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Osteomyelitis-Like Presentation In A Young Girl With Hyperphosphatemic Familial Tumoral Calcinosis – A Case Report

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Abstract

Background: Hyperphosphatemic familial tumoral calcinosis (hFTC) is a disorder of phosphate regulation characterized by ectopic calcifications and inflammatory bone pains.

Case: We describe a 10-year-old Indian girl who presented with clinical features mimicking osteomyelitis and swelling over the right gluteal region and was eventually diagnosed with hyperphosphatemic familial tumoral calcinosis. She was found to have a homozygous mutation c.1097T>G p. Leu366Arg in the *GALNT3* gene. She was started on a low phosphate diet, sevelamer, and acetazolamide and underwent an excision of the right gluteal swelling.

Conclusion: Osteomyelitis-like presentation can lead to undue delay in the diagnosis of hFTC. Physicians and orthopedicians must be aware of this condition to ensure a timely diagnosis and better outcome.

Keywords: Hyperphosphatemic familial tumoral calcinosis, osteomyelitis

Introduction

Familial Tumoral calcinosis (TC) is a rare autosomal recessive metabolic disorder characterized by the progressive deposition of calcium phosphate crystals in periarticular spaces and soft tissues which can occur in the setting of hyperphosphatemia (hFTC) and normophosphatemia (nFTC). Fewer than 100 cases of genetically confirmed hFTC [11]. Three genes, namely, *FGF-23*, *GALNT3*, and *KL* were identified as causative of hFTC [11]. We describe a 10-year-old Indian girl with a mutation in the *GALNT3* gene.

Case:

A 10-year-old Indian girl, born to third-degree consanguineous parents, presented with pain in bilateral lower limbs over four years and right gluteal swelling over two years. Her leg pains were associated with fever and were attributed to osteomyelitis for which she underwent debridement twice. The right gluteal swelling was excised but the swelling reappeared. Her medical history was otherwise, insignificant. There was no history of trauma, abdominal pain, renal insufficiency, or similar family history.

Examination revealed a mass on the lateral aspect of her right hip, 5x6 cm in size, firm in consistency, non-tender, and non-mobile (Figure 1,2). The texture and temperature of the overlying skin were normal. Hip movements were normal. Systemic examination was unremarkable.

Investigation revealed normal hemoglobin, total and differential count, and urine routine. Renal function was normal. A plain X-ray of the right hip showed spotty calcification in periarticular soft tissues (Figure 2). Serum calcium was normal (9.1 mg/dL)

and serum phosphorus was high (7.54 mg/dL). Vitamin D was normal. MRI of the right hip showed a multilobulated lesion with fluid calcium levels in the right gluteus maximus and medius muscles which were suggestive of tumoral calcinosis. Histopathological examination showed foreign body giant cell reaction with calcification. Diagnosis of Tumoral Calcinosis was thus made. A clinical exome by Next Generation sequencing (NGS) showed a homozygous mutation in chr2:166615351A>C c.1097T>G p. Leu366Arg of the *GALNT3* gene. She was diagnosed with hFTC and was initiated on a phosphate-restricted diet, acetazolamide, and sevelamer. The right gluteal mass was surgically excised.

Figure 1: Mass seen over the lateral aspect of right hip

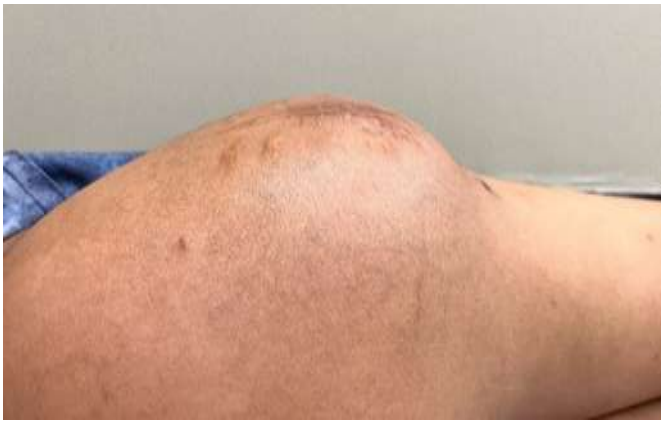
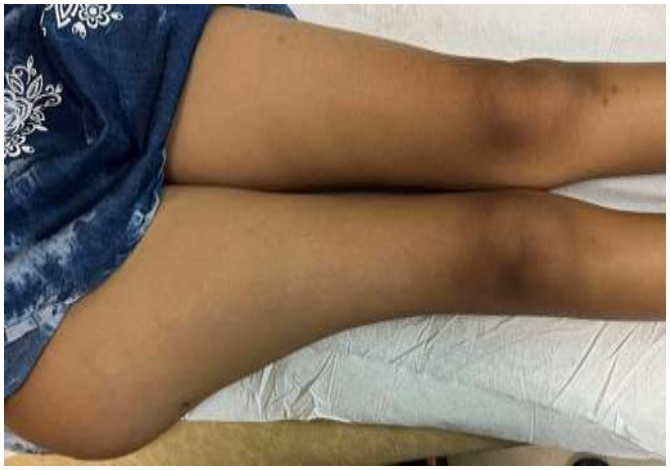
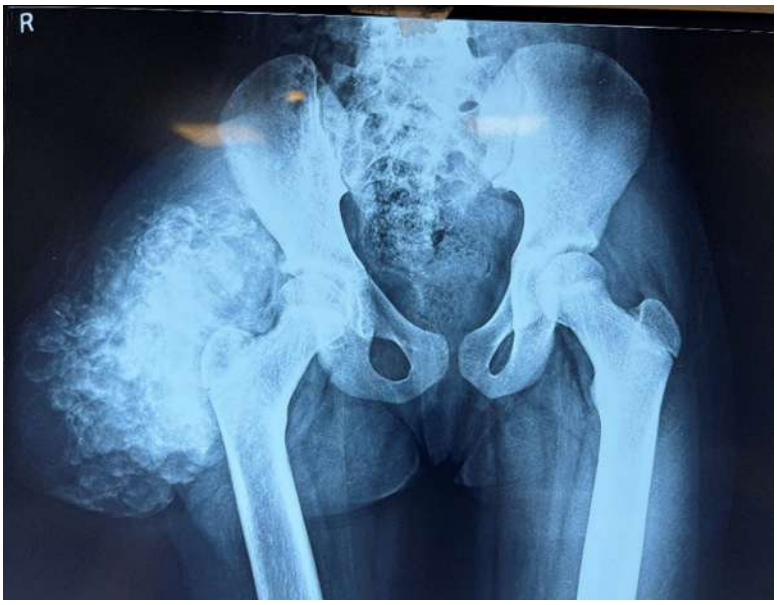


Figure 2: Mass seen over lateral aspect of right hip, 5 x 6cm



Volume 6, Issue 6; November-December 2023; Page No 342-346

Figure 3: X-ray showing spotty calcification in periarticular soft tissues in the right hip region.



Discussion:

Hyperphosphatemic Familial Tumoral Calcinosis is a rare and disabling disorder that results from disturbances in FGF23-mediated phosphate regulation. The primary defect responsible for the metastatic calcification appears to be hyperphosphatemia from the increased capacity of the renal tubule to reabsorb filtered phosphate [1,2,3]. hFTC is caused by loss of function mutations in *FGF23* and *GALNT3* and missense mutations in *αKlotho* [10]. Our patient had a mutation in the *GALNT3* gene. This disorder has been predominantly reported from the Middle-east, African, and European countries [11]. However, only a handful of cases have been reported from the Indian subcontinent [14,15].

The symptoms usually begin in the first two decades of life, however, few cases have been reported in infancy [11,12,13]. Manifestations may vary widely. Tumoral calcinosis (TC) is characterized by swellings on the extensor surface of large joints, though, the involvement of small joints has been noted. Long bone diaphysis has also been affected [4]. Yüksel HY et al showed that TC might be associated with chronic recurrent multifocal osteomyelitis [5]. Even though our patient manifested the classical findings of hFTC, the presence of an osteomyelitis-like picture led to a significant delay in the diagnosis. There was a delay of four years before diagnosis in our patient. The chronicity and recurrence of symptoms seem to affect the quality of life of patients with hFTC.

The biochemical profile of patients with hFTC reveals a normal calcium level, elevated phosphate level, elevated to inappropriately normal serum 1, 25 dihydroxy vitamin D levels, inappropriately increased tubular reabsorption of phosphorus, low-normal serum parathyroid levels, and normal kidney function [11]. Our patient had a similar biochemical profile along with radiographic findings suggestive of tumoral calcinosis.

The index patient had a homozygous mutation in chr2:166615351A>C c.1097T>G p. Leu366Arg of the *GALNT3* gene, which was predicted to be damaging to damaging protein function. The variant is predicted to be damaging by 5 (FATHMM, LRT, Mutation Assessor, Mutation Taster, and SIFT) out of 5 *in silico* missense prediction tools. The identified variant has been previously reported in a compound heterozygous state in two siblings of Indian origin affected by FTC and hyperostosis-hyperphosphatemia syndrome [15].

Treatment options focus on managing blood phosphate, reducing pain and inflammation, and addressing calcifications and their complications.

Volume 6, Issue 6; November-December 2023; Page No 342-346

Phosphate-lowering options include sevelamer, lanthanum, and aluminum hydroxide [6]. Acetazolamide, a carbonic anhydrase inhibitor has been used which acts by increasing calcium-phosphate solubility through lowered serum pH [7]. Patients with inflammatory signs require NSAIDs [11]. Our patient was initiated on sevelamer and acetazolamide. However, she underwent an excision of the gluteal mass. Surgical outcomes are highly variable. The chance of recurrence and poor wound healing remains a major concern [8,9]. On follow-up of 4 months, our patient did not show any new symptoms.

Conclusion:

hFTC is a rare disease characterized by the progressive deposition of calcium phosphate crystals in periarticular spaces and soft tissues. However, an osteomyelitis-like picture can lead to a significant delay in the diagnosis of these patients. Therefore, there is an urgent need to raise awareness amongst physicians and orthopedicians regarding this entity. Serum phosphate can be a simple and readily accessible test for early diagnosis. In the absence of definitive treatment, quality of life continues to remain poor.

Conflicting Interest:

The Authors declare that there is no conflict of interest.

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Authors' contributions:

All authors contributed to the study's conception and design.

JJ- Initial draft, data collection and analysis, literature review

SB –Conceptualization, management of patient, final review of the manuscript

NS- Initial draft, data collection, and literature review

Consent to participate – Consent to participate has been taken.

Consent for publication – Consent for publications has been taken.

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Volume 6, Issue 6; November-December 2023; Page No 342-346

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Volume 6, Issue 6; November-December 2023; Page No 342-346