CASE REPORT

Hyperphosphatemic tumoral calcinosis

Saumyaranjan Mallick,¹ Zohra Ahmad,² Arun K Gupta,² Sandeep R Mathur¹¹Department of Pathology, All India Institute of Medical Sciences, New Delhi, India²Department of Radiodiagnosis, All India Institute of Medical Sciences, New Delhi, India**Correspondence to**Dr Saumyaranjan Mallick,
drsmallick.aiims@gmail.com**SUMMARY**

Tumoral calcinosis (TC) is a rare locally aggressive lesion characterised by extra-articular soft tissue deposition of the calcium phosphate around large joints. The exact aetiology is not known. A 19-year-old boy presented with a painful progressive swelling around the bilateral elbow and left hip joints over a 6-month duration. Routine laboratory results showed a normal haemogram, and normal calcium and high phosphate levels. Imaging showed a soft tissue calcified mass around these joints. The cut surface of the excised mass showed myxoid material with areas of calcification. On microscopy, there were typical features of TC. Our case is being presented due to the rarity of the entity and the peculiar dual energy CT (DECT) finding which are being described for the first time in this pathology.

BACKGROUND

Tumoral calcinosis (TC) is a rare locally aggressive, benign condition first described by Duret.¹ The term TC 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 TC is characterised by extra-articular soft tissue deposition of calcium phosphate. TC may arouse de novo (primary/idiopathic) or secondary to other conditions like renal failure, hypervitaminosis and hyperparathyroidism.⁵ Familial forms of TC have also been described and are usually associated with mutations of genes like GLANT3, FGF23 and *okloto*.⁶

CASE PRESENTATION

A 19-year-old boy presented with swellings in the bilateral elbow and left hip over a 6-month duration. The swellings increased progressively and were associated with pain. His medical history was insignificant except for recurrent episodes of fever. There was no history of trauma, haematuria, abdominal pain, renal insufficiency or similar family history. Physical examination showed tender hard masses in the extensor aspects of the bilateral arms (elbows) (figure 1E) and around the left hip joint. 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 bilateral elbow joints but the motion of hip articulation was normal.

INVESTIGATIONS

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.

Plain radiographs (antero-posterior view) showed large lobulated calcified masses on the extensor aspect of the bilateral elbows and left hip in the periarticular location (figure 2A,B). Non-contrast CT scan demonstrated lobulated calcified masses in the intermuscular planes on the extensor aspects of the left hip and bilateral elbows. No intra-articular extension or bony erosions were noted. To further evaluate the lesions, the patient was subjected to MRI. On T1-weighted images, the lesion showed a diffuse hypointense signal (figure 2C). On T2-weighted images, it was predominantly hypointense with few interspersed nodular hyperintense foci (figure 2D). The hypointense nature on both T1-weighted and T2-weighted images can be attributed to the calcific nature of the deposits, and the foci of T2 hyperintensity suggest the presence of inflammation. On dual energy CT (DECT), the masses showed a blue colour consistent with calcium and the lobulated masses had a cobblestone appearance consisting of multiple distinct lobules of calcium containing material (figure 3J–L). The masses around the left elbow 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 60×40×30 mm in dimension. The cut surface of the tumour was grey-white and gelatinous with areas of calcification (figure 1F).

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 (figures 1G, H). The histomorphological features are consistent with TC.

DIFFERENTIAL DIAGNOSIS

- ▶ Myositis ossificans.
- ▶ Calcinosis of renal failure.

TREATMENT

- ▶ Surgical removal of mass.
- ▶ Phosphate-restricted diet.

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Figure 1 Clinical picture showing a swelling in the posterior aspect of the elbow (E). A gross photomicrograph shows a soft tissue mass measuring 60×40×30 mm. The cut surface shows a myxoid area with calcification (F). Photomicrograph geographic foci of calcification surrounded by palisaded histiocytes and numerous foreign body type giant (G, H&E×200). Photomicrograph shows calcium stained with a Von Kossa stain (H).

OUTCOME AND FOLLOW-UP

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 ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) 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 hyperphosphatemic. The primary TC may be sporadic or familial. The sporadic form is most common and usually occurs in the young adolescent black populations.⁷

Familial hyperphosphatemic TC is an autosomal recessive metabolic disorder where there is a loss of fibroblastic growth factor 23 (FGF23), GalNAc-transferase 3 (GALNT3), an enzyme which initiates O-linked glycosylation and the α kltho 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

Figure 2 Radiographs of the hip (B) and bilateral elbows-anteroposterior view (A) shows periarticular lobulated calcified masses in the left hip and bilateral elbows not extending within the joint. No obvious erosions are noted in the adjacent bones. Coronal T1-weighted MRI of the hip shows hypointense lobulated deposits in the intermuscular plane in the left hip, suggestive of their calcific nature. Coronal T2-weighted MRI of the hip shows a few hyperintense nodular areas of deposits corresponding to inflammation (black arrow) within the intermuscular planes around the left hip joint with interspersed hypointense areas corresponding to calcification (white arrow) with joint effusion.

Figure 3 Coronal dual energy post processed images and volume rendered images show lobulated masses around the left hip with a cobblestone appearance (J and K). Volume rendered dual energy image of the left elbow showing a similar appearance to hip (L).

TC shows a defect in the σ motif domain containing protein (SMAD9).⁸ The exact physiological role of SMAD9 is not clearly known. But it is hypothesised that SMAD9 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 (diaphysitis).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 periosteal 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.

Learning 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.

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Competing interests None.

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