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Multiple ectopic calcifications in subcutaneous tissues with chronic renal failure: A case report

RongKai Zhang[a,1], GuoWei Li[a,1], LuKun Yang[b,1], YingQin Li[c], Jinghuan Ou[d], DaWei Zhang[a], Tao Chen[a], Shaoyan Feng[e,*]

[a] Department of Orthopaedics, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, 519000, China
[b] Department of Anesthesiology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, 519000, China
[c] Department of Radiology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, 519000, China
[d] Department of Allocation, Kaiping Central Hospital, Kaiping, 529300, China
[e] Department of Otolaryngology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, 519000, China

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ABSTRACT

BACKGROUND: Multiple tumor-like ectopic calcifications is a rare syndrome characterized by subcutaneous mass deposits of calcium phosphate in periarticular tissues. Although several cases of the surgical treatment of tumoral calcinosis have been reported, the present case is unique in that multiple ectopic calcifications in subcutaneous tissues were found in a hemodialysis patient who had been operated on a total of five times within a period of 1.5 years.
METHODS: A hemodialysis 60-year-old male presented with multiple tumor-like ectopic calcifications bilateral in the shoulders, right buttock and right thigh. He had been operated on a total of five times within a period of 1.5 years; the operations included a subtotal parathyroidectomy with parathyroid autotransplantation in the right forearm.
RESULTS: Complete excisions of the ectopic calcifications were performed in the left shoulder, right buttock and right thigh, without signs of recurrence in the same sites at follow-up. Incomplete excision of the ectopic calcification in the right shoulder resulted in recurrence in the same site, and the patient was operated on two more times 1.5 years following the initial surgery. Subtotal parathyroidectomy with parathyroid autotransplantation decreased serum levels of PTH, but the levels of serum calcium and phosphorus remained unchanged post-surgery, which appeared not to inhibit the recurrence of ectopic calcification in patients with CRF.
CONCLUSIONS: If conservative therapy failed, then early and complete surgical excision may be a good therapeutic option.

1. Introduction

Multiple tumor-like ectopic calcifications is a rare syndrome characterized by subcutaneous mass deposits of calcium phosphate in periarticular tissues, mostly around larger joints such as the hip, shoulder, or elbow, and occasionally around the joints of the hand, wrist or spine [1]. Tumoral calcinosis (TC) commonly occurs during the disruption of calcium-phosphate metabolism in hemodialysis patients with chronic renal failure (CRF), or during familial tumoral calcinosis and idiopathic sporadic cases [2].

Our case is unique in that multiple ectopic calcifications in subcutaneous tissues were found in a hemodialysis patient who had been operated on a total of five times within a period of 1.5 years; the operations included a subtotal parathyroidectomy with parathyroid autotransplantation in the right forearm.

2. Methods

2.1. Case presentation

In May 2014, a 60-year-old male presented to our department with local, gradually increasing painless swelling and reduced mobility in the bilateral shoulders for two months. His past medical history included a CRF due to adult polycystic kidney disease, high blood pressure, and renal anemia. He had been receiving regularly hemodialysis twice per week for two years. He neither smoked nor drank alcohol. Magnetic resonance imaging (MRI) performed in another hospital revealed that there was an abnormal mass in the subscapular regions of each shoulder (Fig. 1). Clinical evaluation of the swollen shoulders revealed slight limitation of the passive and active range of motion and no apparent tenderness to pressure. No

* Corresponding author.
E-mail address: kaican@163.com (S. Feng).
[1] These authors contributed equally to this work.

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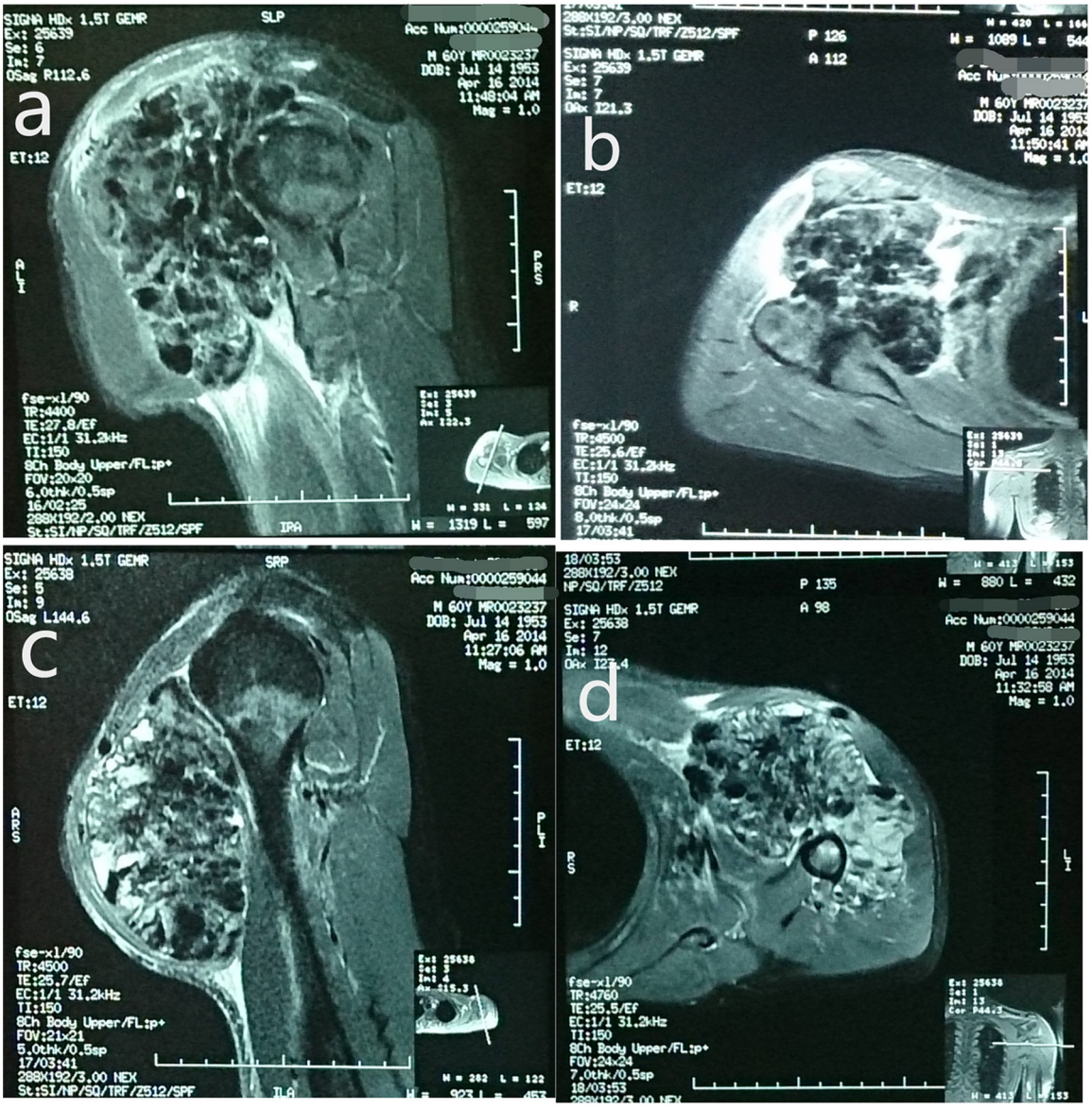

Fig. 1. Preoperative condition. The MRI T1 demonstrated a large ectopic calcification in the right shoulder (a, coronal planes; b, axial planes). The MRI T1 showed a large ectopic calcification in the left shoulder (c, coronal planes; d, axial planes).

muscle weakness was detected. Plain radiographs and computed tomography (CT) scans demonstrated symmetric calcified masses around the bilateral shoulders. In addition, Tc-methylene diphosphonate (Tc-MDP) bone scintigraphy showed increased radiotracer uptake not only in the masses of the bilateral shoulders, which were previously known, but also in the masses of the right buttock and right thigh (Fig. 2). Further CT scans showed calcified masses in the region of the right buttock and right thigh. Laboratory tests showed elevated serum creatinine levels of 1175 μmol/L (reference range, 53–106 μmol/L) and serum urea nitrogen levels of 20.69 mmol/L (reference range, 3.2–7.1 mmol/L).

After a needle biopsy confirmed the ectopic calcification in the right shoulder and surgical contraindications were excluded, the first operation was performed; the tumor was sequentially resected under general anesthesia in the following order: the left shoulder, the right shoulder and the right buttock. At surgery, the mass consisted of thick connective tissue and cavities filled with toothpaste-like material. Furthermore, we found that the TC infiltrated the periarticular tissue of the right shoulder, particularly the rotator cuff and articular capsule, such that a partial excision was performed to avoid postoperative instability and dysfunction of the right shoulder. In contrast, a complete excision was performed in the left shoulder and right buttock due to the clear boundary of the masses covered with velamen (Fig. 3). Considering the patient's poor tolerance of long periods of operation times, we decided to resect the ectopic calcification of the right thigh during the next operation. Postoperative pathology confirmed that the tumors were ectopic calcifications [3]. At the 5-month follow-up, the patient reported no pain during daily activities, and a normal range of motion of the bilateral shoulders had been achieved.

However, the ectopic calcification of the right thigh was gradually growing larger. In October 2014, the patient underwent a complete excision of the mass in the right thigh under epidural anesthesia. During the operation, we found that the mass covered with velamen was divided from the normal tissue (Fig. 4), and the mass consisted of thick connective tissue and cavities filled with a toothpaste-like material. Postoperative pathology confirmed that the mass was an ectopic calcification.

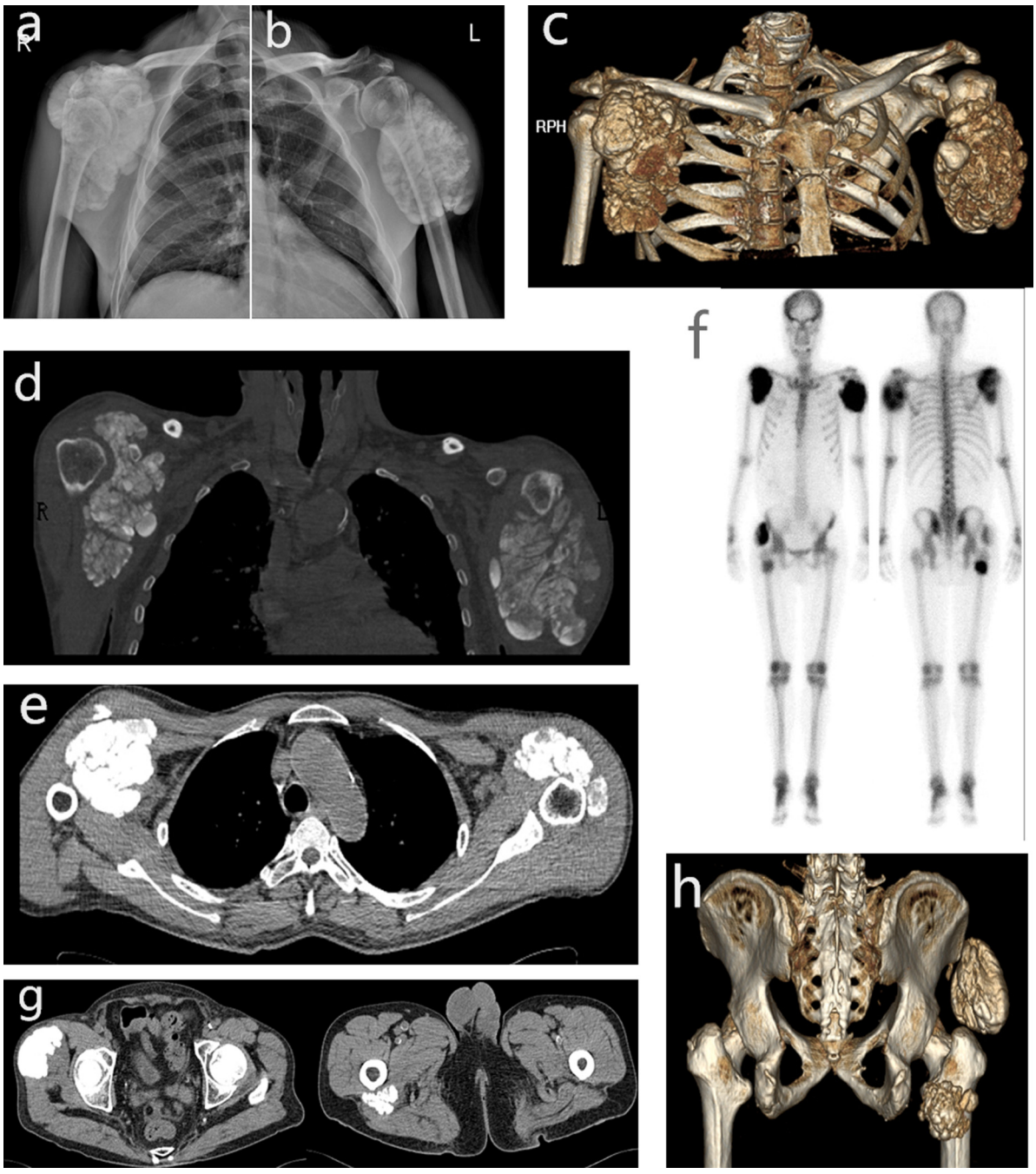

Fig. 2. Plain radiographs of the right shoulder (a) and the left shoulder (b) show the symmetric ectopic calcification. CT scan (d, coronal planes; e, axial planes) and 3-D image (c, anterior) show ectopic calcification in the bilateral shoulders. (f) 99 m Tc-MDP bone scintigraphy revealed the increased accumulation of radiotracer not only in the masses of the bilateral shoulders but also in the right buttock and thigh. CT scan (g, axial planes) and 3-D image (h, posterior) showed ectopic calcification in the right buttock and right thigh behind the greater trochanter.

To the best of our knowledge, the ectopic calcification occurred from the disruption of calcium-phosphate metabolism due to CRF. A series of laboratory tests revealed that serum phosphorus and parathyroid hormone levels were both elevated, with the exception of the normal levels of serum calcium prior to the third operation. In addition, an ultrasound test of the glandula thyroidea revealed that the parathyroid glands were overgrown, which indicated secondary hyperparathyroidism due to CRF. In January 2015, the third surgery, a subtotal parathyroidectomy with parathyroid autotransplantation in the right forearm, was performed under general anesthesia.

At the follow-up, the ectopic calcification of the right shoulder was slowly growing larger, similar to previously described symptoms. The CT and MRI confirmed recurrence of the ectopic calcification in the right shoulder. The fourth and fifth surgeries were performed to resect the ectopic calcification under general anesthesia in April and October 2015, respectively. Consistent with the previous findings of the initial surgery, the ectopic calcification, which was larger than previous calcifications, infiltrated the periarticular tissue of the right shoulder. It was impossible to distinguish the lesions from normal tissue. Furthermore, an incomplete excision was performed twice over two surgeries (Figs. 5 and 6).

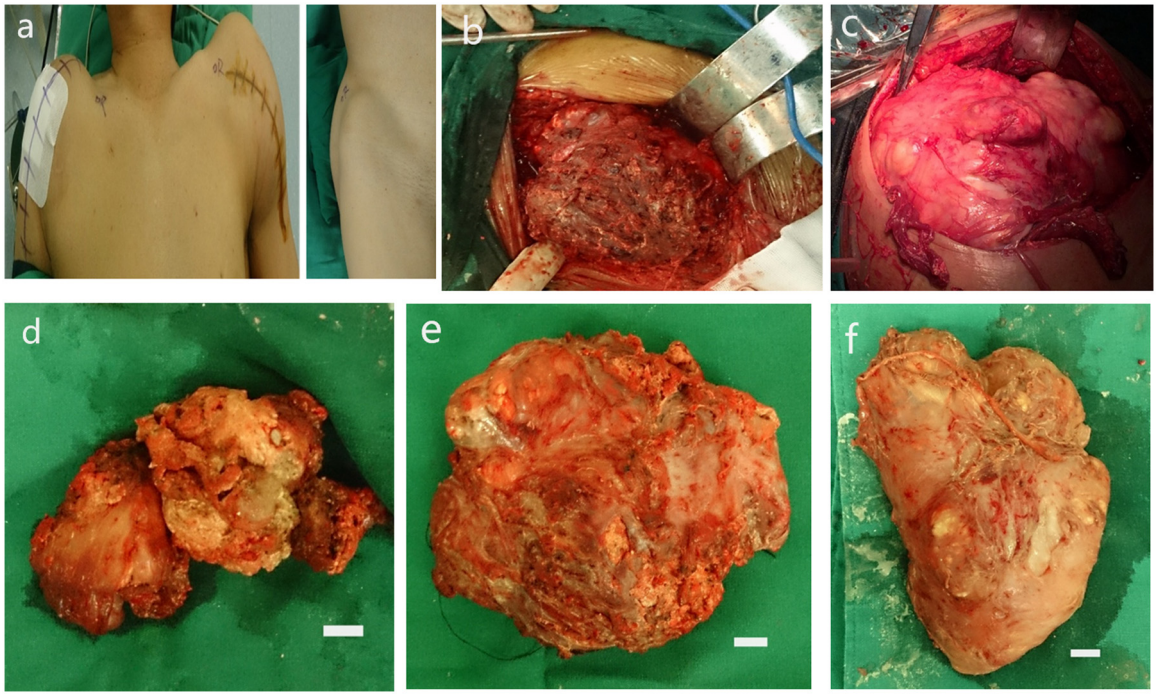

Fig. 3. Preoperative images of the patient show swelling in the bilateral shoulders, right buttock and anteromedial approach (a, b). Intraoperative images: (c) Ectopic calcification infiltrated the periarticular tissue of the right shoulder, particularly the rotator cuff and articular capsule; (d) Ectopic calcification was divided from the normal tissue in the left shoulder; (e) Ectopic calcification resected from the right buttock; (f) Ectopic calcification resected from the right shoulder; and (g) Ectopic calcification resected from the left shoulder. The scale bar represents 1 cm.

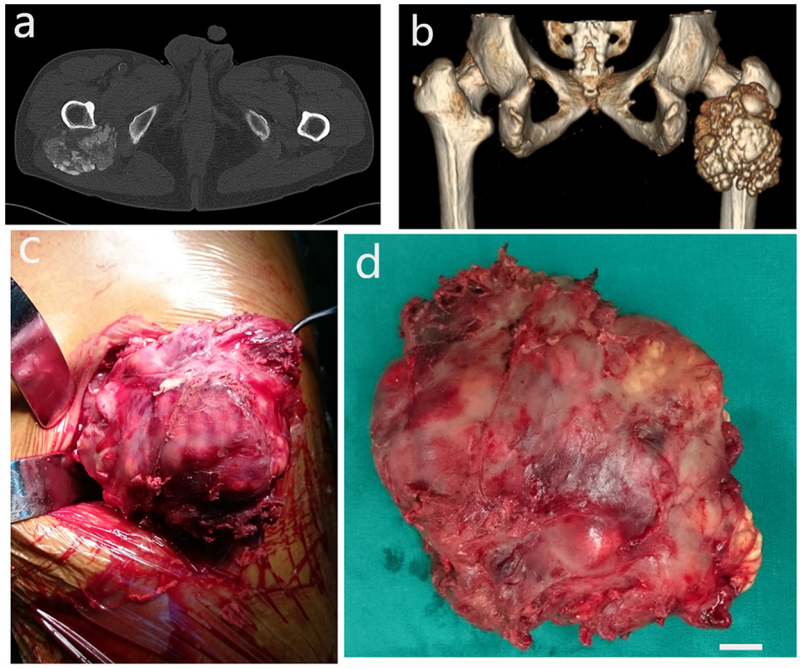

Fig. 4. (a, b) CT scan and 3-D image showed ectopic calcification in the right thigh behind the greater trochanter. Intraoperative images: (c) Ectopic calcification covering with velamen was divided from the normal tissue in the right thigh; and (d) Ectopic calcification resected from the right thigh. The scale bar represents 1 cm.

Postoperative pathology confirmed that the tumors were ectopic calcifications as previously described.

2.2. Statistical analysis

Statistical analysis was conducted using the statistical package for social sciences (SPSS) software, version 19.0 for Windows (SPSS Inc., Chicago, IL, USA). Serum levels of parathyroid hormone (PTH), calcium and phosphorus were measured by laboratory tests and data between pre-surgery and post-surgery were compared by unpaired Student's *t*-tests. All numerical data were expressed as a mean ± standard error of the mean. $P \leq 0.05$ was considered significant.

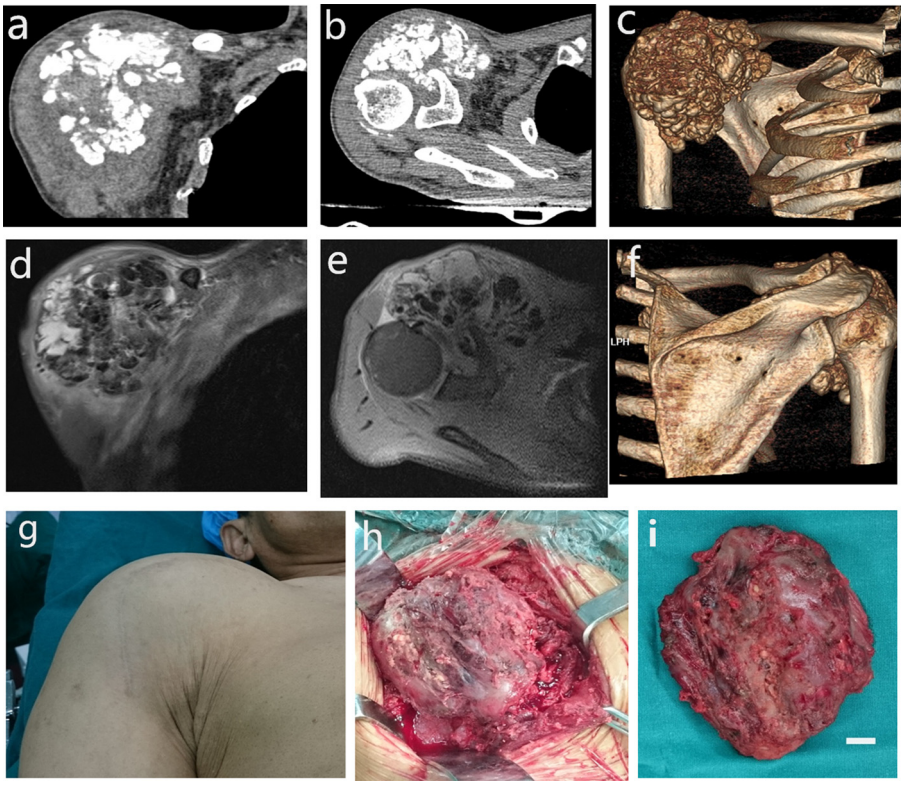

Fig. 5. CT scan (a, coronal planes; b, axial planes) and 3-D images (c, anterior; f, posterior) showed ectopic calcification in the right shoulder. MRI showed ectopic calcification in the right shoulder (d, coronal planes; e, axial planes). (g) Preoperative appearance of the swollen right shoulder. Intraoperative images: (h) Ectopic calcification infiltrated the periarticular tissue of the right shoulder; and (i) Ectopic calcification resected from the right shoulder. The scale bar represents 1 cm.

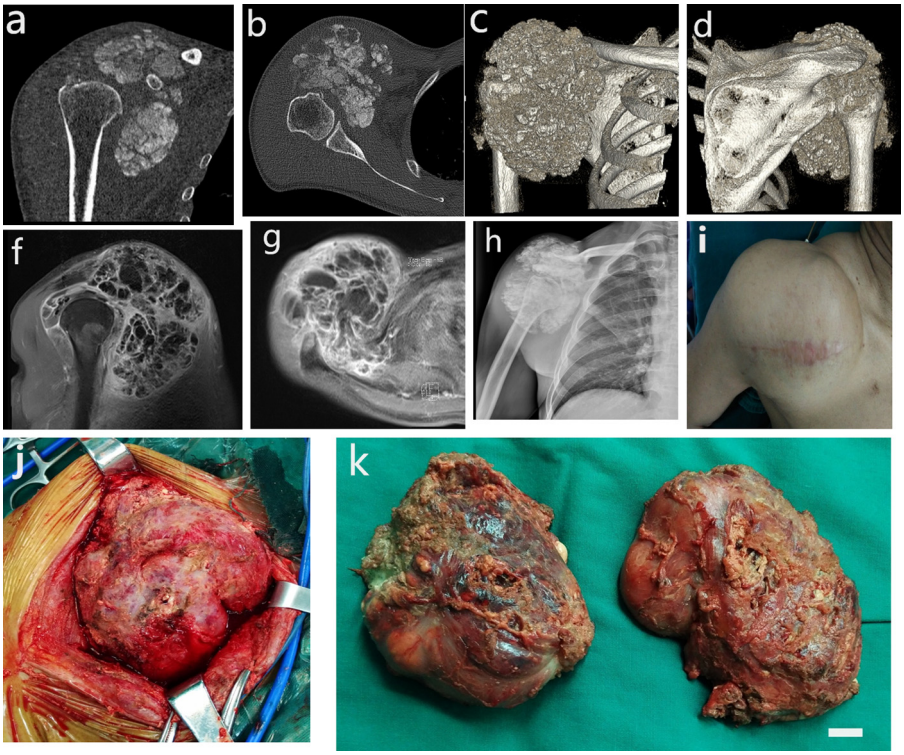

Fig. 6. CT scan (a, coronal planes; b, axial planes) and 3-D images (c, anterior; d, posterior) shows ectopic calcification in the right shoulder. MRI showed ectopic calcification in the right shoulder (f, coronal planes; g, axial planes). (i) Preoperative appearance of the swollen right shoulder. Intraoperative images: (j) Ectopic calcification infiltrated the periarticular tissue of the right shoulder; and (k) Ectopic calcification resected into two parts from the right shoulder. The scale bar represents 1 cm.

3. Results

Complete excisions of the ectopic calcifications were performed in the left shoulder, right buttock and right thigh, without signs of recurrence in the same sites at follow-up. Incomplete excision of the ectopic calcification in the right shoulder resulted in recurrence in the same site, and the patient was operated on two more times 1.5 years following the initial surgery.

Subtotal parathyroidectomy with parathyroid autotransplantation decreased serum levels of PTH, but the levels of serum calcium and phosphorus remained unchanged post-surgery, which appeared not to inhibit the recurrence of ectopic calcification in patients with CRF. The mean serum PTH levels decreased from 132.0 pmol/L (reference range, 1.30–6.80 pmol/L) preoperatively to a mean of 7.55 pmol/L, but the serum levels of calcium and phosphorus remained unchanged (serum calcium (reference range, 2.1–2.9 mmol/L): pre-surgery, 2.50 ± 0.16 mmol/L; post-surgery, 2.65 ± 0.29 mmol/L; pre-surgery vs. post-surgery, $P = 0.37$, $P > 0.05$; serum phosphorus (reference range, 0.8–1.6 mmol/L): pre-surgery, 2.49 ± 0.57 mmol/L; post-surgery, 1.96 ± 0.53 mmol/L; pre-surgery vs. post-surgery, $P = 0.83$, $P > 0.05$). Histology revealed a nodular hyperplasia of the parathyroid glands.

The patient was advised to see doctors every three months. At the follow-up until the date reported for the case, the patient reported no pain during daily activities. Near normal range of motion and good function of the bilateral shoulders had been achieved. However, the right shoulder showed light swelling.

4. Discussion

Tumoral calcinosis (TC) is a rare syndrome characterized by slow growing and painless masses of calcium phosphate deposits within periarticular areas. The mass consists of septal, thick connective tissue and cavities filled with a dense milky substance [4], which causes functional impairment of the joints or mechanical neural irritation [5]. Most reported cases are secondary, particularly due to CRF, which has been described in 1–7% of hemodialysis patients because the patients cannot normally excrete excess phosphorus from the body through the kidneys as a result of secondary hyperparathyroidism [6]. Although the etiopathogenesis of tumoral calcinosis remains poorly understood, it is associated with severe hyperparathyroidism, elevation of serum calcium-phosphorus product or hyperphosphatemia [7]. Histologically, these lesions appear the same [8].

Currently, there are no effective treatments for these patients. However, in addition to plain radiographs, CT scans and MRI, Tc-MDP bone scintigraphy may play an important role in establishing the diagnosis and evaluating the extent of abnormal calcium deposition [3,4]. As an initial therapy, the conservative treatment of underlying metabolic derangements is indicated with the use of phosphate binders, optimization of dialysis and dietetic measures. If this fails, or if the therapeutic outcome is unsatisfactory, parathyroidectomy or surgical resection of the tumoral calcinosis can be performed as a last resort [9]. Parathyroidectomy to treat the disease includes total parathyroidectomy [10], subtotal parathyroidectomy [11] or total parathyroidectomy with autotransplantation [12].

There are two aspects of this case that warrant additional discussion. First, it is well established that in renal failure patients, the occurrence of TC may account for impaired calcium-phosphate metabolism [9]. In the present case, a series of laboratory tests revealed that serum phosphorus and parathyroid hormone levels were both elevated, with the exception of the normal levels of serum calcium. In addition, an ultrasound test of the glandula thyroidea found that the parathyroid glands had overgrown, which indicated secondary hyperparathyroidism. To achieve regression or inhibit the recurrence of TC, subtotal parathyroidectomy with autotransplantation was performed. We found that surgery neither inhibited the recurrence of the ectopic calcification nor decreased the serum phosphorus, regardless of the decreased serum PTH. More recently, isolated cases reported successful rapid regression of calcium deposits in tumoral calcinosis post-parathyroidectomy [13,14], although the procedure of choice remains controversial.

Second, in the present case, four excisions of the TC had been performed. Among them, the complete excisions of the ectopic calcification in the left shoulder, right buttock and right thigh achieved no recurrence in the same site. In contrast, recurrence occurred in the right shoulder due to incomplete excision control. Consistent with this finding, King et al. also concluded that recurrence of the ectopic calcification was common and recurrent lesions were a frequent complication of incomplete excision and typically grew more rapidly than the initial lesion [5]. Our case illustrated the extreme importance of complete excision of the lesions in surgical treatments of TC. It is possible that the remaining calcification triggers the calcium phosphate deposits in the soft tissue as a localized stimulus. Thus, further work is required to elucidate the basis of the relationship between incomplete excision and recurrence of TC.

Although several cases of the surgical treatment of TC have been reported, the present report significantly differs from these studies because it shows different results at different localizations in the same patient. Previously studies have suggested that surgical excision is often limited to patients with significant disability or deformity [8]. Our case suggests that: if conservative therapy failed, then early and complete surgical excision may be a good therapeutic option, which appears to be a minimally invasive surgical option before TC becomes larger in size.

5. Conclusions

Although the result in a single case cannot be taken as an indication of its effectiveness in TC, our case suggests that: if conservative therapy failed, then early and complete surgical excision may be a good therapeutic option. And further investigations are needed to demonstrate recurrence mechanism of TC.

Ethics approval and consent to participate

The present report was approved by the Ethical Review Committee of The Fifth Affiliated Hospital of Sun Ye-san University (Ethical proof NO. 2016020812).

Consent for publication

Written informed consent was obtained from the patient for the publication of this report and any accompanying images. The work in the present report has been carried out in line with the SCARE criteria [15].

Availability of data and supporting materials

Raw data of Images is available from attached files.

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Competing interests

The authors have declared that no competing interests exist.

Authors' contributions

RongKai Zhang, GuoWei Li and LuKun Yang helped with data collection, interpretation and writing the paper. YingQin Li, Jinghuan Ou and DaWei Zhang contributed to study concept/design, data analysis and interpretation. Tao Chen and Shaoyan Feng helped with interpretation and contributed to review of the final manuscript and final submission of the paper. All authors read and approved the final manuscript.

Guarantors

RongKai Zhang, Shaoyan Feng.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijscr.2016.09.041.

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