Retrospective Study of Seven Patients with Tumoral Calcinosis

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Abstract

Introduction: Calcium deposition in the skin has been termed as calcinosis cutis. Tumoral calcinosis is idiopathic form of calcinosis cutis. Etiology of idiopathic calcinosis cutis is unknown. It is characterized by periarticular deposition of amorphous calcium salts around large joints. Our diligent search through literature could not find any consensus on the etiopathogenesis and treatment modalities for tumoral calcinosis.

Materials and Methods: A retrospective study of seven patients of tumoral calcinosis treated with complete surgical excision over a period of 1 year was done. Demographic details were compiled. Routine blood investigations were performed. All patients underwent radiographs and magnetic resonance imaging (MRI) scans of involved part. We did not perform computed tomography (CT) or bone scan in any of our patients. All seven patients underwent surgery and were followed up till 2 years.

Results: In our study, five were female and two were male patients ranging from 31 to 76 years. Size of swelling varied from 2 to 15 cm. Most common location was hip. Serum calcium, phosphorus, and alkaline phosphatase were normal in all patients. Radiographs showed well-outlined periarticular cluster of calcifications in the soft tissues around joint. MRI revealed round to oval multiple cystic lesions around the affected region, but not involving the joint.

Conclusion: Tumoral calcinosis is always the diagnosis of exclusion. It can be normophosphatemic or hypophosphatemic subtype. Large joints are more commonly affected. One can rely on radiographs for diagnosis. MRI for knowing exact location of lesion, its relationship with adjacent structures and planning of surgery is advocated. Complete surgical excision is the only optimum treatment of tumoral calcinosis.

Keywords: Amorphous calcium phosphate, hyperphosphatemia, X-ray film, hip joint, calcinosis, magnetic resonance imaging.

Introduction

Calcium deposition in the skin has been broadly termed as calcinosis cutis, which was first coined by Virchow [1]. Four types of calcinosis cutis have been described in available literature: Dystrophic, idiopathic, metastatic, and iatrogenic [2]. Commonly used term "tumoral calcinosis" is basically the idiopathic form of calcinosis cutis. Inclan 1st time used tumoral calcinosis term in 1943 although it was described previously by Giard, Duret, and Teutschlander separately in their study [3].

Dystrophic calcinosis cutis is mainly associated with infection, inflammation, skin tumors, or connective tissue disorders [4]. Etiology of idiopathic calcinosis cutis is unknown but they are thought to occur in the background of normal serum calcium levels. Elevated serum calcium or phosphorus levels are primarily associated with metastatic calcinosis cutis.

Tumoral calcinosis is characterized by periarticular deposition of amorphous calcium salts and calcium hydroxyapatite crystals mainly around the hip, knee, shoulder, and elbow joint [1]. Surgical excision is the principal treatment modality for tumoral calcinosis.

This study represents our experience of seven cases of tumoral calcinosis seen during the period 1 year in our institution.

Materials and Methods

We retrospectively studied seven patients of tumoral calcinosis diagnosed and histologically proven in our institution over a period of 1 year between May 2015 and April 2016. Demographic details such as age, sex, location and size of swelling, clinical history, and radiological presentations were reviewed as per standard protocol.

Routine blood investigations including complete blood count, serum creatinine, urea, serum calcium, phosphorus, and alkaline phosphatase levels were performed in all cases. All patients underwent radiographs and magnetic resonance imaging (MRI) scans of involved part. MRI was performed with a 1-Tesla MRI system. Four patients underwent ultrasound studies for swelling before MRI. Fine-needle aspiration and cytology or biopsy was not performed in any patients.

All seven patients underwent surgery. Patients were followed up at months 3 and 6 and years 1 and 2. Recurrence rate was

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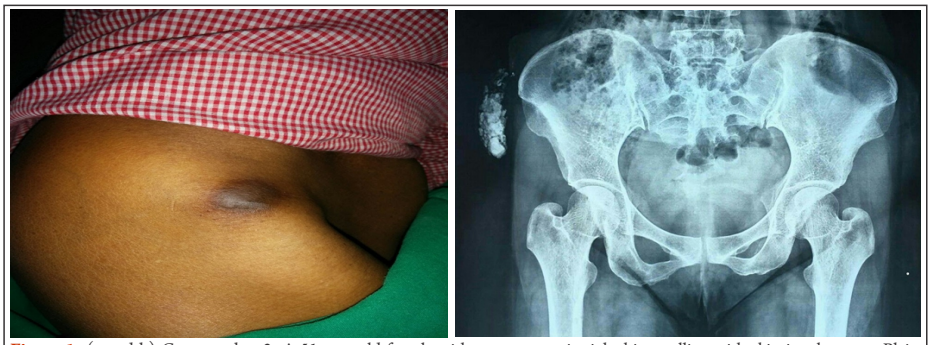

Figure 1: (a and b) Case number 2: A 51-year-old female with post-traumatic right hip swelling with skin involvement. Plain anteroposterior radiograph of pelvis of same patient showing diffuse soft-tissue calcification in the right thigh without involvement of hip joint.

carefully reviewed. Data were compiled in a database using Microsoft Excel.

Results

In our study of seven patients, five were female and two were male patients. Patients ranged in age from 31 to 76 years [Table 1]. A history of trivial trauma was noticed in 1 patient [Figure 1]. None of the patients had any known metabolic disease or proven malignancy before appearance of swelling.

Detail clinical history was reviewed and we noticed that patients in our study presented, an average 14 months after initial onset of symptoms (range: 2–72 months). All patients had complaints of pain as swelling increased in size, but major symptom for hospital visit was gradual increase in the size of swelling [Table 1]. The size of the swelling varied from 2 to 15 cm in largest dimension [Table 1]. Restricted movement of joint was observed in one patient with knee swelling [Figure 2]. The swelling was most often located around hip joint and it was observed in five patients and two of them had bilateral swellings [Figure 1]. One patient each out of seven had swelling located on knee and elbow joint. Skin infection due to pressure effect of swelling was noticed in three cases, two out of them were draining chalky milk like fluid on expression from sinus [Figure 2]. None of the swellings had any ulceration.

Review of physical examination of these patients showed that all seven patients had firm to hard consistency swelling around hip (5), knee (1), and elbow (1). Physical findings revealed that swellings were mobile in all the cases and none of them had any features of fixity to underlying muscle or bone. Skin was adherent to swelling in four patients.

Blood investigations including blood urea, serum creatinine, calcium, phosphorus, and alkaline phosphatase were within normal limits in all seven patients. Radiographs showed well-outlined periarticular calcification in the soft tissues around affected joint. There was cluster of calcifications consisting of multiple small and round opacities with different sizes separated from bone. Radiographs did not show any bony deformation or destruction. Ultrasound studies which were performed in four patients demonstrated well-demarcated soft-tissue masses separated from underlying bone with heterogeneous echogenicity. Swellings were multicystic in all cases containing anechoic or hypoechoic liquid.

MRI study revealed round to oval multiple cystic lesions in the soft tissues around the affected region, but not involving the joint. Lesions showed intermediate to low signal with hypointense foci on T1-weighted MRI, whereas T2-weighted images showed heterogeneous lesions with hyperintense multiloculated cystic structure with hypointense foci. We did not perform computed tomography (CT) scan or bone scan in any of our patients based on our clinical judgment and preliminary diagnosis.

All patients underwent complete surgical excision of lesion after detail pre-operative workup. Elliptical incision was placed whenever it was possible and in four cases, skin was also excised as it was adherent to mass. Mass was excised in toto and primary skin closure was done in all cases. No surgical complications were noted in any of the cases. There was no evidence of recurrence till 2 years of follow-up.

Macroscopic examinations of the excised specimens demonstrated multiloculated whitish creamy to chalky fluid-filled masses of varied sizes. Largest mass was seen around knee joint followed by hip and elbow, respectively. Histopathological study showed typical granular calcified central areas surrounded by macrophages, histiocytes, lymphocytes, and occasional multinucleated giant cells. There was a characteristic fibrous wall separating central area from surrounding granulation tissue.

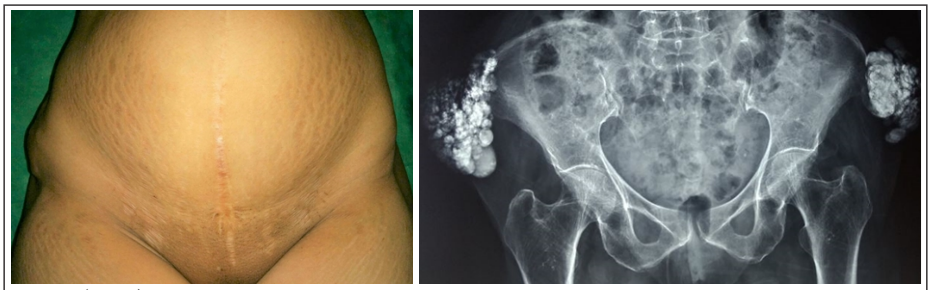

Figure 2: (a and b) Case number 3: A 47-year-old female with bilateral hip swelling without skin involvement. Plain radiograph of the pelvis of same patient including thigh anteroposterior view showing extensive, ribbon-like periarticular calcification in the soft tissues around bilateral hip joint.

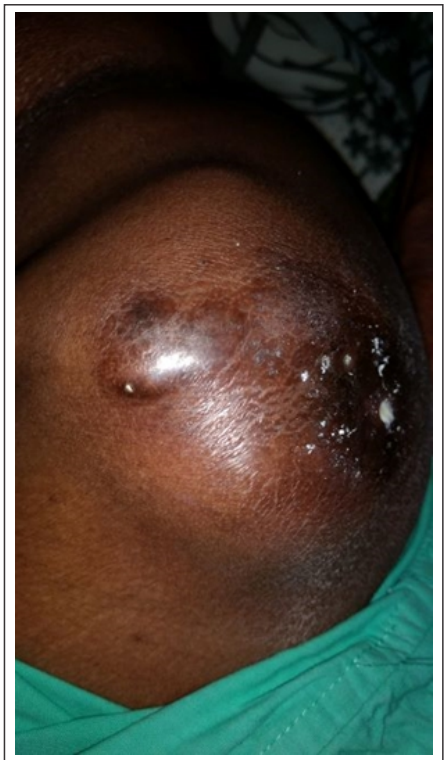

Figure 3: Case number 5: A 59-year-old male with large 13 cm × 15 cm cystic consistency swelling over left knee with skin involvement and whitish chalky discharge.

Physical findings, multiple clinical investigations, and final histology reports were suggestive of the diagnosis of primary normophosphatemic, normocalcemic idiopathic form of calcinosis cutis – "tumoral calcinosis."

Discussion

Calcinosis cutis which is a deposition of calcium salts within the dermis is broadly categorized into four types – dystrophic, idiopathic, metastatic, and iatrogenic [2]. The most common form of idiopathic calcinosis cutis is termed as "tumoral calcinosis." The exact incidence of tumoral calcinosis is still unknown.

Tumoral calcinosis is a benign condition characterized by gradually increasing juxta-articular calcified soft-tissue masses due to deposition of hydroxyapatite or amorphous calcium phosphate crystals [5]. The exact etiology of idiopathic tumoral calcinosis is still unclear; however, diligent literature review suggests the possible linkage with an inborn error of phosphorus and Vitamin D metabolism [3]. Inclan et al. have also described the unique autosomal recessive type of tumoral calcinosis known as familial tumoral calcinosis [6].

Tumoral calcinosis is mainly subdivided in to primary normophosphatemic or primary hypophosphatemic type depending on the serum phosphate levels, although in both these subtypes, serum calcium levels remain normal [7]. We reviewed seven consecutive cases of calcinosis cutis which were idiopathic tumoral calcinosis with normophosphatemia and normocalcemia.

In our retrospective study, we observed that tumoral calcinosis was 70% more common in female than male. Patients age ranged from 31 to 76 years but it was more common in the 4th decade of life. Chaabane et al. in their study of nine patients found that tumoral calcinosis was more common in the first three decades of life without any sex predominance [3]. Another case series of 11 patients found that it was common in male and particularly in the 2nd and 3rd decades with 90% of cases who were seen in <11 years of age [8]. Literature also mentions one case of tumoral calcinosis seen in a 1-year-old child [9].

The most common location for soft-tissue swelling was hip joint (5) followed by knee and elbow joint (1 each) in our seven patients. Among hip joint right side was most commonly involved in four cases, although we could not find any specific relation of it with pathogenesis. Noyez et al. mentioned hip and elbow joint as most common location for appearance of swelling in their study [8]. They also found few cases of tumoral calcinosis involving hands, feet, and knees too. Another study by Niall et al. found hip joint as most common location for swelling like our study [10]. Surprisingly, one study noted that swelling was most commonly seen around elbow followed by hip and feet in their study of nine cases [3].

Two patients in our study had bilateral hip swellings. Another studies also found bilateral swellings in their studies [8, 9]. Fujii et al. in fact mentioned that two-third of patients in their series had multiple swellings [11]. Chaabane et al. mentioned about 80% swellings around elbow joint were bilateral [3]. Exact etiology and pathogenesis for bilateral tumoral calcinosis are not clear.

We noticed that almost all patients in our series had initial complaint of swelling around affected joint which gradually increased over the varied period of time. Pain was associated with large swellings and it was never the preliminary complaint or reason for hospital visit. This finding was consistent with other literature studies of tumoral calcinosis [3, 4, 8]. We found that mean duration of symptoms was 14 months (range: 2–72 months). In a review outcomes of other studies, duration of presentation varied from 2 months to 8 years [2, 3, 4]. Association of history of trauma was seen in one patient in our series, similarly, it was seen in two out of nine cases of another study [3]. We tried to correlate the history of trauma in our one patient and subsequent formation of swelling although, we could not find the enough association like other studies in literature [3].

Size of swelling in our seven patients varied from 2 cm to 15 cm in diameter in its greatest dimension. Largest swelling of 15 cm × 13 cm was seen around left knee who had restricted range of motions. This patient gave the history of 5 years of duration of swelling. At the time of presentation, swelling was cystic in consistency with sinus draining chalky white discharge on expression. Another study found that swelling varied from 4 cm to 15 cm and patient with largest swelling of 10 cm × 12.6 cm around left elbow and had restricted movements [3]. Literature postulates that large tumors may interfere with joint movements and also can lead to pain by nerve compression [9, 12]. Ulcerations or sinuses can occasionally appear in such large swellings.

Routine blood investigations usually indicate normal calcium level, renal function test, alkaline phosphatase, and parathyroid hormone level [13]. Phosphate and Vitamin D levels can be within normal range or slightly lowered. We observed in our all seven patients, calcium, phosphate, as well as rest of blood investigations were within normal limits. One study found five patients in their series had hyperphosphatemia [14].

Tumoral calcinosis appears as well-demarcated, irregular, calcified masses separated by fibrous septae, usually around large joints without any bony involvement on almost all imaging modalities [15]. Plain radiographs are often diagnostic and the first imaging done in tumoral calcinosis as it was performed in our all seven patients. Radiograph findings in our patients were consistent with other reports available in the literature showing characteristic well-demarcated calcified masses of multiple round or oval opacities with different size in the periarticular soft tissue, separated by radiolucent fibrous septa [2, 3, 4, 8]. Salutario et al. mentioned the peculiar "sedimentation sign" seen on radiograph due to X-ray films exposed with a horizontal beam causing mineral portion pooling dependently and creating a fluid calcium level [12, 16].

Due to unusual pattern and location of these swellings, we also performed ultrasonography in four patients. One study also performed ultrasonography in their all nine cases and found that there were multilobulated masses with multiple cavities filled with anechoic or echoic fluid divided by thin septa [3]. We observed similar findings in our series too.

Our diligent search of available literature revealed that the plain radiographs and CT imaging are useful modalities for diagnosing calcified material in tumoral calcinosis. Although majority studies preferred MRI over CT as the swellings in the tumoral calcinosis are located within the soft tissues [17].

MRI findings of various studies in literature and in our patients were similar more or less without any significant difference [1, 2, 3, 4, 8, 14, 16]. We did not perform CT scan or bone scan in any cases. CT findings may vary

Table 1: Detail case history findings

Case	Age	Sex	Primary location of swelling	Other localization of swelling	Clinical features	Investigations	Preliminary diagnosis	Intraoperative size of swelling in centimeters	Treatment
1	39	M	Hip R	-	Swelling Pain	MRI	Calcified granuloma	6 × 7.3	Surgery
2	51	F	Hip R	-	Swelling Pain	USG MRI	Post- traumatic calcified hematoma	2 × 3	Surgery
3	47	F	Hip R	Hip L	Swelling Pain	USG MRI	Bilateral ectopic calcification	4 × 3 3 × 2.6	Surgery Bilateral side – same setting
4	37	F	Hip L	-	Swelling Pain	MRI	Calcified Guinea worm	9 × 8	Surgery
5	59	M	Knee L	-	Swelling Pain Restricted joint movement	USG MRI	Infected cystic calcification	13 × 15	Surgery
6	31	F	Elbow L	-	Swelling Pain	MRI	Calcified granuloma	3.5 × 2	Surgery
7	76	F	Hip R	Hip L	Swelling Pain	USG MRI	Bilateral ectopic calcification	11 × 8.5 4 × 6	Surgery Bilateral side – same setting

M: Male, F: Female, R: Right, L: Left, USG: Ultrasonography, MRI: Magnetic resonance imaging

in tumoral calcinosis according to Chaabane et al. [3]. They found that swellings may consist of cystic components with low attenuation centers and nodular calcified component separated by septations. Fluid calcium levels may be seen. Some studies also performed radionuclide bone scans and found increased uptake of Tc-99m-labeled phosphate in the mass allowing to detect very small and asymptomatic lesions [9, 18].

We emphasize to perform MRI in all cases of tumoral calcinosis additional to bare minimum radiograph whenever and wherever the cost-effectiveness is not an issue. We think that MRI is superior to CT to detect septal enhancement in masses and it also provides definitive information about the location of swelling, its extent, and relation with adjacent soft tissue and bone for better planning of surgery.

Tumoral calcinosis itself is slow growing in nature but it can lead to pain and functional limitations as swelling progresses in size. Definitive treatment should be planned once the diagnosis has been confirmed. Literature believes that spontaneous regression of tumoral calcinosis does not occur and we agree on same. Although, Niall et al. in his study confirmed the total regression of tumoral calcinosis in an infant [10]. Medical treatment suggested in available literature has been proven unsuccessful [8, 9, 12, 19]. Some mentions the use of calcium and phosphate restricted diet and phosphate-binding antacids in hyperphosphatemic tumoral calcinosis subtype having defective phosphate metabolism [9, 10, 11, 20]. Particularly, acetazolamide having pharmacokinetic property of increasing urinary phosphate excretion is been the typical drug of interest in few studies with hyperphosphatemic tumoral calcinosis [19, 20]. We could not find any study advocating these medical treatment for normo- or hypophosphatemic tumoral calcinosis.

We performed complete surgical excision in all our seven cases including those who had bilateral swellings. We think that surgery is the optimum treatment modality with comparatively sound results than no treatment or medical management. Many other studies also supported the role of surgery in tumoral calcinosis [8, 9, 10, 11, 12]. We concluded from available literature that indications for surgery in these patients were pain, recurrent infection, ulceration, and functional impairment due to the swelling.

Recurrence after surgical excision is not uncommon, but according to the various studies, it is mainly due to the inadequate excision on prior setup [10]. Surprisingly, recurrence rate appears to be same irrespective of tumoral calcinosis subtype. Exact recurrence rate post-surgery in tumoral calcinosis still remains unknown due to the less number of cases reported in literature and various different modalities used in different cases.

There is no available consensus for the treatment of tumoral calcinosis. In our reviewed cases, complete surgical excision was done and we did not encounter any recurrence till 2 years of follow-up. One study postulated that one of the main reasons for recurrence in patients who underwent surgery was the surgical intervention done during the active phase of tumoral calcinosis [21]. In some cases, lesions can recur even after multiple attempts of complete surgical excision [20].

Conclusion

We decided to do retrospective study of tumoral calcinosis in our institute as our diligent search found that there are still no accepted consensus about exact etiology, pathogenesis, and treatment of tumoral calcinosis. Tumoral calcinosis is the most common form of calcinosis cutis mentioned in the available literature. We wish to emphasize that tumoral calcinosis is always the diagnosis of exclusion. One has to dig into detail clinical history, blood biochemical and radiographs, and also additional MRI and/or CT investigations before labeling calcinosis cutis as idiopathic tumoral calcinosis. Differential diagnosis of other variants of calcinosis cutis such as chronic renal failure, hyperparathyroidism, chronic vitamin D intoxication, milk-alkali syndrome, collagen vascular diseases, and metastasis should be ruled out carefully.

One has to remember the vast variations in the presentations in case of tumoral calcinosis, it can be normophosphatemic or hypophosphatemic, but serum calcium levels almost always remains normal. Although, hyperphosphatemic tumoral calcinosis is rare form, the presence of high phosphate levels should not vary the diagnosis. Large joints such as hip, knee, and elbow are more commonly affected in it but rarely can also occur in small joints.

We think, one can surely rely on radiographs for confirmatory diagnosis in initial workup of tumoral calcinosis; however, we advocate to do MRI in each case whenever feasible for knowing exact location of lesion, its relationship with adjacent structures and planning of surgery.

We recommend, one should always consider for complete surgical excision in cases of tumoral calcinosis irrespective of its size, location, number, and type. Some schools of thought like us still believe that meticulous complete surgical excision is the only optimum treatment of tumoral calcinosis and with the proper margin recurrence can be prevented.

Prospective studies with large number of cases are necessary to understand the exact etiopathogenesis of idiopathic tumoral calcinosis and to establish the treatment consensus.

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