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Hyperparathyroidism Tumoral calcinosis: A case report

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Abstract
Tumoral calcinosis (TC) is a rare locally aggressive lesion characterised by extra-articular soft tissue deposition of the calcium phosphate around large joints & small joints. The exact aetiology is not known.
A 11–year–old female presented with a painful progressive swelling around the medial aspect of 1st metatarsal right foot over a 6–month duration. Routine laboratory results showed a normal haemogram, and normal calcium and high phosphate levels & para thyroid level. Imaging showed a soft tissue calcified mass around 1st metatarsal medial aspect of right foot. The cut surface of the excised mass showed myxoid material with areas of calcification. On microscopy, there were typical features of Tumoral calcinosis.

Keywords: Hyperparathyroidism, granulomatosis calcinosis, microscopy

Introduction
Tumoral calcinosis (TC) is a rare locally aggressive, benign condition first described by Duret [1]. The term Tumoral Calcinosis was coined by Inclan [2]. This is also known as Teutsecherlaender disease, calcifying bursitis, lipocalcino granulomatosis. This condition mostly occurs in adolescents and young adults, but familial forms affecting infants are also described [3]. Masses are usually found around large joints such as the hips, shoulder and elbow. Only occasional cases of small joint involvement have been reported [4]. Tumoral Calcinosis is characterised by extra-articular soft tissue deposition of calcium phosphate. Tumoral Calcinosis may arouse de novo (primary/idiopathic) or secondary to other conditions like renal failure, hypervitaminosis and hyperparathyroidism [5]. Familial forms of Tumoral Calcinosis have also been described and are usually associated with mutations of genes like GLANT3, FGF23 and αklotho.

Case Report
A 11–year–old female presented with a painful progressive swelling around the medial aspect of 1st metatarsal right foot over a 6–month duration. His medical history was insignificant. There was no history of trauma, haematuria, abdominal pain, renal insufficiency or similar family history. Physical examination showed tender around the medial aspect of 1st metatarsal right foot. The masses were sessile and not attached to the underlying bones. The texture and temperature of the overlying skin was normal. There was mild restriction in movement around the 1st MTP & TMT joint .The patient underwent an excision biopsy and curettage under spinal anesthesia. The skin incision was made on the medial plantar aspect of the first toe from the proximal inter-phalangeal joint (PIP) to the 1st metatarsal base. After meticulous dissection, a chalky white material measuring 5* 2.5*2 cm was noted; it was enmeshed in a tenacious fibrous capsule which adhered to the surrounding soft tissues. On sectioning, the mass showed a yellowish pasty calcareous material and there was a gritty feeling to the material. Upon histological examination, the capsule consisted of a well-defined collagen fiber membrane with an amorphous acidophilic material inside. The mass also contained a crystalline infiltrate of calcium and giant cells. It was identified as an inactive phase of tumoral calcinosis because there was merely calcified material surrounded by dense fibrous material extending into the adjacent tissues. The patient has been followed up for one year postoperatively without any evidence of relapse and noted persisting growth of the bone.

Investigation

The serum calcium, serum albumin, vitamin D and renal function tests were normal while the phosphate level was high (6 mg/dl). His haemogram was normal except for mild lymphocytosis (47%) and monocytosis (10%) with a raised erythrocyte sedimentation rate, suggestive of a chronic inflammatory process. The laboratory examination showed normal calcium (9.0 mg/dl), phosphorus (3.9 mg/dl), serum alkaline phosphatase (311 IU/L) and uric acid (3.5 mg/dl); Parathyroid level 127 pg/ml

Plain radiographs (antero-posterior view) showed large lobulated calcified masses the medial aspect of 1st metatarsal right foot over (figure 1c). No intra-articular extension or bony erosions were noted. To further evaluate the lesions, the patient was subjected to MRI. Mri images showed a diffuse hypointense signal with few interspersed nodular hyperintense foci (figure 2a;2b). The hypointense nature Mri images can be attributed to the calcific nature of the deposits, and the foci suggest the presence of inflammation. The masses around the medial aspect of 1st metatarsal right foot were excised surgically and sent for histopathological examination.

Pathological Findings

Grossly, the tumour comprises a well circumscribed unencapsulated globular soft tissue mass. The tumour was 50×25×20 mm in dimension. The cut surface of the tumour was grey-white and gelatinous with areas of calcification

The H&E stained tissue section from the tumoral mass on light microscopy showed multiple cystic spaces with large geographic areas of calcification surrounded by palisaded histiocytes and numerous foreign body type giant cells. The intervening fibrocollagenous stroma was infiltrated by lymphocytes. The histomorphological features are consistent with TC.

Differential Diagnosis

- Myositis ossificans.
- Calcinosis of renal failure.

Outcome & Followup

The patient was now on a phosphate-restricted diet. There was no new lesion. The follow-up x-ray showed no recurrence in 7 months.

Discussion

TC is a rare disorder characterised by the periarticular soft tissue deposition of a calcium phosphate and hydroxylapatite (Ca_{10} $(PO_4)_6(OH)_2$) resembling neoplasm. The basic defect lies in calcium metabolism. There is a decrease in the excretion of phosphate with excess secretion of vitamin D; however, the exact aetiology is not known. On the basis of the underlying aetiology, the disease can be primary or secondary to other conditions. Depending upon the phosphate level, primary TC can be normophosphatemic or hyperphosmatemic. The primary TC may be sporadic or familial. The sporadic form is most common and usually occurs in the young adolescent black populations [7].

The patient had undergone excision biopsy and the pathological report identified an inactive phase of tumoral calcinosis of the foot.

Familial hyperphosphatemic TC is an autosomal recessive metabolic disorder where there is a loss of fibroblastic growth factor 23 (FGF23), GaINAc-transferase 3 (GALNT3), an enzyme which initiates O-linked glycosilation and the αkoltho gene. This leads to the uncontrolled production of 1, 25 dihydroxy vitamin D resulting in increased phosphate reabsorption from the kidney and intestine [6]. However, normophosphatemic TC shows a defect in the steve α motif domain containing protein (SMAD9) [8]. The exact physiological role of SMAD9 is not clearly known. But it is hypothesised that SAMD9 may be a downstream target of TNF-α signalling, where it mediates pro-apoptotic signals and activates counter-regulatory anti-inflammatory activities. It is also seen that SMAD9 is involved in dystrophic calcinosis, a common form of extraosseous calcification [9]. Metzker *et al* [10] have already demonstrated an inflammatory response in normophosphatemic TC associated with deficiency of SMAD9.

TC can also affect long bone diaphysis (diaphysits) [11]. Bone marrow sclerosis (in children) and periosteal reaction have also been reported. A review of the literature showed that TC may be associated with chronic recurrent multifocal osteomyelitis, which may sometimes be confused with TC because of a periosteoal reaction and a recurrent episode of fever [12]. In some cases, ophthalmic involvement includes a calcified deposit in the eyelid and conjunctiva along with angoid streaks being reported [13]. Apart from large joints, other rare sites include dental (calcification of pulp cavity) and small joints. The joint cavities are usually spared, but the movement restriction is due to the large size of the lesion.

The differential diagnosis considered in this case of soft tissue calcification includes calcinosis secondary to renal failure, which can be differentiated by the renal function test and vitamin D level. Synovial chondromatosis which is usually intra-articular and show ring, arc appearance. Myositis ossificans which is characterised by rapid evolution and lacks lobular morphology.

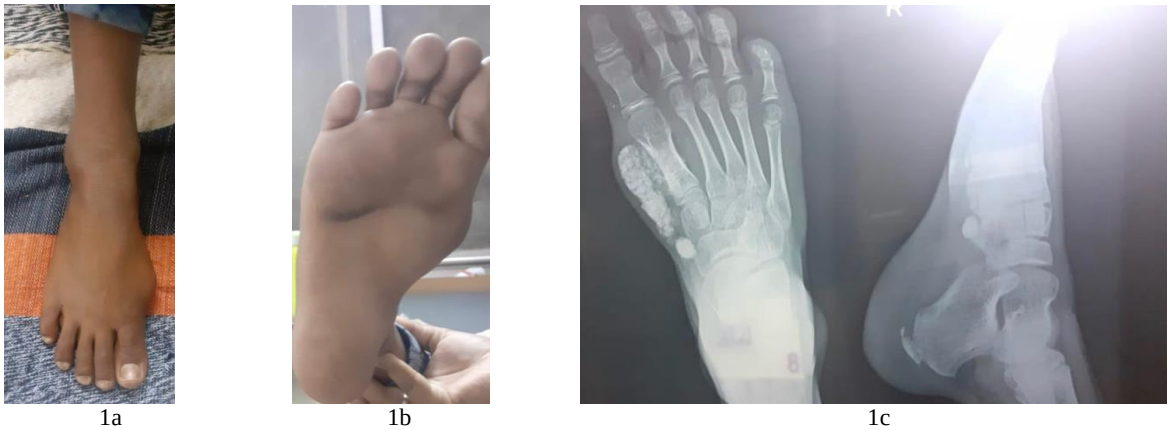
Our recent experience with DECT in such lesions showed them to have a composition consistent with calcium containing material with typical lobulated calcific masses in periarticular locations with areas of low attenuation in between; and the nodular appearance giving rise to a ‘cobblestone appearance’.

Complication related to TC includes pain due to nerve compression, ulceration, bacterial infection and cosmetic disfigurement. Severe complication is very rare and includes loss of vision.

The treatment choice is surgical resection as the use of medical treatment for hyperphosphatemia is controversial. Steroid and radiation use were also suggested by other authors. However, complete surgical removal to prevent recurrence is the best approach.

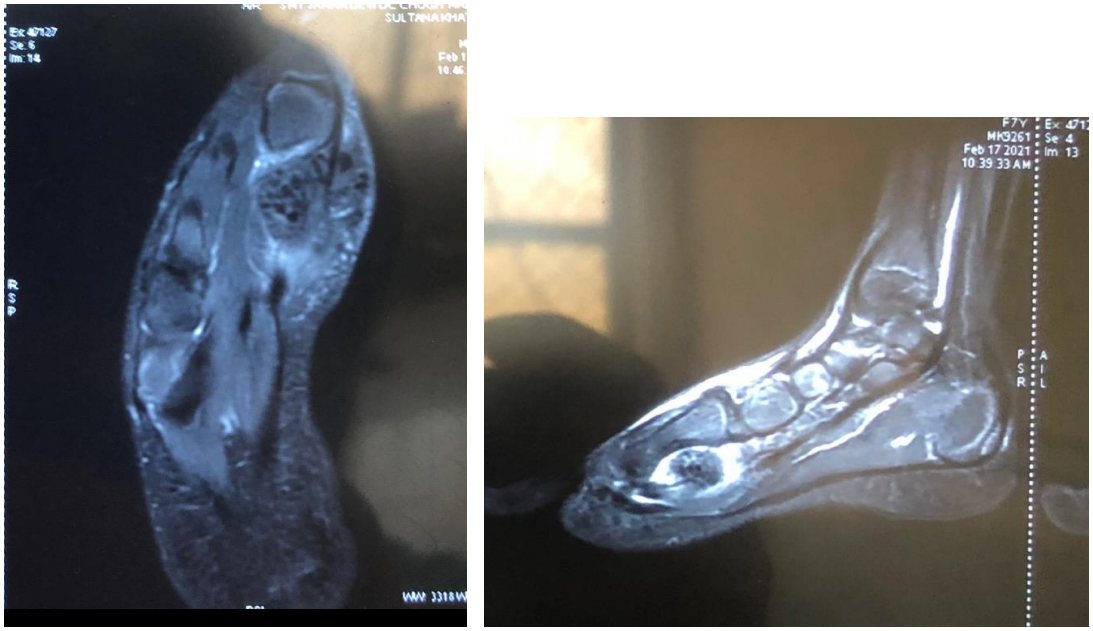
Key Points

- Though tumoral calcinosis is uncommon, it should be considered as a cause of soft tissue calcification, especially around the periarticular region.
- A high index of suspicion and a multidisciplinary approach are required for correct diagnosis and effective treatment.
- A ‘cobblestone’ appearance is a unique observation in dual energy CT, which may be a helpful tool as an additional imaging modality for this rare entity.
- Close follow-up is mandated because of a high propensity of recurrence even after surgical removal.



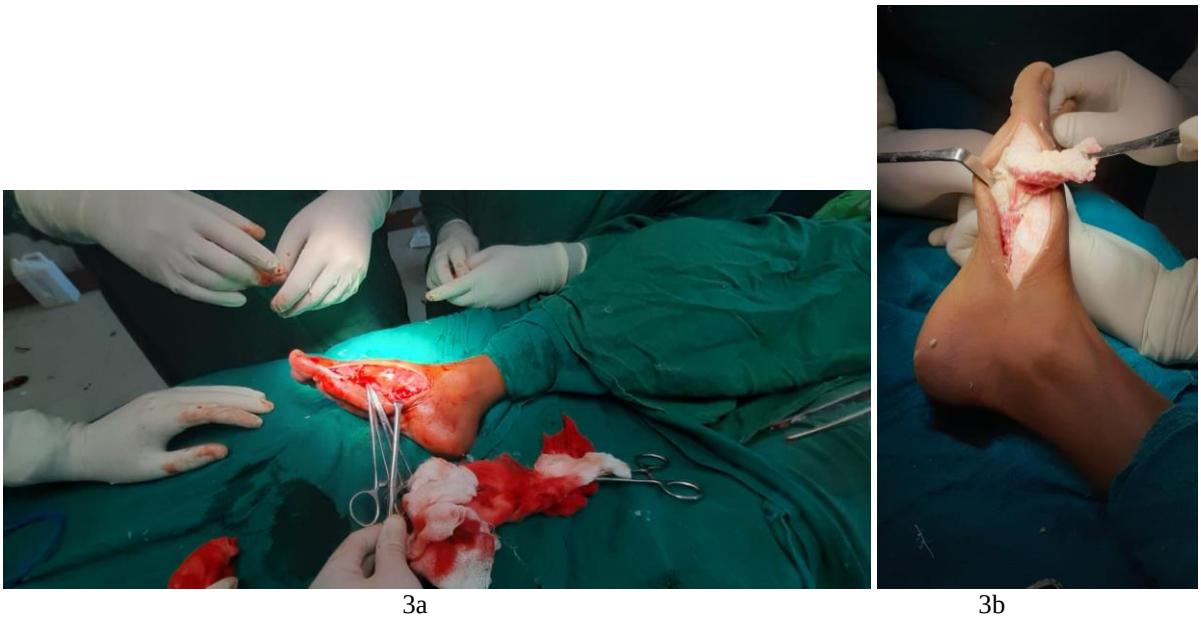
1a 1b 1c

Fig 1: Clinical & radiological images showing swelling over medial & plantar aspect of right 1st metatarsal (1a;1b;1c)



2a **2b**

Fig 2: MRI SECTIONS: Showing well defined lobulated lesion measuring 31*31*55 mm medial plantar aspect of 1st metatarsal displacing FHL Tendon. (2a; 2b)



3a 3b

Fig 3: Surgical excision of tumoral calcinosis swelling (3a; 3b)

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