Progressive osseous heteroplasia
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Section: Musculoskeletal system
Area of Interest: Musculoskeletal bone Musculoskeletal joint Musculoskeletal soft tissue
Procedure: Comparative studies
Procedure: Education
Imaging Technique: Digital radiography
Special Focus: Congenital Calcifications / Calculi Case
Type: Clinical Cases
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Patient: 38 years, female

Clinical History:
A 38-year-old woman with no history of trauma consulted her physician complaining of a lifelong generalized pain, with limited mobility of her right upper limb and a deformity of the right elbow. No contralateral or lower limbs abnormalities. Laboratory tests (serum levels of calcium, phosphate, parathyroid hormone, Vit.D) were normal.

Imaging Findings:
New bone formation with a reticular pattern is observed around the upper right limb (from shoulder to the forearm), affecting the skin, subcutaneous cellular tissue, tendons and muscles (figure 1). Contralateral limb had no abnormalities (figure 2). There is also deformity of the distal humerus, ulna and radius, and a luxation of the radius with neo-articulation of the radius to the humerus (figure 3).
Bone scintigraphy showed uptake in the upper right limb and parasternal right region. Genetic test was positive for GNAS mutation, which helped achieve the diagnosis.

Discussion:
Progressive osseous heteroplasia (POH) is a very rare genetic disorder characterized by dermal ossification during infancy with progressive heterotopic ossification of skeletal muscle and deep connective tissue [1, 2, 3]. It is caused by an inactivating mutation in the GNAS gene, which regulates osteogenesis [1]. Albright hereditary osteodystrophy (AHO), osteoma cutis and fibrodysplasia ossificans progressiva (FOP) are also related to GNAS mutation. POH can be distinguished from other GNAS associated disorders by the progression of heterotopic ossification from skin and subcutaneous tissue into skeletal muscle, the absence of a distinctive habitus associated with AHO (obesity, short stature, shortened fourth and fifth metacarpals, rounded facies, and often mild mental retardation), and the presence of normal endocrine function [1, 2].
POH begins during infancy with the formation of islands of heterotopic bone in the dermis that coalesce into plaques which gradually involve the subcutaneous fat, skeletal muscle, and deep connective tissues. Extensive ossification of the deep connective tissues results in ankylosis of affected joints and growth retardation of involved limbs[1]. Bone scintigraphy shows pathological increase uptake in the regions of calcified soft tissue.
Radiologically, the calcified plaques show a reticular pattern and follow an anatomic progression from proximal to distal (unlike in FOP), and from the subcutaneous tissue into the deep muscle. Characteristically, heterotopic bone formation is unilateral [1].
Diagnosis is provided by the clinical history, the absence of somatic abnormalities, the presence of normal
laboratory tests, the typical radiological findings, and the genetic test (GNAS mutation)[1, 2]. There is no specific treatment. Surgical resection can lead to recurrences. Some researchers investigated the results of bisphosphonate therapy but more long-term studies are needed in this area [1]. Our patient is on treatment for chronic pain.

Written informed patient consent for publication has been obtained.

Differential Diagnosis List: Progressive osseous heteroplasia, Albright hereditary osteodystrophy, Fibrodysplasia ossificans progressiva

Final Diagnosis: Progressive osseous heteroplasia

References:

(2009) GNAS-associated disorders of cutaneous ossification: Two different clinical presentations. (PMID: 19900597)
Description: Deformity of glenoid cavity and scapula's neck (blue-arrow). Polimorphous calcifications in soft tissue of glenohumeral-joint, armpit (green-arrow) and 1st-costal-cartilage (black-arrow). Heterotopic ossifications of the skin/soft tissues (red-arrows). Abnormal elbow with radio dislocated (star). Origin: HGU J.M. Morales Meseguer, Department of Radiology, Murcia, España
Figure 2

Description: Normal findings Origin: HGU J.M. Morales Meseguer, Department of Radiology, Murcia, España
Description: Extensive heterotopic ossification involving the skin, subcutaneous tissue, muscle bundles and sheaths of the tendons (black arrows). Abnormal bone development of the elbow with dislocated radial head (red arrow). Origin: HGU J.M. Morales Meseguer, Department of Radiology, Murcia, España