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Calcinosis Cutis Complicated with Septic Arthritis in a Patient with Rheumatoid Arthritis: A Case Report

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Abstract Calcinosis cutis is a disease characterized by precipitation of calcium and phosphate salts in the subcutaneous tissue. It is classified in four different groups depending on the etiology. The most common subtype is dystrophic calcification and is usually associated with connective tissue diseases, including systemic sclerosis, dermatomyositis or systemic lupus erythematosus. However, only two cases have been reported in relation to rheumatoid arthritis. A female patient, who had been followed for 20 years because of the diagnosis of rheumatoid arthritis, was admitted to the hospital due to the complaints of redness in her right leg and discharge. Many radiopaque mineral deposits were observed in the bilateral soft tissue of the lower extremity by direct radiography. There was no evidence of other connective tissue diseases upon evaluation for the differential diagnosis of calcinosis cutis. Serum calcium, phosphorus, alkaline phosphatase, and parathyroid hormone were normal. Septic arthritis in the right knee was detected on the fifth day of follow-up. The aim of this study was to present a case of calcinosis cutis in a patient with rheumatoid arthritis that presented with soft tissue infection resulting in right knee septic arthritis.

Keywords Rheumatoid arthritis, Calcinosis cutis, Septic arthritis

1. Introduction

Deposition of calcium in subcutaneous tissue, also known as calcinosis cutis, can be related to various conditions such as connective tissue disease, chronic kidney failure, hyperparathyroidism, and malignancy. It is divided into four groups depending on the etiology: metastatic, dystrophic, tumoral, and idiopathic. The most common subtype is dystrophic calcinosis, which is usually related to the underlying connective tissue disease (ACTD) [1]. Dystrophic calcinosis is characterized by normal levels of serum, calcium, and phosphorus. Calcium accumulation can lead to recurrent local inflammation and infection complicated with skin ulcers or nodules and subsequently, can lead to joint contractures and muscle atrophy [2].

There are two cases of calcinosis cutis related with rheumatoid arthritis (RA) in the literature. One is a case report and the other takes place in a case series of calcinosis cutis associated with connective tissue diseases [3, 4]. We aimed to present a new case of calcinosis cutis associated with skin ulcers and complicated with septic arthritis in a patient with RA.

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2. Case

A 65 year old female patient presented with fever, fatigue and erythema, and discharge in her legs. Patient was followed for rheumatoid arthritis for 20 years but, failed to come to control examinations for the last year. During this period, she was administered methotrexate (15 mg/week), leflunomide (20 mg/day), pantoprazole (40 mg/day) and folic acid (10 mg/week) as a treatment regime. She did not have any concurrent diseases such as diabetes or hypertension, and did not smoke or consume alcohol. Physical examination showed edema, tenderness, and warmness on the pretibial area. In addition to erythema, the tibia, 1/3 distal, and 1/3 middle regions had small ulcerated areas on the cutaneous calcified plaques. Yellow discharge was coming from the ulcerated lesions spontaneously. She was hospitalized and ultrasonography (USG) examination showed a heterogeneous appearance, including septations compatible with a soft tissue infection. Cultures of blood, urine, and cutaneous ulcers were obtained. Empirical antibiotherapy (intravenous ampicillin sulbactam) was administered. Lower limb radiography showed multiple milimetric radiopaque mineral deposits (figure 1).

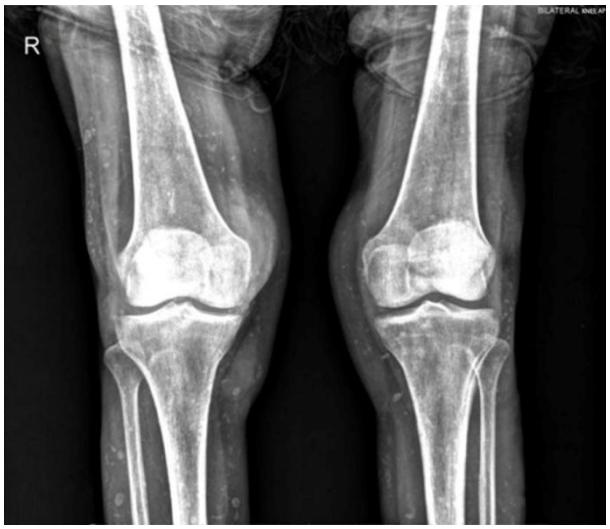

Figure 1. A bilateral anteroposterior knee radiograph that shows widespread microcalcifications on soft tissue

The patient did not describe raynaud phenomenon, dry eye or mouth, and did not have constitutional symptoms, neurologic deficits, or muscle weakness. There was no signs of sclerodactyly, telangiectasia, or muscle weakness in the physical examination. Thyroid USG, breast USG, and thorax and abdomen computed tomography (CT) did not show any pathology. Laboratory studies were as follows: parathormone: 43.2 pg/ml, serum calcium: 9.5 mg/dl, serum phosphorus: 3.4 mg/dl, 24 hour urine calcium: 55 mg/day, alkaline phosphatase: 72 IU/L, sedimentation rate: 54 mm/h, C-reactive protein: 1,47 mg/dl and antinuclear antibody: negative. The urine acidification capacity was normaland Schirmer's test was 17/20mm. Cultures obtained from the cutaneous ulcers before empiric antibiotheraphy showed E. coli growth, and treatment was switched to intravenous piperacillin tazobactam (on the third day of empirical antibiotherapy).

On the third day of piperacillin tazobactam treatment, the patient's right knee developed edema, erythema, and warmness. Sedimentation and CRP levels substantially increased (respectively, 109 mm/h, 12.5 mg/dl). We performed synovial fluid sampling, which was purulent and there was leukocytosis with neutrophil dominancy (WBC: 24.000, 82% neutrophil). Synovial fluid cultures were obtained, and the AARB was negative. No growth was observed for the tuberculosis culture. We stopped piperacillin tazobactam, and initiated meropenem (3x1 gr) and teicoplanin (2x400 mg 2 days, 1x400 mg for rest) antibiotics. The joint was drained and washed arthroscopically by an orthopedic surgeon. No growth was seen on cultures from synovial fluid. The echocardiography did not reveal any signs of infective endocarditis. In our case, calcinosis cutis lesions were most common in the lower extremities. In addition, the ulcerated calcinosis lesions were infected. Overall, the skin was healthy and there was no evidence of infection in the area of the non-ulcerated calcinosis lesions. Septic arthritis table developed after the soft tissue infections (on the sixth day of empirical antibiotherapy), which was dependent on the ulcerated calcinosis cutis lesions.

We interpreted the patient's condition as calcinosis cutis associated with RA and skin ulcerations, resulting in soft tissue infection and septic right knee arthritis. After proper antibiotherapy, the patient's lesions healed leaving skatris (figure 2, 3). There was no need for debridement, and diltiazem and colchicine were started for long term treatment.

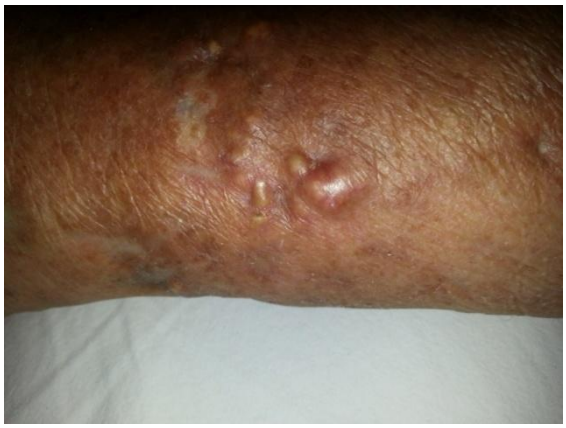

Figure 2. Pretibial soft tissue calcinosis cutis lesions and skatris after treatment

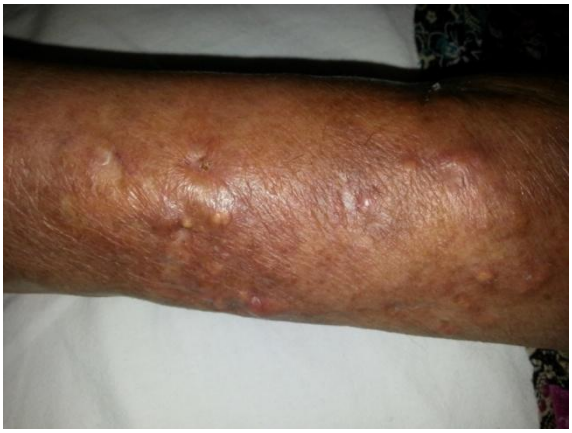

Figure 3. Pretibial soft tissue calcinosis cutis lesions and skatris after treatment

3. Discussion

Calcinosis cutis is divided into four groups metastatic, dystrophic, tumoral, and idiopathic, which depend on the etiology. The metastatic calcification is related to abnormal serum calcium-phosphorus levels and is observed in normal tissues. Moreover, it has been linked to other conditions such as malignancy, hyperparathyroidism, and hypervitaminosis D (2,5). Calcification is usually widespread, and sometimes may be present only on skin and subcutaneous soft tissue. The most common cause of metastatic calcification is chronic kidney disease (CKD). Secondary to CKD, hyperparathyroidism leads to higher levels of serum calcium and phosphate, which cause metastatic calcifications [6].

Tumoral calcinosis has two subtypes: 1) Primary

normophosphatemic tumoral calcinosis and 2) primary hyperphosphatemic tumoral calcinosis. Primary normophosphatemic tumoral calcinosis is not familial and serum calcium-phosphorus levels are typically normal. In general, this type of calcinosis has a singular lesion and usually involves trauma. On the other hand, primary hyperphosphatemic tumoral calcinosis is a rare familial disease. In most case, the serum phosphorus levels are high, but calcium levels are normal. In addition, trauma history is not present, and it is characterized by multiple lesions before the second decade. The hyperphosphatemia association is caused by a decrease in renal clearance and an increase in tubular reabsorption [7].

Dystrophic calcification is the most common subtype of calcinosis cutis and is usually associated with ACTD. It is present in normal metabolism and commonly develops in traumatized tissues. In addition to case reports regarding this subject, studies have shown and evaluated the relationship between ACTD and dystrophic calcification.

The calcinosis cutis probability is 25% in systemic sclerosis [8], 30-70% in juvenile dermatomyositis [9], and 40% in systemic lupus erythematosus [10]. However, there are only two cases of calcinosis cutis related to RA in the literature [3, 4]. Although normal physiologic tissue concentrations of calcium and phosphate are close to their saturation, tissue calcification is unusual due to the presence of endogenous inhibitors of calcification [11]. Dystrophic calcification etiology is not known; however, several studies were conducted about this subject. One study showed increased calcium binding amino acid and gamma carboxyglutamic acid levels in calcinosis patients [12], while another showed increased IL-1β levels [13]. Kim [14] on the other hand, concluded that apoptosis most likely underlies the mechanism of both physiological and pathological calcification. Interstingly, dystrophic calcifications develop in tissues that change in structure to suitable conditions for calcification, such as hypoxia, trauma, hypovascularity, and tissue structural damage. Genetic predisposition and advanced age can also contribute to this tendency. Presently, there is not a standard pharmacological treatment for prevention or treatment of calcinosis cutis. Warfarin, colchicine, bisphosphonates, or diltiazem can be used either alone or in combination considering the clinical condition of the patient [2]. For small superficial lesions, carbon dioxide laser therapy is an option, but surgical resection may be necessary for larger and more complicated lesions.

4. Conclusions

Dystrophic calcinosis cutis is observed in connective tissue diseases such as systemic lupus erythematosus, scleroderma, and dermatomyositis. Calcinosis accumulation is known for its role in recurrent local infections and skin ulcerations. Joint contractures may develop secondary to recurrent infection attacks. In the literature, only two cases of calcinosis associated with rheumatoid arthritis have been reported. It should be kept in mind that calcinosis cutis may also be observed in RA patients similar to our case study. In addition, it should be noted that calcinosis accumulation may cause complications such as skin ulceration, soft tissue infections, muscle atrophy, joint contractures, and even septic arthritis. In our case, calcium accumulation caused skin ulcers and soft tissue infection leading to right knee septic arthritis. Besides other connective tissue diseases, RA can be associated with calcinosis cutis and result in severe complications such as septic arthritis.

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