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Retinoic acid arthropathy: An unusual cause of elbow pain

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Retinoic acid arthropathy typically presents in the axial skeleton as flowing ossification along the anterior longitudinal ligament and as a condition of pelvic hyperostosis. When the appendicular skeleton is involved, radiographic findings usually present late and are typically asymmetric. We present an unusual case of retinoic acid arthropathy presenting in both elbow joints. Radiologists should consider this diagnosis when faced with hyperostosis that is not explained by sports-related history.

Case report

A 49 year-old woman presented with severe, sudden, sharp pain in her right elbow after performing triceps exercises. The pain decreased from a 7/10 to 3/10 severity over the course of one week. However, the patient noted increasing bony prominence over her right lateral elbow. On physical examination, there was a tender bony prominence over the lateral epicondyle. Bilateral elbow radiographs demonstrated hyperostosis, especially involving the proximal ulnas, bilateral triceps tendon insertions, and the right lateral humeral condyle (Figs. 1-3). No fracture, dislocation, joint effusion, or radiographic evidence of triceps tendon tear was evident in the right elbow (Fig. 3).

Figure 1. 49-year-old woman with retinoic acid arthropathy. Anteroposterior radiograph of the right elbow shows hyperostosis, especially involving the lateral humeral epicondyle at the origin of the extensor tendons (white arrow). Hyperostosis is also seen involving the sublime tubercle (yellow arrow).

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Figure 2. 49-year-old woman with retinoic acid arthropathy. Anteroposterior radiograph of the asymptomatic left elbow shows hyperostosis at the sublime tubercle (arrow).

Figure 3. 49-year-old woman with retenoic acid arthropathy. Lateral radiograph of the right elbow shows hyperostosis involving the olecranon process, but no soft-tissue swelling adjacent to this site, joint effusion, or fracture.

Although no prior elbow radiographs were available for comparison, radiographs of the thoracic spine from two years prior also showed flowing ossification of the anterior longitudinal ligament with relatively maintained disc spaces (Fig. 4). An AP radiograph of the pelvis from one year prior showed multiple sites of hyperostosis, including at the iliac crests (Fig. 5).

Figure 4. 49-year-old woman with retinoic acid arthropathy. Lateral radiograph of the thoracic spine shows flowing ossification of the anterior longitudinal ligament of several thoracic vertebral bodies. The disc spaces and vertebral body heights are normal.

Initial differential-diagnostic considerations included diffuse idiopathic skeletal hyperostosis (DISH) or sports activity requiring bilateral overhead throwing. Investigation of recent clinical notes revealed a history of autosomal recessive congenital icthyosis (lamellar icthyosis) requiring long-standing treatment with 13-cis-retinoic acid. Although the patient's radiographic findings are in keeping with DISH, her young age and long history of retinoic acid

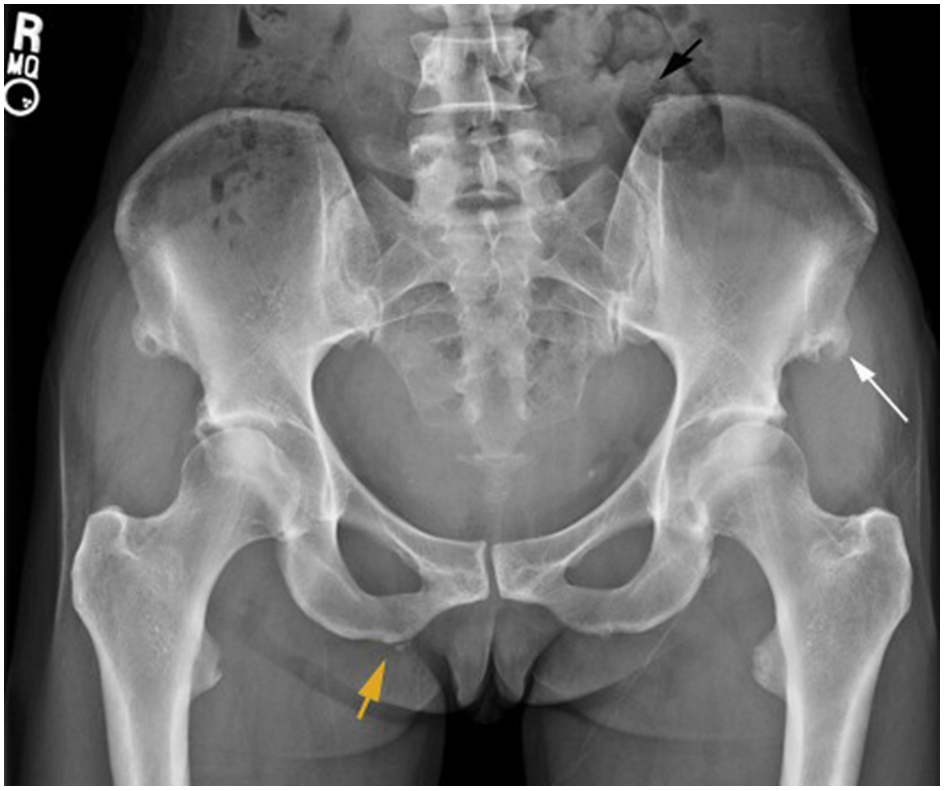

Figure 5. 49-year-old woman with retinoic acid arthropathy. AP radiograph of the pelvis shows enthesopathy at the iliolumbar ligament insertions (black arrow), anterior superior iliac spines (white arrow), and hamstring tendon (yellow arrow) attachments bilaterally.

therapy strongly suggest retinoic acid arthropathy as the correct diagnosis.

Discussion

Pittsley and Yoder first described the relationship between use of 13-cis-retinoic acid and skeletal abnormalities in 1983 (1). Their patients developed ossifying diatheses, which resembled DISH on radiographic examination. Over time, foci of hyperostosis increase in size and number (2). The most common site of involvement for retinoic acid arthropathy is the axial skeleton, particularly the cervical spine. The ossification progresses to involve both the anterior and posterior longitudinal ligaments (3). The radiographic appearance is nearly identical to DISH, a more common condition characterized by ossification at the bony attachments of muscles, ligaments, and tendons (4).

After four to five years, ossification progresses to involve the appendicular skeleton, where it is initially a unilateral process. Eventually, however, it is seen bilaterally, although it is usually asymmetric (2). Additional findings include extraspinal calcification, costochondritis, periostitis, premature physeal closure, and sacroiliitis (5). No association has been noted between symptoms and radiographic findings (6, 7). Approximately 20% of patients report the symptoms of fatigability, drowsiness, or musculoskeletal pain, usually mild in severity (8).

The underlying pathophysiology of retinoic acid arthropathy is related to the effects of chronic hypervitaminosis A on bone, since 13-cis-retinoid acid (isoretinoin) is a vitamin A derivative. The mechanism for hyperostosis is unclear, although recent experimental results raise the possibility of stimulation of progenitor osteoblastic cells, which are the cells responsible for bone production (9, 10). Alternatively, chronic hypervitaminosis A has been associated with osteoporosis and risk of fracture (11, 12). Thus, another hypothesis is that the vitamin-A-induced osteopenia stimulates osteoblastic activity (9).

Our patient's bone-mineral density measured normal. However, the case is interesting for involvement of the elbow joints. The appendicular involvement fits her long-term treatment of icthyosis with retinoic acid and serves to remind radiologists to consider retinoic acid arthropathy and hypervitaminosis A when faced with a case showing findings resembling DISH.

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