Ultrasonographic Diagnosis of Tumoral Calcinosis in End-Stage Renal Disease
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ABSTRACT
We report the case of a young 25-year male, a known case of end-stage renal disease (ESRD), undergoing irregular dialysis sessions, who presented with multiple swellings along the extensor surfaces of large joints of body including shoulders, sacrum, wrists and elbows. The swellings were initially painless, but later became painful on movements alone, were causing hindrance in movement and the sacral lump was causing difficulty in lying supine. On evaluation by laboratory investigations, he revealed borderline hyperphosphatemia and hypocalcemia. The patient was referred by the treating physician to radiology department for assessment and evaluation of the periarticular swellings. Musculoskeletal ultrasound revealed multiple, large, hypoechoic shadows in subcutaneous location around both shoulders, elbows, wrists and sacrum. The needle aspirate showed thick whitish liquefied material which revealed amorphous, basophilic, clumps of dystrophic calcification on cytology. He was on irregular treatment and dialysis sessions. He was diagnosed as a case of tumoral calcinosis on the basis of history, examination and investigations. He was recommended surgical excision of the large swellings which were causing hindrance in his activities of daily living. He was put on phosphate lowering drugs and diet. Regular hemodialysis sessions were scheduled, but the patient had a fast downhill course and died within a month of diagnosis of tumoral calcinosis.


INTRODUCTION
Tumoral calcinosis is a rare familial condition characterised by solitary or multiple painless, periarticular masses caused by a hereditary metabolic dysfunction of phosphate regulation associated with massive periarticular calcinosis.¹

The true incidence is unknown. Most of the data comes from case reports or small case series.² The condition predominantly affects young black patients with an equal male to female ratio. Although the pattern of inheritance is still debated, the generally accepted mode of transmission is autosomal dominant with variable expressivity. However, recent discoveries in the field of genetics have identified autosomal recessive mutations, specifically of genes, GALNT3 and FGF23, which induce metabolic dysregulation of phosphate, suggesting a posttranslational defect.²

Although this term is used liberally to describe any massive periarticular calcification,² the classic tumoral calcinosis lesions were characterised as lobular, densely calcified masses confined to the soft tissue, generally on the extensor surface of the joint in the anatomic distribution of a bursa. The most common locations of tumoral calcinosis in descending order are the hip, elbow, shoulder, foot, and wrist.² It may appear spontaneously or secondary to chronic renal insufficiency, hyperparathyroidism, hypervitaminosis D, and other metabolic disorders.¹ Histologically, these lesions appear same² regardless of the etiology, which explains why periarticular calcifications of different nature are often called tumoral calcinosis. The treatment of massive periarticular calcinosis depends largely on its underlying cause. This case emphasises the importance of recognising and documenting this rare entity.

CASE REPORT
The patient was a 25 years old male, a known case of end-stage renal disease (ESRD), since last 2 years, presenting with complaint of rapidly growing swellings around large joints including shoulders, sacrum, wrists and elbows. The swellings, located around his shoulders and sacrum, were of major concern as they were disturbing his positioning and movement. Initially, he observed the swelling around right wrist one year back, which gradually increased in size. Then, he noticed swelling around left shoulder and then in the right shoulder, which was initially painless, but later on became painful on movements only. The left elbow and sacral region were involved later. The swelling at sacrum was causing difficulty in lying supine and sitting upright. The right shoulder swelling measured 9x11 cm, left shoulder 8x10 cm, left elbow and right wrist 7x6 cm and sacral swelling spanned over an area of 7x10 cm (Figures 1, 2 and 3). These swellings were non-tender
with overlying shiny skin. Multiple lobulations could be seen grossly, particularly in the wrist, shoulder and sacral swellings.

His laboratory investigations revealed markedly deranged renal profile. His hemoglobin was 6.1 g/dl with normal leukocyte count. Serum calcium was 7.8 mg/dl (normal 8.5 - 10.5 mg/dl) and slightly raised S. phosphorus levels of 5.0 mg/dl (normal 2.5 - 4.5 mg/dl in adults). His uric acid levels, bilirubin and alanine aminotransferase (ALT) were within normal range. Hepatitis screening was positive for hep 'C'. His ultrasound kidney, ureter, bladder (KUB) showed ESRD, bilateral nephrolithiasis, left-sided hydronephrosis and right-sided moderate pleural effusion. Echocardiographic findings revealed moderate pulmonary hypertension, mild mitral and aortic regurgitation with mild pericardial effusion.

His X-ray shoulder revealed multiple, large, lobulated amorphous calcific density areas, seen around both shoulders, wrists, elbow joints and sacrum. Small fluid levels (milk of calcium) were also noted in these areas (Figures 1, 2 and 3). Underlying joints appeared normal. Musculoskeletal ultrasound revealed multiple, large, hypoechoic shadows along the bursae of both shoulders, elbow and subcutaneously over the wrist and sacrum. These areas showed dense septations and fine internal echoes bordered by well defined hyper echoic rim. Multiple, small, dense areas were also noted in these locations (Figures 1, 2 and 3). On Doppler, no vascularity was noted in these swellings. Ultrasound-guided aspiration of liquefied material from sacral swelling using 20-G lumber puncture (LP) needle revealed 3 ml of thick whitish fluid, which showed no pus cells on Leishman stain, no organism on gram stain and no AFB on ZN stain. Bacterial culture did not reveal growth of any organism after 48 hours. The cytology showed amorphous basophilic clumps of dystrophic calcification. Direct microscopy revealed occasional red blood cells (RBCs), and irregular shaped cells. Keeping in view the history, examination and investigations, a final diagnosis of tumoral calcinosis was made.

He was reviewed by a panel of doctors including physician, nephrologist, pathologist, radiologist and rehabilitation specialist. He was on hemodialysis irregularly showing poor compliance to both oral medications and dialysis. Though twice a week sessions were recommended, but he failed to comply with the schedule. He underwent multiple blood transfusions to correct anemia. His past history revealed surgery for nephrolithiasis at the age of 7 years. There was family history of hypertension and renal stones on maternal side.

He had been receiving hemodialysis sessions for five years before he first visited to our facility. The patient was offered phosphate lowering medicines and surgical removal of swellings along with regular hemodialysis sessions twice a week.

The purpose of this case report is to bring in the importance of tumoral calcinosis as a disorder of metabolic dysfunction, which may be secondary to chronic renal failure or may result in ESRD.

**DISCUSSION**

The term tumoral calcinosis was introduced in 1943 by Inclan et al.\(^3\) It is a familial condition characterised by solitary or multiple, painless, periarticular masses.\(^4\) Massive periarticular calcinosis of the soft tissues is a unique but not rare radiographic finding. Diagnosis is difficult with imaging alone and relies on a combination of typical radiologic features and biochemical profile.\(^5\) Many of the mimics of periarticular calcification in renal patients share the radiologic features of tumoral calcinosis, including similar distribution, size, and morphology. Therefore, one approach to differentiating tumoral calcinosis from its mimics is by categorising soft-tissue calcification in terms of serum chemistry.\(^6\)
Tumoral calcinosis has a typical appearance on radiographs, i.e. amorphous, cystic, and multilobulated calcification located in a periarticular distribution.\(^2\)

High resolution ultrasound (US) has been widely used in the evaluation of musculoskeletal disorders based on its culminating resolution of superficial structures, excellent delineation of muscles, tendons and ligaments and allowance for real time guided interventions. Hence, US imaging has been proposed as an alternative diagnostic method,\(^7\) in the recent literature in various soft tissue lesions. As the lesions of tumoral calcinosis are superficial to the joints, and mostly along the bursae of large joints, hence the musculoskeletal ultrasound is a very useful modality in determining the extent, contents, and underlying joint status. The aspiration of these swellings reveal thick liquefied chalky white material which shows a calcific amorphous centre surrounded by a cellular zone of fibroblasts, chronic inflammatory cells, histiocytes and osteoclast like giant cells during the active phase. In the inactive phase, there is calcified material bordered by thick fibrous tissue with cystic spaces.\(^6\)

Medical treatment is preferred over surgery in patients with tumoral calcinosis who have multiple swellings. Surgical excision of the tumoral calcinosis lesion is a well-documented treatment, but high rate of recurrence is common, particularly when it is actively progressing.\(^2\)

Surgical excision is associated with postsurgical complications that include infection and fistula formation.\(^9\) Surgical excision and phosphate deprivation (using aluminum hydroxide) along with acetazolamide has proved to be the most effective therapy. Phosphate depletion in both normo- and hyper-phosphatemia has proved to have variable success.\(^10\)

To the best of authors’ knowledge, this is the first case report on tumoral calcinosis from Pakistan. This report highlights the importance of diagnosing this disorder earlier and differentiating it from other calcifications, so that the management is started earlier. Secondly, it shows the importance of musculoskeletal ultrasound, which is becoming increasingly popular in detecting soft tissue pathologies of diverse etiologies.

REFERENCES