【 CASE REPORT 】

Successful Treatment of Tumoral Calcinosis by Lanthanum Carbonate

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Abstract:

Tumoral calcinosis (TC) is a rare benign but aggressive disorder with variable response rates and high recurrence rates despite medical or surgical treatments. We herein report a case of a 28-year-old woman with underlying systemic lupus erythematosus (SLE) who developed diffuse tumoral calcinosis that was successfully treated by lanthanum carbonate. The formation of tumoral calcinosis depends on the supersaturation of calcium and phosphate. Lanthanum carbonate not only has an excellent phosphate-lowering ability but also low gastro-intestinal calcium absorption. It can be considered an effective alternative treatment for tumoral calcinosis if surgical treatment is not feasible.

Key words: tumoral calcinosis, lanthanum carbonate

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Introduction

Tumoral calcinosis (TC) is a rare locally benign but aggressive disorder with an obscure etiology characterized by massive extra-articular soft tissue deposition of calcium phosphate. TC often involves large joints, such as the hip, elbow, and shoulder (1). The treatments of TC include medical and surgical treatments but show variable response rates. We herein report a case in which TC was effectively treated by lanthanum carbonate.

Case Report

A 28-year-old woman visited an out-patient clinic due to a 6-month history of indurated masses over the left hip and bilateral scapula. Due to left hip pain, her ambulation was restricted. She had been diagnosed with systemic lupus erythematosus (SLE) at the 18 years of age with an initial presentation of nephrotic syndrome. Class V lupus nephritis (membranous) was confirmed by a renal biopsy and treated with steroids and mycophenolate mofetil (MMF). Her estimated glomerular filtration rate [GFR; by Modification of Diet in Renal Disease (MDRD)] was 110 mL/min/1.73 m², and her urinary protein loss was around 0.5 mg/day. Her medication history did not include a calcium supplement or vitamin D.

An examination revealed a 3×4-cm mass in the right scapular region, a 5×6-cm mass in the left scapula region and a 7×8-cm mass at the lateral aspect of the left hip. These masses were characterized as firm to hard and were immobile, with tenderness on palpation. The laboratory examination findings were as follows: serum creatinine 0.4 mg/dL, adjusted serum calcium 8.8 mg/dL, phosphate 5.3 mg/dL, albumin: 3.5 g/dL, intact parathyroid hormone 26.9 ng/L(16-67 ng/L) and 25-dihydroxyvitamin D 25 pg/mL (>20, sufficient). The tubular maximum reabsorption of phosphate corrected for the GFR (TMP/GFR) was 7.95 mg/dL (normal range 3.8-5 mg/dL).

Plain radiograph of the chest showed several lobulated calcified masses at the bilateral scapular and right perihilar regions. Plain radiograph of the pelvis showed huge lobulated calcified masses in the bilateral hip and pelvic regions (Figure a). TC related to SLE was initially suspected, and the rheumatologist increased the doses of steroid and MMF. The SLE disease activity index (SLEDAI) was adequately controlled in the range of 2-4 in the subsequent period, but progressive TC was still noted.
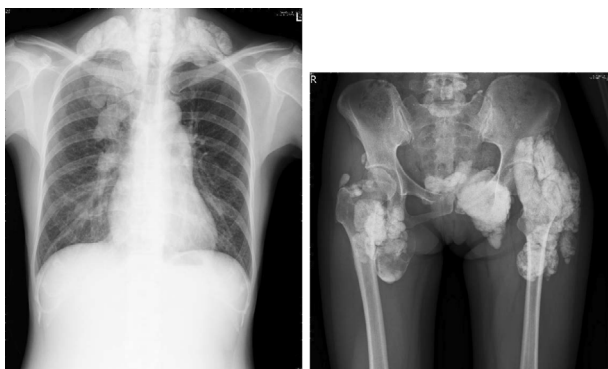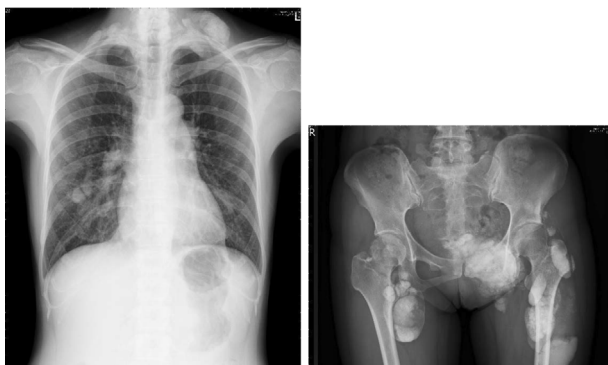
a. Before treatment

b. After treatment

Figure.   **Before treatment: Chest radiograph showed several lobulated calcified masses at bilateral scapula and right perihilar region (a, left). Pelvic radiograph showed huge calcified masses in bilateral hips and pelvic region (a, right). After treatment: Progressive resolution of calcified masses in chest radiograph (b, left) and bilateral hip and pelvis (b, right).**

Due to symptomatic TC with pain, surgical removal was suggested. However, the patient refused surgical intervention for fear of the complications. Due to persistent hyperphosphatemia, lanthanum carbonate treatment was prescribed in combination with a low-phosphate diet. Her serum phosphate level was maintained in the range of 3-4 mg/dL in the subsequent period. After three years, progressive resolution of TC was observed (Figure b).

Discussion

TC is a rare locally benign but aggressive disorder with an obscure etiology characterized by massive extra-articular soft tissue deposition of calcium phosphate. TC often involves large joints, such as the hip, elbow, and shoulder (1). Primary TC was originally described as a familial or hereditary condition caused by autosomal recessive mutations in genes involving phosphate metabolism. Familial hyperphosphatemic TC is an autosomal recessive metabolic disorder involving the loss of fibroblastic growth factor 23 (FGF23) or GaLNAc-transferase 3 (GALNT3), whereas normophosphatemic TC shows a defect in sterile α motif domain-containing protein (SMAD9) (2, 3). Loss of function of FGF23 or GALNT3 results in the uncontrolled production

of 1,25-dihydroxy vitamin D with subsequently increased phosphate reabsorption from the kidney and intestine.

SMAD9 may be a downstream target of tumor necrosis factor (TNF)-α signaling. A defect in SMAD9 is associated with the inflammatory response in normophosphatemic TC and is involved in the pathogenesis of dystrophic TC (4). The most common forms of secondary TC are related to chronic kidney disease, especially in dialysis patients, and patients with hyperparathyroidism, hypervitaminosis or dystrophic TC associated with connective tissue diseases (1).

In their review of TC, Fathi et al. (5) stated that the differential diagnosis of primary TC should exclude connective tissue disease first, especially in the setting of normal serum calcium and phosphate levels. In our case, the etiology of TC was initially thought to be related to the underlying SLE. However, TC still progressed gradually despite the lupus activity being adequately controlled. Findings on further workup suggested that hyperphosphatemia with increased renal tubular reabsorption of phosphate might be associated with the progression of TC. However, one limitation associated with this report was that tests for 1,25(OH)2D, FGF23, GALNT3 and alpha-klotho could not be performed at our hospital.

The treatments of TC include surgical and medical interventions. The main approach for managing primary TC is early surgical treatment. However, the high rate of recurrence warrants repeated excision. In addition, partial excision due to the involvement of important neurovascular structures often results in rapid recurrence. Huge lesions require extensive excision, which is often complicated by delayed wound healing or secondary infection (5). Considering the high rate of recurrence after surgical excision, medical treatment may be reasonably considered before surgical intervention, especially in cases of hyperphosphatemia.

Medical intervention for TC with hyperphosphatemia through a phosphate-restricted diet and the use of phosphate binders, such as aluminum hydroxide, has shown varying success (6). Combination therapy with acetazolamide was previously reported to induce mild metabolic acidosis without changes in the serum phosphate level while effectively slowing tumor growth in a patient with hyperphosphatemic familial TC (7). For cases of secondary TC, medical treatments include calcium and a phosphate-restricted diet, low-calcium dialysates for dialysis patients and phosphate binders. Sodium thiosulfate or intravenous pamidronate has also been used in the treatment of secondary TC with varying success (8, 9).

To our knowledge, lanthanum carbonate was never been used to treat TC. In the present case, the non-calcium-based phosphate binder lanthanum carbonate was used to treat TC, and the patient's TC had markedly regressed after three years of treatment. The periarticular soft-tissue deposition of TC was mainly composed of calcium phosphate and calcium-hydroxylapatite (Ca10(PO4)6(OH)2), the formation of which depends on the supersaturation of calcium and phosphate. Behets reported on the difference in gastrointesti-

nal calcium absorption after the ingestion of several calcium-free phosphate binders. Lanthanum carbonate had a significantly lower net calcium absorption and lower rate of hypercalciuria than sevelamer carbonate (10). Hoenderop et al. found that lanthanum carbonate was the best-performing calcium channel blocker of all substances studied and induced no increase in the calcium absorption in the gut, in contrast to other currently used phosphate binders (11). Furthermore, Malluche et al. reported improvement in the bone turnover as well as restoration of the bone reservoir function when using lanthanum carbonate (12). The decreased calcium loading and improvement of the bone reservoir function, which facilitates the influx of calcium into the bone with decreased calcium deposition into the soft tissue, may explain the resolution of TC in our patient. We believe that the dramatic shrinkage in the size of the TC in our patient was due to not only the phosphate-lowering effect but also the decreased gastro-intestinal calcium absorption induced by lanthanum carbonate.

In conclusion, lanthanum carbonate can be considered a reasonable alternative treatment for TC if surgical treatment is not feasible.

This study was approved by the institutional review board of the Chang Gung Medical Foundation (IRB Number: 201702340 B0).

The authors state that they have no Conflict of Interest (COI).

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