



Calcinosis Cutis: Case Series of Five Patients

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Abstract

Calcinosis cutis is an uncommon disorder characterized by the deposition of insoluble calcium salts in the skin and subcutaneous tissue. There are five types of calcinosis cutis, namely metastatic, dystrophic, idiopathic, iatrogenic calcinosis and calciphylaxis. We report a case series comprising of five patients (four females and one male). There were 5 cases of dystrophic calcification with connective tissue disorder being the primary diagnosis in these cases.

Keywords: *Calcinosis, Dystrophic, Dermatomyositis.*

Introduction

Calcinosis cutis is an uncommon disorder characterized by the deposition of insoluble calcium salts, such as hydroxyapatite crystals or amorphous calcium phosphate crystals in the skin or subcutaneous tissue and rarely deeper tissues such as muscle and tendons. Calcinosis cutis is of five subtypes namely dystrophic calcification, metastatic calcification, idiopathic calcification, iatrogenic calcification and calciphylaxis⁽¹⁾. Calcium deposits in the skin and subcutaneous tissue are seen in a variety of connective tissue disorders most commonly scleroderma, dermatomyositis, overlap syndromes and rarely systemic lupus erythematosus⁽²⁾, undifferentiated connective tissue disorder, mixed connective tissue disorder and rheumatoid arthritis⁽³⁾. This condition is associated with substantial morbidity

and can cause pain secondary to ulceration or over areas adjacent to the joints. Treatment is mainly unsatisfactory and no therapeutic options have convincingly prevented or reduced calcinosis⁽⁴⁾.

Case Reports

Case 1

A 69 years male admitted in Dermatology indoor department with erythroderma secondary to dermatomyositis. He was a known case of dermatomyositis for one and half years. He also had multiple painless, non-itchy, non-scaly, non-oozy lesions over lower back and thighs for 2 months. The lesions were gradually progressing in size and number. On examination, there were multiple ill-defined erythematous nodules and plaques of size varying from 1*1cm to 5*5 cm approximately with no surface changes. On

palpation, these were non-tender, indurated, and hard in consistency. Radiography of lower back and thigh region revealed foci of calcification in the soft tissue in the lower back and thigh with normal underlying bones. Incisional biopsy of lesion in thigh revealed granules and deposits of calcium in the dermis and subcutaneous tissue supporting the diagnosis of calcinosis cutis.

Case 2

A 62 years female, a known case of diffuse cutaneous progressive systemic sclerosis for the past 14 years was admitted with the history of painful ulceration over outer aspect of ankles for 2 months. Over bilateral lateral malleoli, there were two ill-defined erythematous plaques of size 1.5*1.5cm to 2*2.5cm approximately with central ulceration and discharge of chalky white material. X-rays ankles revealed soft tissue calcification over both lateral malleoli with no bony involvement.

Case 3

A 14 years female with the diagnosis of diffuse systemic sclerosis since 10 years of age, presented with ulcerated lesions over both knees for 4 months. On examination, over extensor aspects of both knees, there were two ulcerated plaques of size 3*2cm approximately with yellowish slough at base. There was history of discharge of chalky white material from the lesions. She had developed semi-flexion deformities over metacarpophalangeal and interphalangeal joints bilaterally. Her routine were conducted and all were within normal limits. X-ray bilateral knees revealed foci of calcification in soft tissue anterior to knee joint and underlying bones showed no abnormalities. She was managed with weekly doses of methotrexate and diltiazem. On follow up visits, there was marked improvement in the lesions of calcinosis cutis.

Case 4

A 33 years female, who was a known case of Dermatomyositis for 10 years, presented with

multiple erythematous indurated plaques of variable sizes over sacrum and thighs for 8 months and a plaque over sacrum for past 6 years. Her X-ray gave evidence of spicules of calcification in soft tissue adjacent to left hip region and proximal thigh. She was diagnosed as a case of Dermatomyositis with calcinosis cutis. Patient was managed with oral steroids and azathioprine for Dermatomyositis and oral calcium and risodronate for calcinosis cutis. The patient was also prescribed tablet diltiazem 60mg thrice a day that was increased to 90mg thrice a day, due to poor response. But the patient developed side effects such as headache, dizziness, flushing and stomach upset. Thereafter, the dose of diltiazem was decreased to 90mg twice a day. The lesions over thigh responded well whereas the lesions over sacrum showed poor response, where even after 5 years of therapy a well demarcated, erythematous indurated, fixed plaque was persisting over the sacral area with evidence of hypo pigmentation and atrophy at places (Figure 1).



Figure 1: Clinical photograph of patient of Dermatomyositis with calcinosis showing indurated, depressed, atrophic plaque over sacral area

Case 5

A 24 years female, who was a known case of Mixed connective tissue disorder with grade 4 lupus nephritis for 5 years presented with six months history of red to flesh coloured hard nodular lesions over both buttocks and thighs.

Radiological evidence of foci of calcification in soft tissues above bilateral iliac crest (Figure 2a), buttocks and thighs (Figure 2b) was demonstrated and a diagnosis of calcinosis cutis was made. Patient was managed with oral steroids, hydroxychloroquine, calcium and risedronate. The patient was also started on tablet diltiazem 60mg TDS but owing to poor response, the dose was increased to 90mg TDS. On follow-up visits, there was minimal improvement in the lesions.



Figure 5(a): calcinosis cutis above iliac crests



Figure 5(b): Calcinosis cutis over bilateral buttocks and thighs

All our patients of dystrophic calcification were initiated on calcium channel blockers, diltiazem and bisphosphonates like risedronate. Our two patients showed improvement with resolution of lesions, while one patient had resolution only in thigh lesions and no improvement over sacral lesions. One patient had minimal response and one was lost to followup.

Discussion

Among the five types reported in literature, dystrophic calcification is the most common type of calcinosis cutis⁽⁵⁾. It refers to deposition of calcium salts locally in dead and degenerating tissues with normal serum calcium levels and absence of derangements in calcium metabolism. Calcinosis occurring in connective tissue disorders is dystrophic type⁽⁶⁾ seen commonly in dermatomyositis, scleroderma, overlap syndromes and rarely in lupus erythematosus. Exact etiology is not known but it is proposed that it is related to the release of alkaline phosphatase by damaged lysosomes in necrotic tissues. Alkaline phosphatase acts on organic phosphate, which usually inhibits crystal formation thus allowing calcium deposition⁽⁷⁾. Other than connective tissue disorders, it can be seen in infections such as onchocerciasis and other inflammatory processes. Metastatic calcification⁽⁸⁾ is the deposition of calcium salts in otherwise normal tissues. It almost always results from hypercalcaemia due to derangements in calcium metabolism. Iatrogenic calcification occurs due to intravenous leakage of calcium gluconate or as calcium salts deposits in skin following procedures such as electromyography or electroencephalography. The fifth type of calcinosis cutis is idiopathic calcification, which occurs in the absence of any tissue or metabolic abnormalities. Several clinical presentations have been recognized without a definite cause such as idiopathic scrotal calcinosis, subepidermal calcific nodules, tumoral and military calcinosis⁽⁹⁾.

Our series comprised of five patients, out of which four were females and one was a male patient.

Hence, a male female ratio of 4:1 was observed. Calcinosis cutis is more common in females as compared to males as seen in our cases. Two patients were primarily diagnosed as dermatomyositis, two as scleroderma, one as mixed connective tissue disorder hence classifying as dystrophic calcinosis cutis. In dermatomyositis, calcification is observed in 40-70 percent of cases. It usually presents as firm dermal or subcutaneous papules or nodules, which are most prominent around sites of repeated microtrauma over extensors such as elbows, knees, buttocks and hands. Large subcutaneous calcium deposits can appear over the trunk also. Complications include pain, cosmetic disfigurement, persistent ulceration, secondary infection and mechanical compromise⁽⁶⁾.

In scleroderma patients, calcinosis cutis are commonly associated with limited cutaneous systemic sclerosis i.e. CREST syndrome, an acronym for calcinosis, raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia⁽⁵⁾. In our series, both patients belonged to diffuse cutaneous systemic sclerosis. Histologically, all cases of calcinosis cutis show similar morphology with the lesions comprising of large and small deposits of calcium⁽¹⁰⁾.

Treatment of calcinosis cutis is challenging. Spontaneous resolution has been reported only in 14 cases of dermatomyositis⁽¹¹⁾. Surgical excision is treatment of choice for localized disease. However, recurrence is known to occur. Intralesional steroids, carbon dioxide laser, extracorporeal shock wave lithotripsy, intralesional and topical sodium thiosulfate include treatment modalities of localized disease. For extensive lesions, systemic therapy may be administered in the form of calcium channel blockers, diltiazem. Diltiazem is probably the most used medical treatment till now. In responder patients, the response may be observed relatively quickly after months of treatment⁽¹²⁾. Bisphosphonates including etidronate, pamidronate, alendronate and risedronate⁽¹³⁾ are possible treatment options. Even in our patients,

three patients showed response to risedronate and diltiazem therapy. Warfarin, minocycline, ceftriaxone, aluminium hydroxide, colchicine, probenecid, intravenous immunoglobulins and autologous stem cell transplantation have been tried. Fetuin –A ($\alpha 2$ - Hereman-Schmid glycoprotein) and myo-inositolhexaphosphate (InsP6, phytate) are being considered as treatment modalities but require further investigations⁽¹⁴⁾. A recent review of 4 patients with juvenile dermatomyositis has demonstrated efficacy of monoclonal antibody, rituximab in the treatment of severe calcinosis⁽¹⁵⁾.

Conclusion

Calcinosis cutis is a rare disease. Sometimes, symptoms may be very mild and disease is diagnosed accidentally on radiography. Patients of connective tissue disorders, especially those with long duration of the disease must be screened for this condition. This will help to decrease morbidity associated and enable proper management of such patients.

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