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Tumoral calcinosis in an 8-year-old girl: A case report

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ABSTRACT

Introduction: Tumoral Calcinosis is a rare, benign metabolic disorder, characterized by the deposition of calcium phosphate crystals in extra-articular soft tissues. Less than 400 cases have been described globally, with only around 10 % being described in the pediatric population. Large bilateral masses are exceedingly rare.

Case report: We present a case of an 8-year-old female with bilateral 15 × 10cm posterior chest wall masses, who presented following a one-year history of enlargement. The patient had no medical or family history. A diagnosis of primary hyperphosphataemic tumoral calcinosis was suspected based on biochemistry and imaging. The patient had a raised phosphate and normal parathyroid hormone level, while ultrasound and Computed Tomography scans showed multilocular, calcified lesions with solid and cystic components. Core needle biopsy confirmed a diagnosis of tumoral calcinosis. Staged surgery was undertaken to resect the masses, which had extensive regional invasion. Clear margins were attained, with a rim of normal tissue on histology. The patient developed recurrent bilateral 15 × 20cm masses one year later, having defaulted post-operative treatment with Acetazolamide and Aluminium Hydroxide. Further surgery and medical management with the above agents was required. Six months post-surgery for the recurrence, no further recurrence was noted, but following poor adherence to her medical therapy another year later, there has been recurrence on the right, measuring 5 × 5cm. Treatment with Acetazolamide and Aluminium Hydroxide continue, with close observation for further growth.

Conclusion: A combination of targeted medical therapy with Acetazolamide and Aluminium Hydroxide, and early surgical resection, may limit the risk of recurrence in hyperphosphatemic tumoral calcinosis in the pediatric population.

1. Introduction

Tumoral Calcinosis is a rare clinical and histological diagnosis, especially in the pediatric population. Large, bilateral symmetrical cases are exceedingly uncommon. With a low level of clinical suspicion, diagnosis and management can be challenging. Lesions may mimic far commoner neoplastic conditions, and few clear treatment guidelines exist. We present a case of an eight-year-old female with large bilateral tumoral calcinosis lesions of the posterior chest wall.

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2. Case report

An eight-year-old female was referred by the pediatric endocrine unit to the pediatric surgery outpatient unit at our tertiary facility. She presented with a one-year history of rapidly enlarging posterior chest wall masses. This was associated with discomfort and impaired shoulder range of motion, lethargy and weight loss. The patient had no known comorbidities, and no significant family history.

Examination revealed a clinically well patient with normal vital signs. Two large symmetrical posterior chest wall masses overlying both scapulae were visualized. Both masses measured approximately 15 × 10cm (Fig. 1). They were irregularly shaped, soft, non-tender, non-mobile, and no overlying skin changes were present. Bilateral passive shoulder range of motion was mildly limited due to mass effect. There was no evidence of focal neurology.

Biochemical analysis revealed a normal white cell count, haemoglobin and platelets. Renal function was normal. Phosphate levels were elevated at 2.36 mmol/l (normal 1.33–1.92 mmol/l), with a normal calcium. Parathyroid hormone (PTH) was decreased at 0.9 pmol/l (normal 2.3–9.3 pmol/l). No pre-operative medical therapy was recommended by the endocrine unit.

An ultrasound was performed, showing multilocular lesions with no features to suggest malignancy. A core needle biopsy was performed, which demonstrated fibrous tissue bundles, free lying areas of calcification, as well as small areas of psammomatous calcifications. Giant cells, macrophages and reactive fibroblasts were also seen. These findings were in keeping with a diagnosis of tumoral calcinosis. A Computed Tomography (CT) scan was ordered, allowing for delineation of the lesions before surgical intervention. Macrolobular masses of the posterior chest wall were noted, with a mix of solid and cystic components, and areas of calcification. Invasion of the muscle layers of the chest wall was noted, with no intra-thoracic extension.

After a multi-disciplinary team discussion, the decision was made to resect one lesion at a time due to the size of the masses and significant muscle infiltration demonstrated on imaging. The left sided lesion was resected first – there was extension into the subscapular region with muscle involvement (Fig. 2). The mass was excised along with involved muscle, and a drain left in situ. No complications were noted. The drain was removed on the third post-operative day, and the patient was discharged the following day, with a clean wound and minimal pain. There was no neurological fallout and no impaired range of motion. The patient was reviewed two weeks later and was noted to have a well healed wound and no impaired range of motion. Histology confirmed a tumoral calcinosis diagnosis – numerous lobular aggregates of calcific substance evoking giant cell reactions. Clear margins were noted on histology, with a rim of non-pathological tissue.

The right sided mass was resected 6 weeks later. There was also subscapular extension, as well as extension into the axillary space, with muscle infiltration. The mass and surrounding involved muscle were once again resected, with a drain left in-situ. The drain was removed on the third post-operative day, with the patient being discharged the following day. Routine follow up two weeks later was uneventful, with a well healed wound. Histological findings were the same. The patient continued outpatient physiotherapy and was discharged from pediatric surgery for continued follow up by the endocrine unit. The patient was started on acetazolamide, a carbonic anhydrase inhibitor which aids in anion excretion, as well as aluminium hydroxide, used for its phosphate binding properties.

The patient defaulted medical treatment, and one year after her initial presentation, re-presented with recurrence of the masses bilaterally.

On examination, both masses had recurred, measuring 15 × 20cm. They now had overlying areas of skin excoriation. Biochemical analysis showed a normal PTH and calcium, but a raised phosphate of 2.16 mmol/l. Renal function was normal. A decision was made for surgical intervention, and a staged procedure was once again undertaken, with the left side being operated on prior to the right. During resection of both masses, extension was noted subscapularly, into the axillary space, with further extension anteriorly up to the

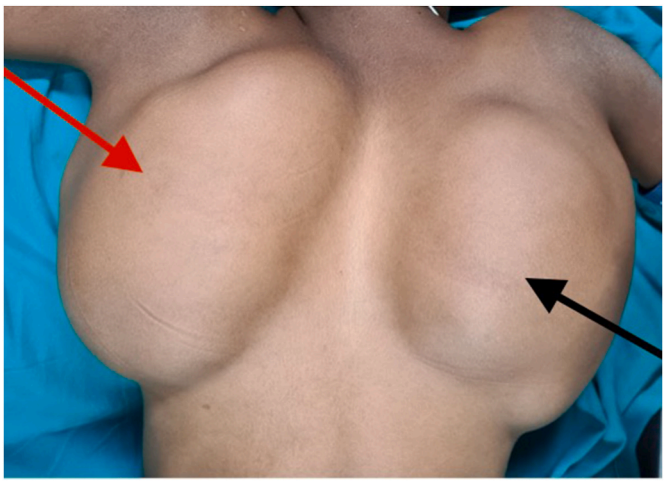


Fig. 1. Index Presentation - bilateral posterior chest wall masses.
Red arrow – left sided mass.
Black arrow – right sided mass.



Fig. 2. Intra-operative findings of left sided lesion – extensive subscapular extension with muscular invasion.

mid-axillary line. Muscle invasion was seen to be more extensive, and the masses themselves were more fibrotic than the initial lesions. Both procedures were uneventful, with macroscopic margins attained, but positive margins noted on histology. Post-operative course was the same as for her index surgeries.

On discharge, the patient was re-initiated on Acetazolamide as well as Aluminium Hydroxide by endocrinology. Follow up until 6 months post operatively was uneventful, with well healed wounds, and no recurrence (Fig. 3). 1 year post-operatively, there has been no further recurrence on the left, with a focal area of recurrence on the right measuring 5 × 5cm. Poor adherence to medical therapy has been noted. Medical management, adherence counselling and observation will continue.



Fig. 3. Wounds 6 months post second surgery for recurrence.

3. Discussion

Tumoral Calcinosis is a rare clinical and histological condition, characterized by calcium salt deposition in extra-articular soft tissue regions [1]. Regions most commonly involved include the elbow, shoulder and hip [2,3]. Multifocal lesions are not uncommon, but large symmetrical bilateral masses – as with the index patient - are exceedingly rare, having previously been described in an adult [4]. It is most common in young adults, with cases typically seen in African, Latin American and Middle Eastern populations [5]. Presentation is usually that of a firm, painless, enlarging mass, with associated disfigurement and movement difficulties due to mass effect [1,6].

The etiology of the disease is still not entirely clear, but three main origins have been described, split into primary (which has two subtypes) and secondary [7]. Primary tumoral calcinosis can be divided into normophosphatemic and hyperphosphatemic types. The normophosphataemic variant has been linked to possible repetitive minor trauma in the regions affected [7,8]. The hyperphosphatemic variant is linked to defects in phosphate excretion, and may have a genetic element to it, with around 70 familial cases described, linked to the Fibroblast Growth Factor gene [6]. Lack of genetic testing availability meant we were unable to ascertain a genetic component in our patient. Secondary tumoral calcinosis is usually seen in chronic renal disease, most commonly attributed to secondary or tertiary hyperparathyroidism [7,8]. Despite the different possible etiologies, clinical presentation is similar [3].

The diagnosis of tumoral calcinosis can be challenging, with lesions having a broad differential, mimicking multiple neoplastic or rheumatological disorders, such as sarcoma, tophaceous gout and myositis ossificans [3]. Perhaps unsurprisingly, our patient was initially referred as a suspected sarcoma. There are multiple modalities to aid in diagnosis, with imaging being the cornerstone. In smaller limb lesions, plain radiography may show multilobulated cystic calcifications around the joint involved [3,9]. Ultrasonography may show multiloculated cystic lesions and posterior acoustic shadowing. It can also be used to assess response to medical treatment in smaller lesions [5,9]. CT scans may show cystic locules and fluid-fluid layering caused by calcium deposition - the "sedimentation sign." Both ultrasound and CT were used to confirm diagnosis in our index patient. Axial imaging is also useful for surgical planning, with relations and extension of the lesion being key. Very rarely is there intra-osseous extension, another key feature differentiating it from other lesions [3]. Magnetic Resonance Imaging (MRI) and bone scintigraphy using radio-labelled phosphate – to detect smaller lesions and early recurrence - can also be used where resources allow [3]. Biopsy or FNA can reveal areas of fibrosis, calcium deposits and psammomatous calcifications, with typical cells including osteoclasts, giant cells and macrophages [3,10].

Treatment differs depending on the suspected type of tumoral calcinosis.

For both primary subtypes, early surgical excision was previously the preferred treatment. There is, however, a high rate of recurrence, often requiring multiple surgeries [2,3]. Control of phosphate levels both pre- and post-operatively may help with preventing recurrence [8]. This is typically achieved using phosphate binding agents such as aluminium hydroxide, along with acetazolamide, a carbonic anhydrase inhibitor, to induce phosphaturia [3,11]. Medical therapy has been advocated pre-operatively, as recurrence may be decreased if non-metabolically active lesions are excised [3,8,12]. Our index patient didn't receive pre-operative therapy, possibly leading to her early, severe recurrence.

A review of limited cases in pediatric patients has shown successful outcomes with a variety of treatment choices. Early surgical excision alone has been used in both primary subtypes with good outcomes [13,14]. Early aggressive resection in normophosphatemic variants can reduce the rate of or even prevent recurrence, whilst hyperphosphataemic variants have shown an overall good response to early surgical resection and medical management with phosphate binders and acetazolamide therapy [4,11,13,15]. Topical sodium metabisulfate, a compound shown to inhibit calcium oxalate agglomeration, along with acetazolamide therapy has led to regression of smaller lesions, negating the need for surgery [13,16]. None of these patients, however, had such large bilateral lesions.

Large lesions can prove surgically challenging if there is extensive invasion – as with the index patient - or involvement of neurovascular structures [12]. Bulk resection may aid in symptom relief, but recurrence of growth tends to occur at a faster rate [3,12]. Post-operative course can be challenging, with complications including infection, sinus tract formation and poor wound healing [3,12].

4. Conclusion

Tumoral calcinosis must be considered as a differential diagnosis in pediatric patients presenting with multi-focal soft tissue lesions. In primary hyperphosphatemic variants, a multi-disciplinary approach is imperative, as pre-operative medical therapy may prevent or minimize post-surgical recurrence in large lesions, or even negate the need for surgery with smaller lesions.

CRediT authorship contribution statement

M. Savadier: Writing – original draft, Investigation. **N. Maistry:** Writing – review & editing. **D.S. Harrison:** Writing – review & editing, Supervision, Conceptualization.

Statements

Informed consent was obtained from the patient's parents.

All authors attest that they meet the current ICMJE criteria for Authorship.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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