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Large Subcutaneous Calcification in Systemic Lupus Erythematosus: Treatment with Oral Aluminum Hydroxide Administration Followed by Surgical Excision

A 32-year-old woman with a long-standing systemic lupus erythematosus had multiple subcutaneous nodules on her axillae, iliac crests and limbs. Three years ago, these nodules began to appear and slowly became larger. Some of them amassed to form a large, fungating, lobulated mass on her right iliac crest. Roentgenographic and histological examination showed that they were calcium deposits. She was initially treated with aluminum hydroxide administration for nine months, which resulted in moderate decrease in size and softening in consistency, but not complete resolution. Then, the mass on the right iliac crest was excised, with an excellent early result.

Key Words: *Calcinosis; Lupus erythematosus systemic; Aluminum hydroxide*

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INTRODUCTION

Calcinosis cutis is a common feature of certain connective tissue diseases such as dermatomyositis and scleroderma, but is rarely reported in association with systemic lupus erythematosus (SLE) (1). In most previously reported cases, the deposition of calcium was usually seen under the cutaneous lupus lesions, and the amounts were relatively small (2, 3). The pathophysiology of this condition is unknown and no reliable therapy is currently available, especially for extensive or large subcutaneous calcification associated with SLE. We herein describe a case of large subcutaneous calcification in a patient with SLE, who was successfully treated with oral administration of aluminum hydroxide, followed by simple excision.

CASE REPORT

A 22-year-old woman was admitted to our department in December 1988, with a history of proximal muscle weakness, edema, myalgia, arthralgia, and oral ulcer. Laboratory studies revealed the following abnormalities: hemoglobin (8.0 g/dL), hematocrit (26.6%), leukocyte count (3,800/μL), erythrocyte sedimentation rate (33 mm/hr), glutamic oxalacetic transaminase (62.3 U/L), glutamic pyruvic transaminase (87.3 U/L), and lactic dehydrogenase (780 U/L). The levels of aldolase and creatine phosphokinase were normal. The antinuclear antibody test was positive in a titer of 1:80, homogeneous pattern, and anti-DNA antibody was 48 U/ mL (upper limit: 5.3 IU/mL). Other antibody tests including anti-ENA Ab, anti-Sm Ab, anti-nRNP Ab, and anti-SSB Ab were all negative, except for anti-SSA Ab. Electromyography of the quadriceps muscles revealed the typical myogenic pattern. Histological examination of a muscle biopsy showed unremarkable findings. Based on these findings, the diagnosis of SLE with myositis was made and the patient was treated with low-dose orally administered prednisolone and hydroxychloroquine, and had done well thereafter.

In August 1995, she began to develop multiple yellowish-white nodules and plaques protruding over the axillae, iliac crests, and limbs. Gradually, the nodules increased in size and number and eventually coalesced, most impressively over the right iliac crest, where they formed a large lump, 9×6.5 cm in size (Fig. 1A). Multiple biopsy specimens taken from the iliac crests and axillae commonly showed distended lobules containing amorphous basophilic material in the dermis and subcutaneous tissue (Fig. 2), which proved to be calcium with von Kossa's stain. She suffered from complications of ulceration, infection, and abscess formation, with extrusion of chalky material from the biopsy sites for 1 month

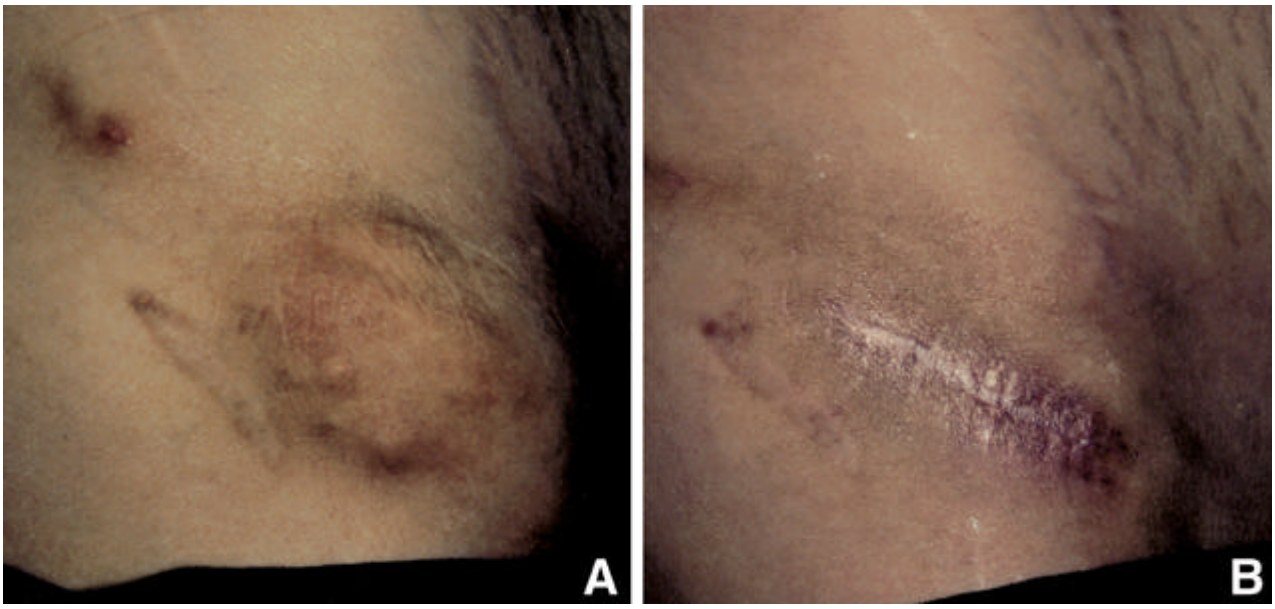

Fig. 1. A: Large (9×6.5 cm) lobulated subcutaneous calcified mass on the right iliac crest. B: Postoperative follow-up.

after the biopsy. At this time, she was treated with prednisolone, colchicine, and hydroxychloroquine, but was ineffective in calcification.

In February 1998, she revisited our department to treat a lump of calcinosis cutis overlying the right iliac crest that interfered with movement at the waist and hip. Subsequent biopsy was performed and histopathologic findings confirmed calcinosis cutis. Roentgenographic examination disclosed soft tissue calcification over the axillae, iliac crests, and limbs (Fig. 3). Serum calcium, inorganic phosphorus and magnesium levels were within normal limits. Orally administered aluminum hydroxide (Amphogel®) was instituted at a dose of 600 mg, three times a day. Clinical improvement occurred within six months. During this period, the size of the lump over the right iliac crest decreased to 5×4.3 cm, and the stony hard consistency changed into a soft to firm one. However, by the end of nine months of therapy, there was no further improvement of lesions. Serum calcium and inorganic phosphorus levels were within normal

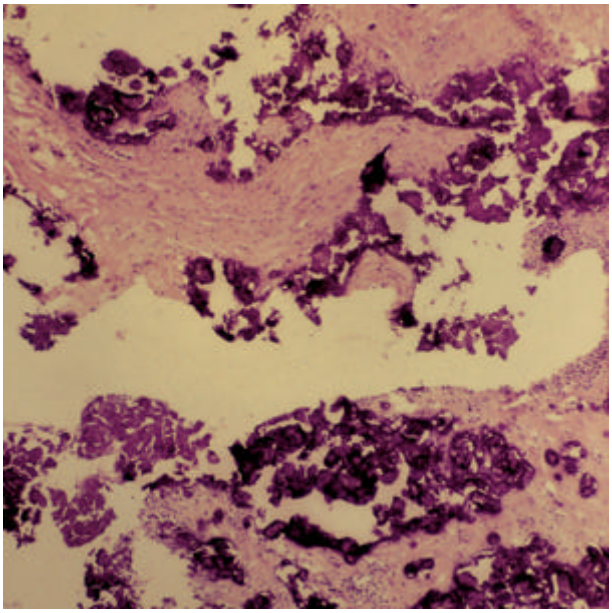

Fig. 2. Biopsy specimen shows calcium deposits in the subcutaneous tissue (H&E, ×100).

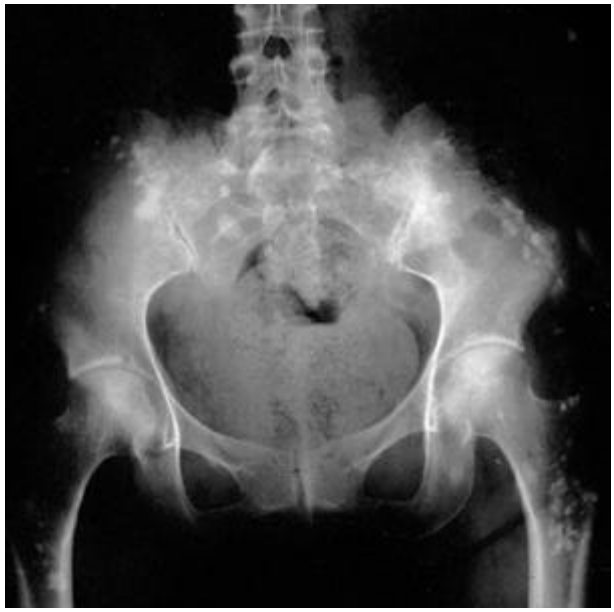

Fig. 3. Roentgenography of the pelvis demonstrates numerous subcutaneous calcification around hip joint areas.

ranges during the course of therapy. At this time the large lump over the right iliac crest was excised, and then inner calcium contents were extruded, debrided and simply closed, with an excellent early result. Wound healing was delayed because of poor blood supply and consistent bloody discharge. However, follow-up after three months revealed that surgery is beneficial to patient's comfort and function (Fig. 1B).

DISCUSSION

Cutaneous deposition of calcium salts in the skin and subcutaneous tissue occurs in a variety of clinical settings. It is generally classified into 4 subsets: metastatic calcinosis, dystrophic calcinosis, idiopathic calcinosis, and iatrogenic calcification (4). In dystrophic calcinosis, the values of serum calcium and phosphorus are normal and the internal organs are usually unaffected (1, 4). In contrast to the relative frequency of this event in patients with connective tissue diseases such as scleroderma, dermatomyositis or CREST syndrome, calcinosis cutis is very rarely seen in SLE (1). In 1969, Kabir and Malkinson (2) were the first to describe two patients with LE and calcinosis cutis. Since then, to our knowledge, about 32 cases have been reported (2, 3, 5-9). In Korea, Park et al. (10) reported a calcinosis cutis limited to discoid LE, but there was no reported case of large extensive calcinosis cutis in association with SLE.

Clinically, calcinosis cutis in SLE typically occurs in women late in the course of long-standing, severe disease (3, 5). It has a predilection for the extremities and buttocks and is usually limited within the dermis or subcutaneous fat tissue of small areas (2, 7). The calcification is also found in deeper soft tissue and peripheral vasculature (3, 5). The calcium deposits may ulcerate and extrude a thick, white granular material (1, 4). Spontaneous resolution occurs very rarely (11). This case fulfilled the American Rheumatism Association criteria for SLE, although muscle symptoms were the principal findings at her initial visit. This patient developed large and extensive calcifications seven years after SLE was diagnosed. In particular, the calcification over the right iliac area was manifested as an unusual large lump. Such large calcification is usually seen in dermatomyositis or tumoral calcinosis (12), but rarely noted in SLE (5, 8).

The pathophysiology of calcinosis cutis remains unclear, but apparently involves abnormally high mitochondrial calcium phosphate levels, resulting in crystal deposition and cell death (4). In dystrophic calcinosis, local tissue abnormalities, such as alterations in collagen, elastin, or subcutaneous fat, may precipitate calcification (1). On the cellular level, mitochondria serve as a nidus for calcinosis and have a high affinity for calcium and phosphate to levels that allow crystalization (1). High levels of intracellular calcium may result from membrane damage, leading to a large influx of calcium. It is also possible that cell necrosis creates a more acidic environment that lacks certain calcification inhibitors (1).

Various treatments of calcinosis cutis have been attempted with varying degrees of success. Warfarin has a limited success in the early circumscribed lesion (13). Steroids, and the chelating agent, diphosphate, have not been uniformly successful (14, 15). Aluminum hydroxide has been reported to be successful in the treatment of calcinosis cutis in juvenile dermatomyositis (16). This compound, by forming insoluble aluminum phosphate, may decrease the intestinal absorption of phosphate, which results in phosphate depletion, and may help to reverse the precipitating reaction. Recently, diltiazem has been used to treat calcinosis cutis and dramatic improvement with regression of calcification has been reported after a prolonged treatment (17).

Besides these medical therapies, some reports have documented the benefits from surgical management of calcinosis cutis. Indications for surgical treatment include painful masses, recurrent infection, ulcerations, functional impairment, and cosmetic concerns (18). Most recently, Cousins et al. (8) reported an excellent result from surgical intervention of calcinosis cutis universalis in a patient with SLE. Our patient was treated with oral aluminum hydroxide and a favorable response was seen during the first six months, but, thereafter, there was no further improvement of lesions. Thus, after nine months of treatment with aluminum hydroxide, the large mass over the right iliac crest was excised, and then inner calcium contents were squeezed, debrided and simply closed, with an excellent result. Wound healing was somewhat delayed, but follow-up has confirmed that surgery is beneficial to patient's comfort and function. Taken together, we empirically recommend that oral aluminum hydroxide and subsequent surgical intervention may be the most ideal therapy for the treatment of large calcinosis cutis. Wound healing, although a potential problem, does not constitute a contraindication to operative treatment.

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