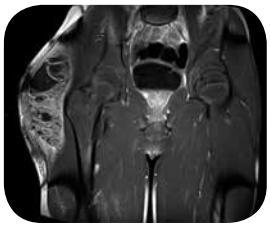

Hyperphosphatemic Tumoral Calcinosis: Case presentation and Clinical-radio-pathological Correlation

Calcinosis tumoral hiperfosfatémica: Presentación de un caso y correlación clínico-radiopatológica

Ana María Henao González[1]
Julián Garzón[2]
Oscar Messa[3]
Karina Ruiz[4]
Ennya L. Leonel Triana[5]

Key words (MeSH)

Calcinosis
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Palabras clave (DeCS)

Calcinosis
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Hiperfosfatemia

Summary

Introduction: Hyperphosphatemic tumoral calcinosis is a rare, benign condition characterized by calcified masses in the periarticular tissues which is associated with high blood phosphate levels as a result of increase in renal tubular reabsorption. *Case presentation:* In this report we describe an unusual case of hyperphosphatemic tumoral calcinosis in an adolescent who had history of trauma in the gluteal region and was surgically treated. *Discussion:* Tumoral calcinosis, also known as Teutschlaender disease, belongs to a broad spectrum of entities characterized by calcified soft tissue masses, which according to their location, morphology of the calcifications, signal intensity characteristics and sparing of the bony structures, should be considered as a diagnostic possibility. *Conclusion:* Due to the large number of differential diagnoses, such as surface osteosarcoma, chondrosarcoma, myositis ossificans, among others, radiological and histological findings are crucial in the diagnosis and proper management of this entity. This has to go along with the proper classification of the patient as hyperphosphatemic, normophosphatemic or with secondary hyperphosphatemia in order to guarantee an optimal treatment.

Resumen

Introducción: La calcinosis tumoral hiperfosfatémica es una condición rara, benigna, caracterizada por masas calcificadas en los tejidos periarticulares asociada a niveles altos de fosfato en sangre por aumento en la reabsorción tubular renal. *Presentación de caso:* Se presenta un caso inusual de calcinosis tumoral hiperfosfatémica en un adolescente con antecedente de trauma en la región glútea quien fue manejado quirúrgicamente. *Discusión:* La calcinosis tumoral, también conocida como enfermedad de Teutschlaender, hace parte del amplio espectro de entidades que cursan con masas calcificadas de tejidos blandos y que por sus características de localización, morfología de las calcificaciones, intensidad de señal y respeto óseo debe ser considerada como posibilidad diagnóstica. *Conclusión:* Debido a la gran cantidad de diagnósticos diferenciales, como el osteosarcoma de superficie, condrosarcoma y miositis osificante, entre otras, los hallazgos radiológicos e histológicos son determinantes en el diagnóstico y manejo apropiado de dicha entidad. Esto debe ir de la mano con la clasificación adecuada del paciente como hiperfosfatémico, normofosfatémico o con hiperfosfatemia secundaria, con el fin de garantizar un tratamiento óptimo.

[1]Doctor. Third year resident of the postgraduate course in radiology, Pontificia Universidad Javeriana. Bogotá, Colombia.

[2]Doctor. Radiologist, Department of Radiology and Diagnostic Imaging. National Cancer Institute. Bogotá, Colombia

[3]Doctor. Pathologist, National Cancer Institute. Bogotá, Colombia

[4]Doctor. Fourth year resident of the postgraduate course in pathology, Universidad de Cartagena. Bogotá, Colombia

[5]Odontologist. Second year resident of the postgraduate course in pathology and oral surgery, Pontificia Universidad Javeriana. Bogotá, Colombia

Introduction

Hyperphosphatemic tumor calcinosis is a rare condition, generated by the deposition of calcium phosphate crystals, of which there is little published information. This entity appears as a benign calcified tumor mass, located in the soft tissues of the periarticular regions, associated with high blood phosphate levels, secondary to a mutation in the genes coding for proteins that perform tubular reabsorption. Multiple secondary etiologies have also been described, including chronic renal failure and hyperparathyroidism. The most frequent locations are shoulders, hip and elbows (1-5).

This paper describes the case of a young patient with this condition and discusses the importance of radiological and histological findings to be considered within the spectrum of differential diagnoses of calcified soft tissue masses.

Case presentation

A 14-year-old male patient, who consults for the appearance of a non-painful, right thigh mass that relates to mild trauma seven months ago. There are no other antecedents or symptoms of importance.

The physical examination identifies a large mass in the lateral region of the proximal third of the right thigh, slightly painful and without inflammatory signs. In addition, the oral cavity showed signs of gingivitis and changes in the enamel structure, such as areas of hypoplasia and hypomineralization (figure 1).

An x-ray is performed in which calcifications are observed, well defined, located in the right periarticular coxofemoral region, without erosion of the cortical bone or signs of fracture (figure 2). For the adequate characterization of this lesion, a magnetic resonance (MR) with contrast medium, gadolinium, is used, in which a mass with very heterogeneous signal intensity is observed in T1 and T2-weighted sequences, areas with marked low signal due to the presence of calcium, as well as cystic component, liquid-calcium levels and, as in the radiograph, without compromise of the cortex of the adjacent bone (figures 3 and 4). This lesion enhances the septa following the administration of contrast medium (figure 5). There is no evidence of restriction in the diffusion sequence (figure 6).

In the blood tests of this patient, high phosphorus was found in 7.5 mg / dl (normal range 2.5-4.5 mg / dl), calcium levels with normal values (9.66 mg / dl) and without alterations of renal function.

The patient underwent orthopedic surgery, which consisted of complete excision of a mass of approximately 24 × 14 × 6.5 cm, approximately 875 grs, light brown color, soft consistency and multinodular surface.

In the anatomopathological findings, a yellowish-white, lobed mass with a milky material outlet was observed at the time of the cut (figure 7). Microscopically, calcifications were found surrounded by a chronic inflammatory reaction with multinuclear giant cells of the 'foreign body' type. No osteocartilaginous component was found, fusocellular proliferation with "zonal" change as in ossifying myositis or areas of atypia, mitosis or necrosis to be considered as of malignant origin (figure 8). With the radiological, clinical and histopathological findings, the definitive diagnosis of hyperphosphatemic tumor calcinosis is reached.

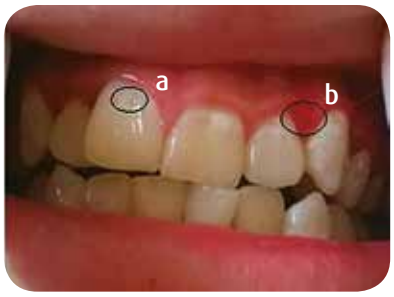

Figure 1. (a) Hypomineralization of the enamel in the cervical third of the upper anterior teeth. b) Areas of gingivitis.

Figure 2. Radiograph: Large mass of soft tissues on the lateral aspect of the proximal third of the femur, with lobulated, confluent calcifications that resemble "clouds".

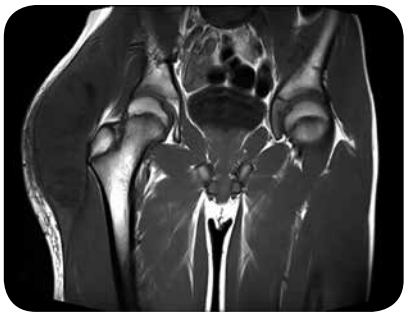

Figure 3. Coronal plane MRI enhanced in T1: Mass located in the gluteal muscular plane, with heterogeneous signal intensity and some low signal foci.

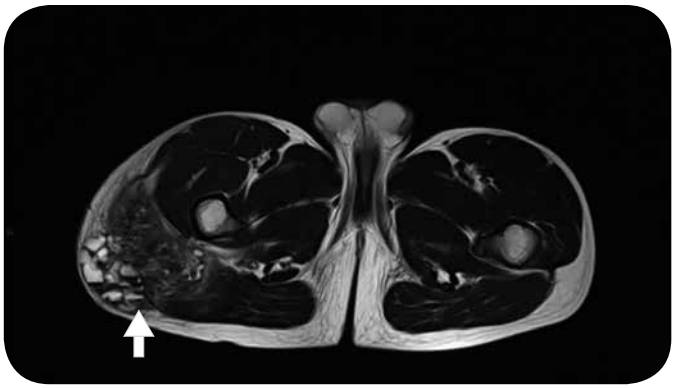

Figure 4. Axial plane, T2-weighted sequence: High signal mass, heterogeneous, with cystic component showing liquid-calcium levels inside (arrow).

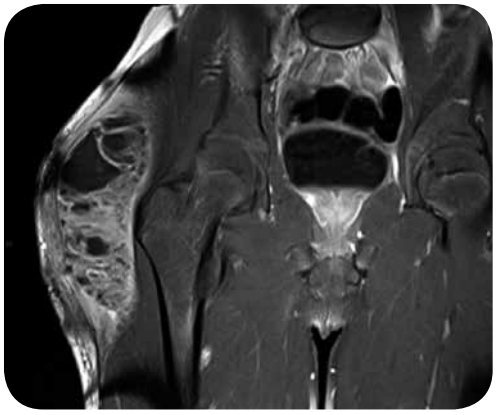

Figure 5. Heterogeneous enhancement after administration of contrast medium; Preservation of cortical integrity is observed.

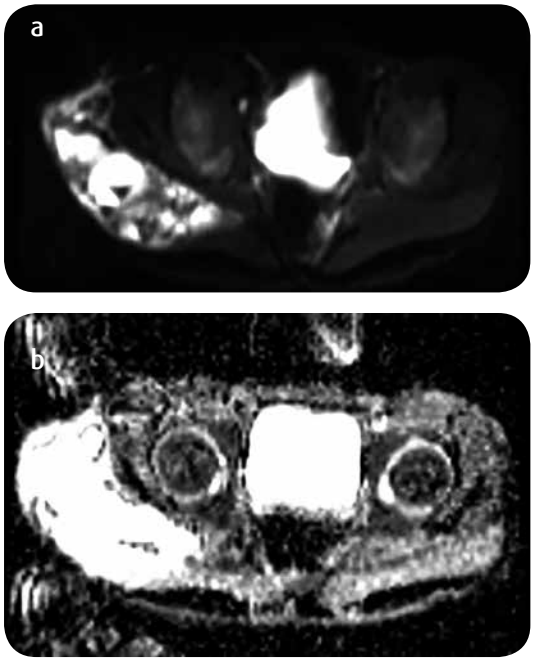

Figure 6. a) Diffusion sequence and b) ADC map: Absence of mass restriction.

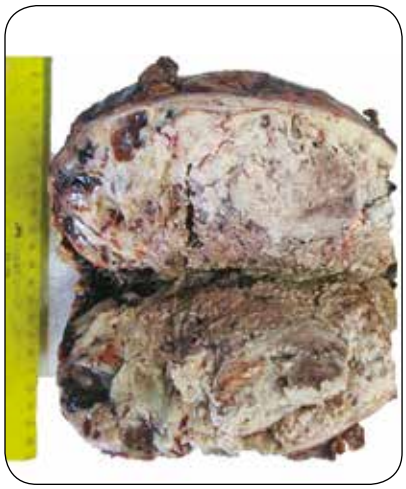

Figure 7. Macroscopic view of the tumor lesion. Surface is observed with areas of liquefaction and calcifications.

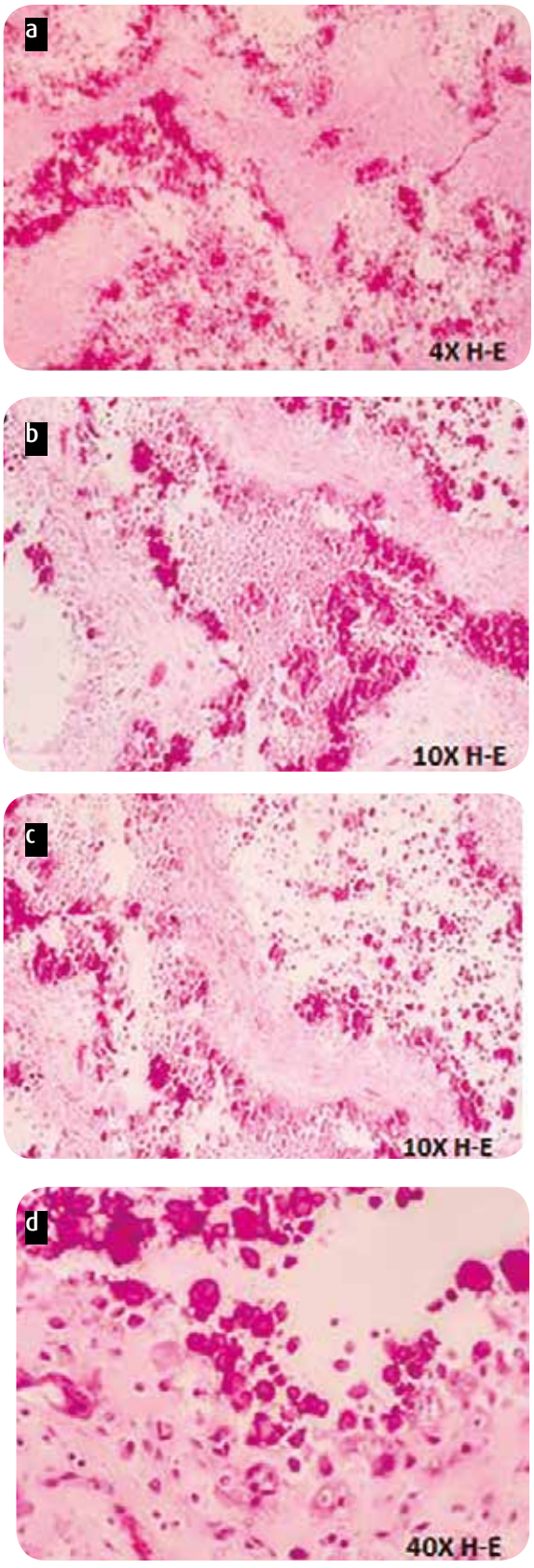

Figure 8. a) Panoramic view in 4x. b and c) Increase in 10x: Histiocytes and cystic cavities with calcifications. d) Increase of 40x.

Discussion

Tumor calcinosis is a rare, generalized and progressive disease in which calcium salts are not deposited at the usual sites, which is why it is classified into heterotopic calcifications. It was first described by Duret in 1899 as a large calcified and multilobulated mass of soft periarticular tissues. It is commonly found in adolescents as a non-painful, firm and mobile mass characteristically located in the soft tissues of the periarticular regions of the hip, shoulders and elbows, and foot involvement is uncommon (1-5).

Under normal conditions, serum phosphate levels depend on three factors: intestinal absorption, skeletal storage and renal resorption. Primary tumoral calcinosis may be of the hyperphosphatemic or normo-phosphatemic variety. The primary hyperphosphatemic variety is an autosomal recessive disorder, by mutation of the genes FGF23, GALNT3 and KL (1,4-6). Phosphate reabsorption in the kidneys is carried out in the proximal tubules by means of sodium-phosphate type II and type III cotransporters. The sodium-phosphate cotransporter type II is responsible for 70-80% of phosphate reabsorption (7,8). This process is regulated by the fibroblast growth factor 23.0 encoded by the FGF23 gene, which is mutated in this pathology (6-8).

Secondary tumoral calcinosis is associated with conditions such as hyperparathyroidism, chronic kidney disease, vitamin D toxicity, milk-alkali syndrome and osteolysis (1,6).

It appears more frequently between the first and second decade of life, in the afro-descendant community. Clinically it manifests with a non-painful mass, which decreases the range of motion of the adjacent joint. The relationship between trauma and hyperphosphatemic tumor calcinosis is rare, but may appear in the normophosphatemic variety (1).

In the oral cavity it can manifest with root malformations that include tartar and obliteration of the pulp, with local thickening of the roots of the permanent teeth, specific findings for this disorder that can serve as a phenotypic marker; These malformations seem to fit somewhere between the classic descriptions of dental dysplasia type I and II (DD-I and DDII), a hallmark of hyperphosphatemic diseases, such as tumor calcinosis (9).

Laboratory tests in these patients demonstrate hyperphosphatemia (less common normophosphatemia), normocalcemia, normal or elevated vitamin D levels, normal parathyroid hormone and normal renal function (1).

Conventional radiography is the first diagnostic study in which there are typically amorphous and multilobulated calcifications described in the literature to appear as "in clouds", located on the extensor surfaces of the periarticular regions. The radiolucent line interposed between the conglomerate of calcifications and the cortical bone shows respect for the bone (figure 2). Computed tomography (CT) helps to characterize the cystic component with liquid-calcium levels, which some authors call "a sign of sedimentation" (1). MRI shows a mass with a very heterogeneous cystic component, both in T1 and T2, by the calcified zones that reflect high intensity signals (figures 2 and 5), with characteristic levels of liquid-calcium (the latter is very low signal in all sequences) (figure 5), as well as heterogeneous and septa enhancement after administration of contrast medium (figure 7). In the diffusion sequences these lesions do not restrict (figure 8) (1,10-13).

In macroscopic pathology, a mass of cystic composition is described, with yellow lump material corresponding to the crystals of calcium hydroxyapatite (1) and in histology is characterized by the aggregation of foamy histiocytes; These are transformed, with the participation of collagenolysis, into cystic cavities coated by osteoclasts, such as giant cells and histiocytes. Movement and friction are key forces in the generation of periarticular lesions. In this process there are two calcifying events, possibly driven by concurrent hyperphosphatemia or endogenous hypervitaminosis D. The first occurs in membranous antiprotease fragments, which contain large cytoplasmic vesicles in osteoclast giant cells and mononuclear cells, which cover the cavities of tumor calcinosis; The second, in tumor calcinosis loci, membranous debris and lining cells of the cavity and erythrocytes. Finally, the cavities are filled with calcified material, lose their synovial lining, are encapsulated by fibrous tissue and ossify (1,14).

The difficulty in this patient is due to the possible differential diagnoses for his age and to the clinical manifestation as well as the radiological findings (1,11,12,15). In the evaluation of this case we consider in the differential diagnosis the following entities:

Surface osteosarcoma, or juxtacortical: one of the histological variants of osteosarcoma, which in turn is divided into paraostal and periostal, and may appear in patients of greater age range than classic osteosarcoma. This tumor has a broad cortical base, cortical thickening and is composed of mature bone matrix that is characteristically of central location. Although both are masses with calcified soft tissue component, in osteosarcoma there is contact and compromise of the cortical, without evidence of a radiolucent line separating them; in addition, the morphology of "cloud" calcifications and their random location do not coincide with the dense central calcifications (osteoid matrix) observed in the osteosarcoma. In MRI, although both are heterogeneous lesions in T1 and T2 and enhance after administration of contrast medium, osteosarcoma presents diffusion restriction and liquid-calcium levels are not characteristic.

Ossifying myositis corresponds to the formation of soft tissue bone due to different etiologies but, mainly, secondary to trauma; It is considered that there are progenitor cells producing osteoid in the affected soft tissues, which with a stimulus such as trauma become osteoblasts and form osteoid. In pictures different patterns are found depending on the stages of evolution: initially, subcutaneous plane edema and distortion of the muscular plane. Subsequently, between the third and fourth week, development of periosteal reaction; Six to eight weeks, peripheral bone formation and central immature bone; and from one and a half to six months, development of mature peripheral bone. In radiography the peripheral arrangement of calcifications and the evolution in time of the images do not coincide with the pattern described in tumor calcinosis. In MRI, myositis ossificans may show liquid-liquid, but not liquid-calcium levels.

Conclusions

Hyperphosphatemic tumor calcinosis is a rare entity that should be considered within the spectrum of differential diagnoses of patients

with calcified soft tissue masses. Complete physical examination, including the oral cavity, and characteristic imaging findings, such as lobular calcifications that respect cortical and fluid-calcium levels, are essential for a proper diagnostic approach and treatment.

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Correspondence

Ana María Henao González
Calle 138 # 10A-10
Bogotá, Colombia
anitahego@hotmail.com

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