 months of isotretinoin (0.5 mg/kg/day) [4]. For acne, isotretinoin is generally prescribed during 6 months, but in case of intolerance, the dose is lowered and therapy duration increased. Similarly, our patient was treated with low doses for 7 years (0.2 mg/kg/day), suggestive of a cumulative skeletal toxicity of retinoids [5,6]. Back and joint pain are the main reported symptoms. The treatment of retinoid hypersostosis is mostly based on retinoid discontinuation, to prevent further aggravation of the structural damage, which is considered irreversible [7].

RH must not be mistakenly diagnosed as spondyloarthritis [2], because both entities manifest with similar spinal ankylosis in young patients. Our patient did not meet any of the ASAS classification criteria for spondyloarthritis [8]. Syndesmophytes in ankylosing spondylitis are small, with less well-defined margins, smoothly fused to the underlying cortex, in addition to romanus lesions and erosive sacroiliitis. Whereas in RH, vertebral ossification bridges

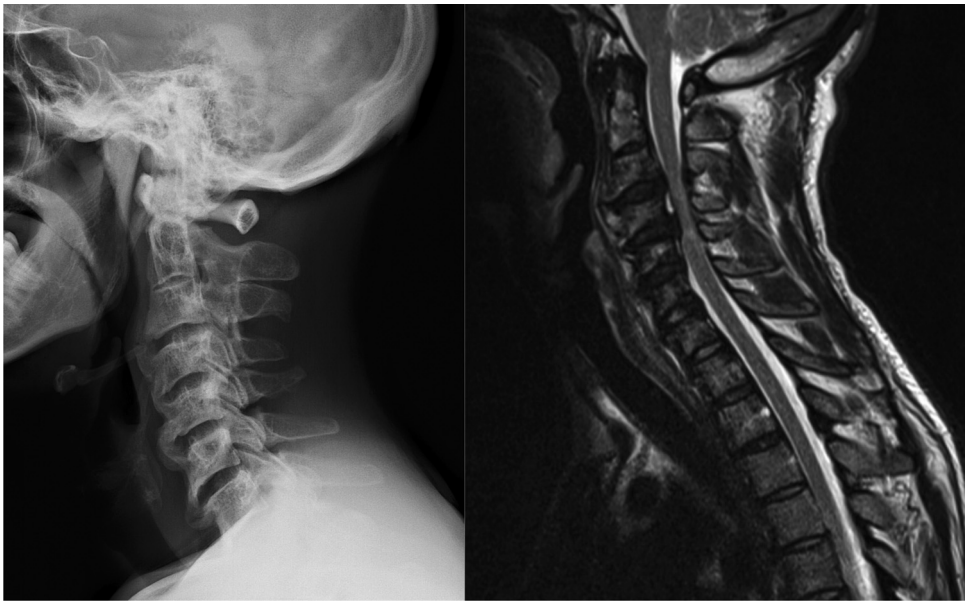

Fig. 1. Cervical X-ray: extensive ossification of the anterior and posterior longitudinal ligaments, with exuberant bridging of vertebra, responsible for complete cervical ankylosis and cervical spinal stenosis (on the left). T2 weighted sagital cervical MRI: compressive C4-C5 cervical myelopathy, revealed by an enhanced centro-medullar signal of the spinal cord. Severe C3-C4 and C4-C5 narrowing, caused by a hypertrophic ossification of the posterior longitudinal ligament (on the right).

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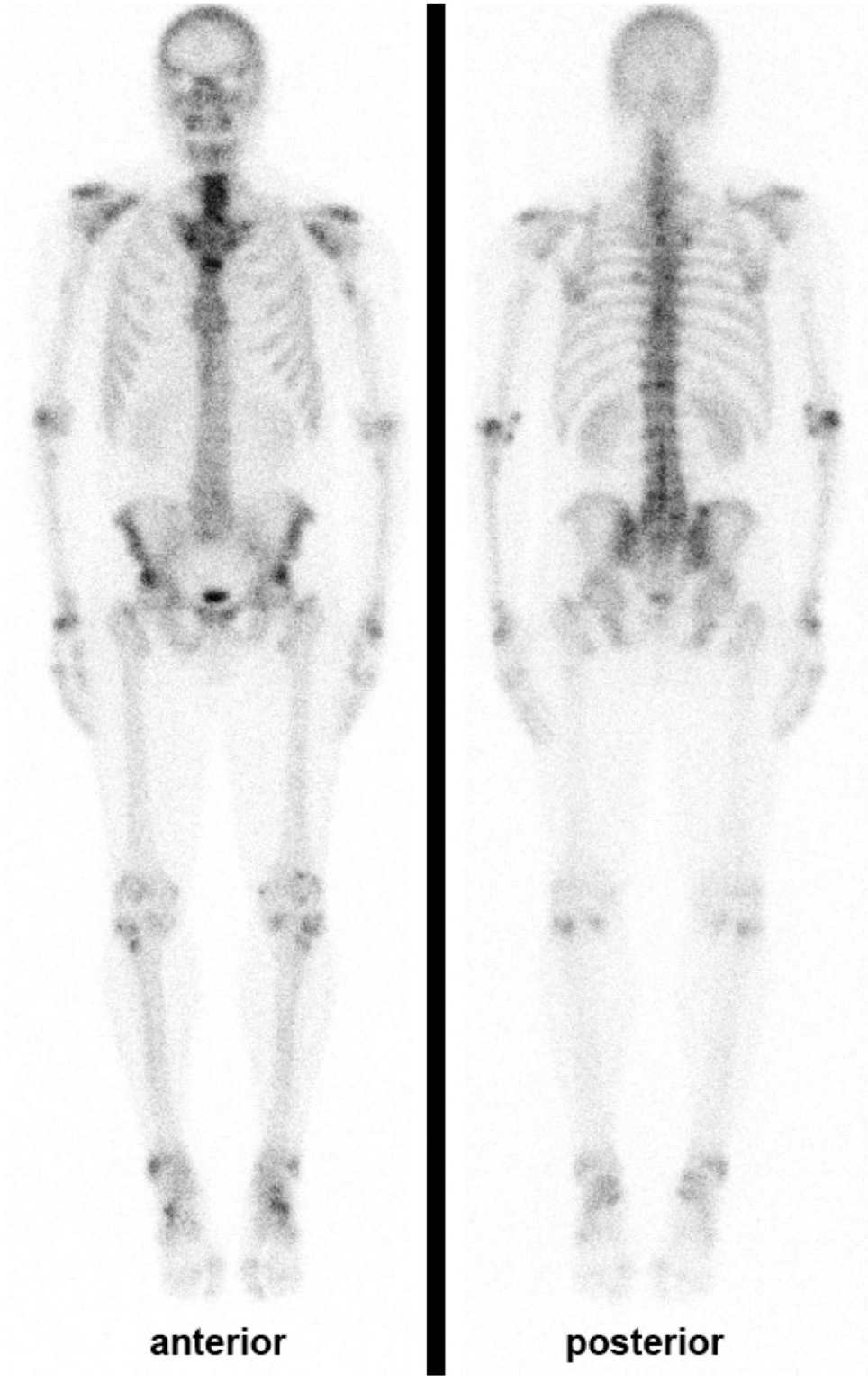

Fig. 2. Full body bone-scan: multiple moderately intense, hyper-fixating localizations of all the periosteal junctions with ligaments or tendons (anterior cervical spine, manubriosternal angle, greater and lesser trochanters, acetabulum, anterior sacro-iliac joint, and periarticular entheses of shoulders, elbows, knees, and ankle joints).

are large, bumpy and associated with exuberant anterior sacroiliac hyperostotic bridging, without involvement of the sacroiliac joint.

Pathogenesis of retinoid induced hyperostosis remains unclear. Prolonged retinoid intake has a similar effect on bone as vitamin A (retinol) intoxication. Retinoids effect is mediated through retinoid acid receptors, modulating peptide growth factors receptors expression, thus enabling mesenchymal cell differentiation and favouring enchondral ossification [6]. There is no inflammatory process involved in RH. The effect of vitamin A on bone formation appears to be non-linear: low retinol concentrations inhibits osteoblast formation, whereas higher dosages induce osteogenic differentiation, compatible with a hyperostosis phenotype [9,10].

Considering retinoid widespread use, physicians (especially rheumatologists and dermatologists) should be aware of this skeletal effect, because of its irreversible damage and potential risk for complications, such as pain and neurological compression. RH is asymptomatic during several years, however slowly progressing, until a symptomatic threshold is reached. This advocates for systematic X-ray evaluation during retinoid treatment, in case of rheumatological manifestations. Once diagnosed, although the skeletal structural effects are irreversible, retinoid discontinuation is essential to stop disease progression.

Disclosure of interest

The authors declare that they have no competing interest.

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