

Genetic Whispers in Hyperphosphataemic: Tumor Calcinosis in a 30-year-old

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Abstract

Presentation

We present a case of Hyperphosphataemic Familial Tumoral Calcification (HFTC). A 30-year-old Indian male patient presented to our Rheumatology clinic complaining of joint pains involving his left elbow, right hip, and ankle. Examination was normal apart from a tender left elbow with firm swelling on the extensor surface and Positive Faber's test at his right hip. Laboratory analysis showed negative HLA-B27, normal routine parameters except for raised phosphate level. X-rays showed soft tissue calcifications at left elbow and right hip with faint calcifications around right knee and ankle. Dermatomyositis and Heterotopic Calcification Screen were negative.

Diagnosis

Elbow swelling showed Calcium Phosphate crystals on histology. He was diagnosed with HFTC on the basis of positive genetic testing for homozygous GALNT3. His Fibroblast growth factor 23 (FGF-23) levels remained elevated.

Treatment

He received dietary modifications with phosphate binders and referred to Endocrinology.

Discussion

HFTC is a rare condition to consider in patients presenting with features of tumoral calcinosis who also have unexplained hyperphosphataemia. It can be confirmed by genetic testing.

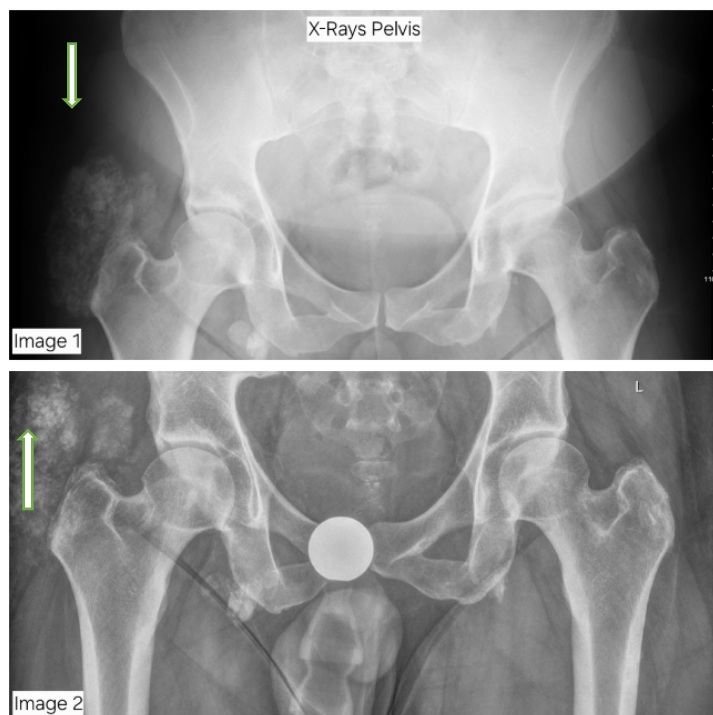


Figure 1 showing progressively worsening calcifications superior-lateral to the greater trochanter on the right.

Introduction

HFTC is a rare genetic disorder causing painful swellings in periarticular soft tissues due to ectopic calcifications, especially in trauma-prone areas like the elbows, shoulders, and weight-bearing joints where excess raised phosphate becomes deposited in the form of Calcium Hydroxyapatite Crystals in soft tissues of the joints^{1,2}. It can be caused either by mutations in gene FGF 23 which is produced in bones and acts on kidneys by regulating the absorption of phosphate by acting directly on renal proximal tubule to induce phosphaturia through the activation of ERK1/2-SGK1 Signaling pathway or through mutations to the *GALNT3* and *KL* genes, which regulate the production of FGF23. Normophosphatemic tumoral calcinosis is caused by a mutated *SAMD9* gene. Although control of hyperphosphatemia is thought to reduce these ectopic calcifications, no disease-specific therapy has demonstrated consistent benefit, as illustrated by this case.

Case Report

A 30-year-old male patient originally from India with a previous diagnosis of ankylosing Spondyloarthritis was referred by his General Practitioner to our clinic with progressive mechanical joint pain affecting hips, knees, and right ankle. He also reported the gradual development of a painful swelling at the extensor surface of left elbow, which he ascribed to direct pressure caused by using a computer mouse. Clinical examination revealed a firm tender swelling on the extensor aspect of his left elbow. Despite a positive FABER's test, there were no clinical, radiographic, or serological features suggestive of ankylosing spondylitis, with normal sacroiliac imaging and negative HLA-B27. However, X-ray imaging of his symptomatic joints showed unexpected findings of multiple periarticular calcifications at the left elbow and right hip. Laboratory analysis showed inappropriately raised phosphate (2.32mmol/L, Normal range of 0.8 to 1.5mmol/L) with normal calcium and PTH levels. A connective tissue disease screen, including evaluation for dermatomyositis, was unremarkable, and he had normal inflammatory markers.

His radiology images were discussed in multidisciplinary musculoskeletal radiology meeting, and the calcifications were deemed consistent with tumor calcinosis. Surgical excision of the left elbow lesion confirmed calcinosis cutis on histological examination. He had further investigations including echocardiography and ultrasound abdomen which showed calcifications in his aortic knuckle and kidneys. His phosphate levels remained persistently elevated and other endocrinological causes (hypoparathyroidism, pseudohypoparathyroidism) were ruled out. Genetic analysis confirmed Familial Hyperphosphataemic Tumoral Calcinosis with presence of homozygous GALNT3 mutations. He was trialed on phosphate binders to help reduce his serum phosphate levels and was referred to endocrinology for further management.

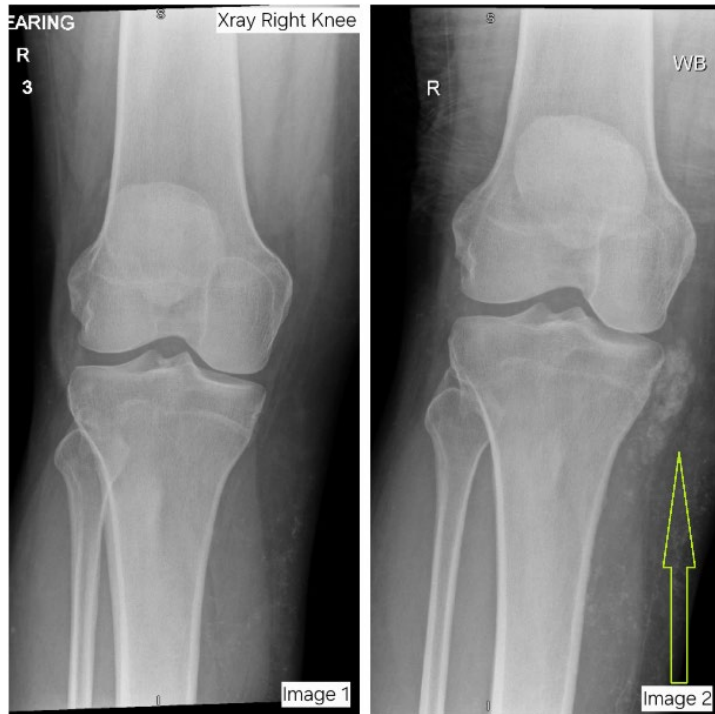


Figure 2 showing progressive X-rays of right knee revealing calcifications at medial condyle of tibia as shown by the arrow.

Discussion

This case highlights a rare presentation of tumoral calcinosis and the role of genetics in diagnosis and management. Symptomatic treatments including surgical excision of painful ectopic calcifications remain a mainstay of therapy, in addition to reducing dietary phosphate intake and through the promotion of phosphate excretion utilizing non-calcium containing phosphate binders^{1,2}. Systemic involvement may occur, with vascular calcifications predisposing to peripheral vascular insufficiency³, ischemic heart disease, or cerebrovascular accidents⁶, and dental abnormalities also reported⁴⁻⁵. Genetic counselling is required as HFTC is inherited in an Autosomal Recessive manner. At conception, each sibling of an affected individual has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.

Declarations of Conflicts of Interest:

None declared.

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