A Rare Case of Disseminated Idiopathic Calcinosis Cutis

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Practice Points

- The balance of extracellular calcium and phosphate levels is well regulated through physiological mechanisms.
- Abnormalities or misregulation of this balance can lead to pathological deposition of calcium-containing salts.
- When this deposition of calcium salts occurs in the skin, it is known as calcinosis cutis.

Idiopathic calcinosis cutis is an uncommon condition characterized by calcium deposits in the dermis, subcutis, and muscles that most commonly are localized in one area. We report the rare case of a 16-year-old adolescent girl who exhibited unusually widespread calcium deposits. The laboratory results showed a normal biochemistry profile. Ultrasonography revealed calcifications in the fat tissue under the skin but not in deeper tissues or muscles. The histopathologic evaluation showed deep cutaneous and subcutaneous calcium deposits. Laboratory investigation revealed normal calcium, phosphate, and parathyroid hormone levels. Calcium excretion in a 24-hour urine sample was normal, but phosphate excretion was slightly low. Scintigraphic research showed no pathology in the thyroid and parathyroid glands but revealed soft-tissue calcification. A chest roentgenogram, blood tests, and testing of stools for occult blood showed no indication of internal malignancy. On the basis of these findings, the diagnosis of idiopathic calcinosis cutis was made. We discuss the pathogenesis, clinical and histologic picture, and differential diagnosis of calcinosis cutis.

Cutis. 2013;91:291-294.

Calcinosis cutis is characterized by the cutaneous deposition of calcium phosphate crystals in various areas of the body.[1] There are 4 major classifications based on etiology including dystrophic (calcium and phosphorus levels are normal and tissue damage is present), idiopathic (calcium and phosphorus levels are normal and no tissue damage is present), metastatic (presence of hypercalcemia or hyperphosphatemia), and iatrogenic calcinosis cutis. A few rare types have been variably classified as dystrophic or idiopathic, including calcinosis cutis circumscripta, calcinosis cutis universalis, tumoral calcinosis, and transplant-associated calcinosis cutis. The pathogenesis of calcinosis cutis is not completely understood.

Idiopathic calcinosis cutis is uncommon and may present as solitary or multiple lesions that appear sporadically or in association with Down syndrome (milialike idiopathic calcinosis cutis); it most often appears during childhood or adolescence or in transplant recipients (transplant-associated calcinosis cutis), most commonly noted following renal transplantation.[2-4] In metastatic calcinosis cutis, the first manifestations often are bone demineralization and visceral and/or nonvisceral calcification, mostly with mural deposits in arteries and arterioles. Chronic renal failure is the most common setting in which metastatic calcification occurs, but it also may

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The authors report no conflict of interest.

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be associated with primary or secondary hyperparathyroidism, paraneoplastic hypercalcemia, or sarcoidosis. Cutaneous involvement is rare.[5] Iatrogenic causes of calcinosis cutis include extravasation of intravenously administered calcium chloride or calcium gluconate and trauma-induced deposition of calcium in the skin, subsequent to electromyography or electroencephalography.[6]

Dystrophic calcinosis cutis is a much more common form of calcinosis cutis in which calcification usually is localized to a specific area of tissue damage, though it may be generalized in some cases. It occurs without calcium or phosphorus metabolic abnormalities. A primary abnormality is damaged, inflamed, neoplastic, or necrotic skin. Calcium salts are deposited secondary to local inflammation; tissue damage from mechanical, chemical, infectious, or other insults (eg, burns, arthropod bites, acne lesions, varicose veins, rhabdomyolysis); and degeneration. Secondary calcinosis cutis also may appear in cases of generalized tissue damage, such as connective-tissue diseases. Rothe et al[7] described 3 patients with long-standing systemic lupus erythematosus who developed extensive calcinosis cutis.

Case Report

A 16-year-old adolescent girl presented with concerns of hardening of the skin on the arms and legs. Her parents reported that the lesions had started on her upper extremities about 1 year prior to presentation and subsequently had spread to her lower extremities. There was no family history of similar lesions. On physical examination, numerous flesh-colored nodules and plaques measuring approximately 1 to 3 cm in diameter were noted on the arms and legs (Figures 1 and 2). Some of the lesions were painful ulcers and were comprised of scar tissue (Figure 3). There were no internal organ symptoms or concerns and the patient reported no muscle weakness or stiffness. Radiologic examination showed no bone pathology, but widespread calcification in the soft tissues was noted.

Ultrasonography revealed calcifications in the fat tissue under the skin but not in the deeper tissues or muscles. A biopsy was performed and histopathologic evaluation showed deep cutaneous and subcutaneous calcium deposits (Figure 4). Laboratory investigation revealed normal calcium, phosphate, and parathyroid hormone levels. Results of biochemical examinations were normal for blood sugar, urea, uric acid, creatinine, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, γ-glutamyltransferase, lactate dehydrogenase, blood proteins, total lipids, triglycerides, and high-density lipoprotein and low-density lipoprotein levels. A

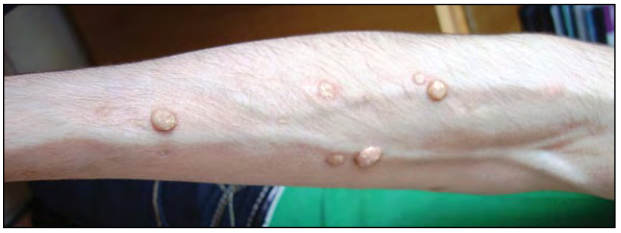

Figure 1. Flesh-colored nodules measuring approximately 1 cm in diameter on the right forearm.

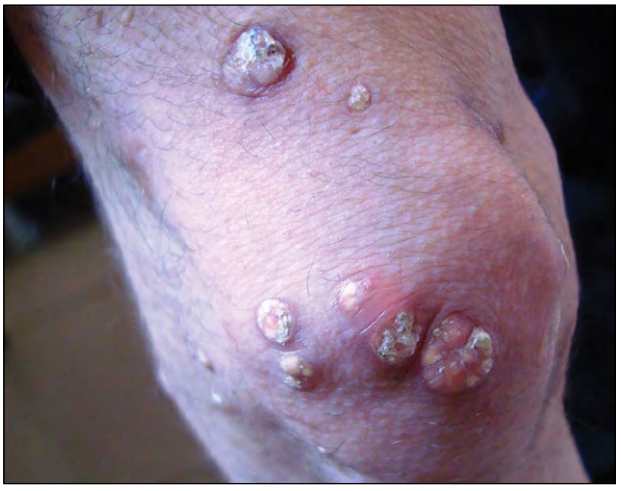

Figure 2. Flesh-colored calcified nodules and plaques on the right leg.

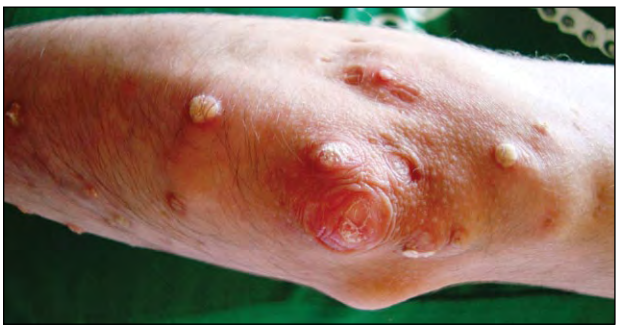

Figure 3. Calcified nodules with ulcers and scar tissue on the posterior aspect of the left forearm.

VDRL test was negative, and routine urine examination was normal. Slight anemia and an elevated erythrocyte sedimentation rate (32 mm/h; reference range, 0–20 mm/h) were noted. Calcium excretion in a 24-hour urine sample was normal, but phosphate excretion was slightly low (0.31 g/d; reference range, 0.4–1.3 g/d). Screening tests for collagen-vascular disease, including antinuclear antibody, anti-DNA, antineutrophil cytoplasmic antibodies, anti-Ro, anti-La, anti-Sm, and anti-Scl-70 antibody levels, were normal. Tuberculin skin tests were negative. Scintigraphic research showed no pathology in

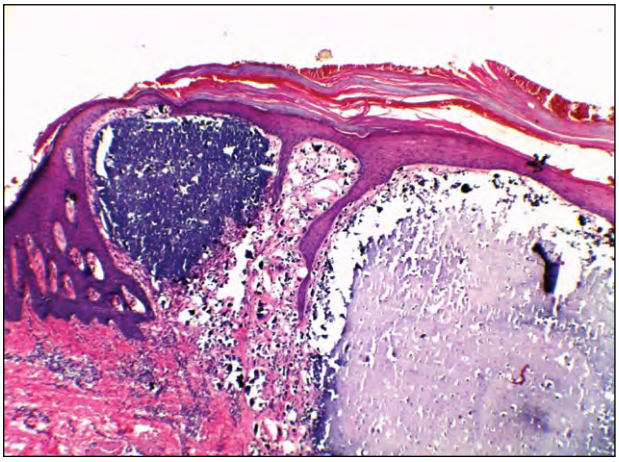

Figure 4. Calcium deposits in the superficial and mid dermis (H&E, original magnification ×200).

the thyroid and parathyroid glands but revealed soft-tissue calcification. A chest roentgenogram, blood tests, and testing of stools for occult blood showed no indication of internal malignancy. On the basis of the clinical, radiologic, and histopathologic findings, a diagnosis of idiopathic calcinosis cutis was made. The patient underwent surgical removal of some of the minor lesions and currently is under observation.

Comment

Calcification is the deposition of insoluble calcium salts; when it occurs in cutaneous tissues, the condition is known as calcinosis cutis. Deposited calcium foci also are known as subepidermal calcified nodules.[8,9] Calcium deposits in the skin can be classified as dystrophic, idiopathic, metastatic, or iatrogenic. In metastatic calcification, the precipitation of calcium salts in normal tissue is secondary to an underlying defect in calcium and/or phosphate metabolism. Some of the inciting factors of increased serum calcium levels include calcium supplements, primary hyperparathyroidism, excessive vitamin D intake, milk-alkali syndrome, sarcoidosis, and malignancy. Renal failure is mostly implicated in increased serum phosphate levels.[8,9] In our patient, we did not consider metastatic calcification because serum phosphate and calcium levels were within reference range, and the biochemical and radiologic findings gave no indication of any primary systemic disease. Cutaneous calcification also may be iatrogenic.

Calcified nodules may appear at sites of extravasation, probably because of an elevated concentration of calcium in the tissue and tissue damage following intravenous calcium chloride and calcium gluconate therapy.[10] Minor trauma and prolonged contact with calcium salts can lead to calcinosis cutis in a variety of settings.[11,12] It also has occurred in patients undergoing electroencephalography with saturated electrode paste containing calcium chloride,[13] in skin graft donor sites following the application of calcium alginate dressings,[14] and following liver transplantation.[15] Our patient reported no history of these conditions. For this reason, iatrogenic calcinosis cutis was excluded from the differential diagnosis.

Dystrophic calcification is associated with normal serum calcium and phosphorus levels and affects previously injured tissue (eg, sites of infection or local tissue trauma).[8] No primary skin injury or infection was detected in our patient. Connective-tissue disorders frequently are associated with calcinosis cutis. It is more commonly associated with juvenile rather than adult-onset dermatomyositis, occurring in 44% to 70% of children as opposed to 20% of adults.[16] Calcification tends to occur 2 to 3 years after disease onset and most frequently appears on the elbows, knees, shoulders, and buttocks.[17] Surprisingly, Wananukul et al[18] reported 2 cases of calcinosis cutis with onset 8 and 3 years before other clinical manifestations of juvenile dermatomyositis. The calcium deposits may be painful and can ulcerate; they also may exude a chalky material, form sinuses, and/or become chronically infected. Calcium salt deposition may become quite extensive, progressing along fascial planes of skin and muscle, forming what is referred to as an exoskeleton and leading to remarkable morbidity and mortality. Although it is uncommon, calcinosis cutis has been described in all clinical subsets of lupus erythematosus.[7,19-21]

Scleroderma and CREST syndrome (calcinosis, Raynaud phenomenon, esophageal motility disorders, sclerodactyly, and telangiectasia) are notable examples of conditions that frequently are associated with calcinosis cutis. No connective-tissue disorders were detected in our patient, and screening tests for collagen-vascular disease were negative; thus dystrophic calcification was not taken into consideration.

Idiopathic calcinosis is characterized by calcium deposits in the dermis, subcutis, and muscles without an underlying metabolic disorder or tissue injury.[8,9] The ultrastructural morphology of localized skin calcifications without associated disease and with normal serum calcium and phosphate ion values is still unknown.[12] Calcium and phosphate excretion may be low. In histologic sections prepared with von Kossa stain, calcium depositions appear first in the adipose tissue and collagen fibrils. These depositions move into the cutis and subcutis and make diffuse salt aggregates. Radiograph examination or sonography of the extremities and trunk for dense shadows due to calcium is important. Biopsy also plays an important role. The lesions may be

ulcerated and painful, as described in our patient. A creamy material containing calcium phosphate and calcium carbonate may drain from ulcerous lesions. This condition is known as lipocalcinogranulomatosis. Draining sinuses develop while the ulcers heal. Usually there is no infection, malignancy, or tissue injury, and biochemical parameters also are within reference range.[8,9] Thibierge-Weissenbach syndrome, systemic sclerosis in childhood, dermatomyositis, myositis ossificans progressiva, and gout must be kept in mind for differential diagnosis.

A low-calcium diet, excision of small lesions, and intravenous EDTA therapy (1200 mg daily for adults) with monitoring of renal function may be helpful for treatment.[8]

Conclusion

Our patient was diagnosed with idiopathic calcinosis cutis because of normal laboratory and clinical findings; however, the triggering factors for the disease remain unclear. We present this case to raise awareness of the presentation, etiopathogenesis, and course of this rare type of calcinosis cutis.

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