Dystrophic calcinosis cutis in pseudoxanthoma elasticum

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Pseudoxanthoma elasticum (PXE) is a genetic disorder in which elastic fibers become calcified with prominent cutaneous, ocular, and cardiovascular features. Calcinosis cutis is an acquired disorder of calcium deposition in cutaneous tissues that occurs as one of the following forms: dystrophic, metastatic, idiopathic, and iatrogenic. We report a case of a woman with PXE who developed widespread dystrophic calcinosis cutis in areas affected by PXE. Although tumoral calcification and nephrolithiasis have been reported in patients with PXE, only one other case in the English-language literature of PXE and calcinosis cutis has been reported and this case was characterized by small, milia-like papules on the front of the neck, without significant discomfort, whereas our patient had widespread involvement that was very painful and pruritic. On 6-month follow-up, this patient had only mild improvement after treatment with an anti-itch lotion and aluminum hydroxide, with which she was noncompliant. (J Am Acad Dermatol 2008;58:707-10.)

Pseudoxanthoma elasticum (PXE) is an inherited disease associated with dystrophic calcification of elastic fibers, primarily in the skin, eye, and cardiovascular system.[1,2] The characteristic cutaneous findings are yellowish papules coalescing into plaques on the neck, axillae, antecubital fossae, abdomen, groin, and thighs, at times referred to as chicken skin because of its appearance, with redundant skin folds.[3] Angioid streaks as a result of rupture of elastic laminae in Bruch's membrane in the eye can cause loss of central vision, and blood vessel involvement can lead to early cardiac disease, cerebrovascular events, peripheral vascular disease, and gastrointestinal bleeding.[3,4] Histologically, fragmented calcified elastic fibers are seen in the affected elastic tissue of the dermis, the eye, and arterial walls.[2] Despite the collections of calcium in the dermis, calcinosis cutis (CC) is an extremely rare occurrence in this disorder. We report a patient with PXE who developed widespread dystrophic CC forming painful and pruritic nodules with epidermal extrusion in several areas.

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OBSERVATION

A 57-year-old woman with a medical history significant for PXE, diagnosed by history and clinical examination in 1979 and confirmed with a biopsy in 2001, presented with a greater than 5-year history of intensely pruritic and painful cutaneous nodules of the abdomen, axillae, and groin. Treatment with topical corticosteroids had been unsuccessful. Along with the classic cutaneous findings associated with PXE, the patient reported a history of retinal hemorrhages resulting in blindness in one eye. One year before presentation, the patient noted a significant increase in the intensity of her pruritus and reported the extrusion of a yellow chalky material from several of her cutaneous nodules.

Her medical history included Crohn's disease controlled with mesalamine, and gastroesophageal reflux disease for which she was taking metoclopramide, ranitidine, and esomeprazole. Her other medications at the time of referral were methadone, clonazepam, and raloxifene.

Cutaneous examination revealed multiple yellow papules coalescing into plaques located on her neck, axillae, antecubital fossae, and popliteal fossae. In the axillae, and on her abdomen and groin, there were erythematous, firm nodules with central crusting. Several of these nodules demonstrated a chalky substance centrally (Figs 1 and 2).

A biopsy specimen had been taken by her referring physician, and staining with Verhoeff-van Gieson and von Kossa's stains revealed short, broken, and frayed elastic fibers, with small, black,

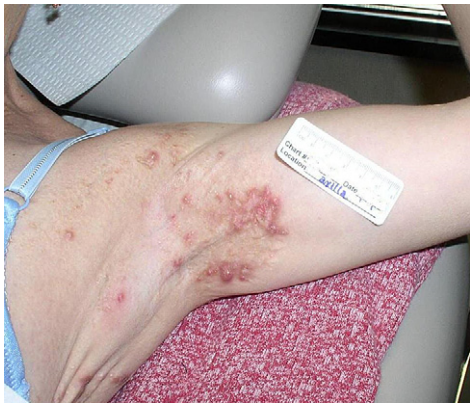

Fig 1. Firm, erythematous, painful nodules of calcinosis cutis involving left axilla on background of conventional pseudoxanthoma elasticum.

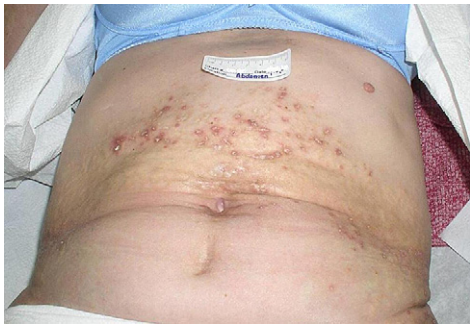

Fig 2. Calcinosis cutis and pseudoxanthoma elasticum of central abdomen. Firm, erythematous nodules with focal areas of yellow chalky material centrally.

granular microdeposits of calcium along these fibers. There were larger, more solid aggregates of calcium within the dermis. The final diagnosis was CC associated with the calcification and degeneration of dermal elastic fibers consistent with the known diagnosis of PXE (Figs 3 to 5).

Laboratory findings included normal serum calcium and phosphate levels: 9.1 mg/dL (8.5-10.6 mg/dL) and 3.6 mg/dL (2.5-4.5 mg/dL), respectively. A slightly elevated intact parathyroid hormone level of 76 pg/mL (12-65 pg/mL) was noted.

A trial was started of 600 mg of aluminum hydroxide 3 times daily to be used for at least 6 months with instructions to avoid any exogenous calcium products with the exception of dairy foods in moderation. On 6-month follow-up, the patient reported a mild improvement in her pruritus and in the inflammation around the nodules of calcium deposits despite sporadic use of aluminum hydroxide.

DISCUSSION

CC is the deposition of insoluble calcium salts in cutaneous tissues.[5] It can occur in dystrophic,

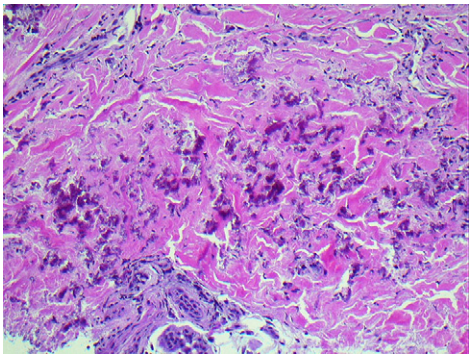

Fig 3. Numerous, short, wavy, fibrillar to slightly granular material with eosinophilic to slightly basophilic appearance present between normal pink bundles of collagen, corresponding to calcified, fragmented elastic fibers. (Hematoxylin-eosin stain; original magnification: ×10.)

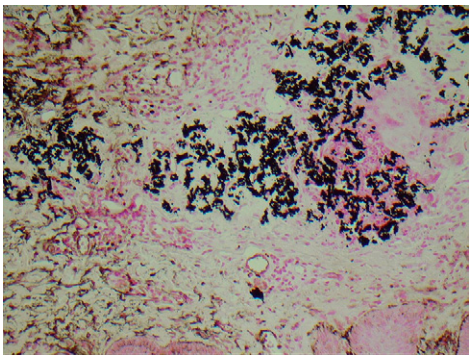

Fig 4. Confirmed presence of black, granular microdeposits of calcium along elastic fibers. (Von Kossa's stain; original magnification: ×4.)

metastatic, idiopathic, and iatrogenic forms.[5] Dystrophic CC occurs with normal levels of calcium and phosphate, and it is seen in skin that has been damaged or traumatized.[5] Although not fully understood, the current hypothesis is that the abnormalities in the structure of skin and subcutaneous tissues precipitate calcification.[5] Abnormally high mitochondrial calcium phosphate levels result in crystallization and cell death.[6] On a cellular level, one possibility is that membrane damage as a result of the initial disease process allows an influx of calcium into the cells, and the intracellular concentration of calcium increases to the point of calcium crystallization.[5] Alternatively, as the cells become necrotic and damaged, the resulting acidic environment halts the function of calcification inhibitors.[5] Dystrophic calcinosis occurs quite commonly with connective tissue diseases and has been seen in CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias) and generalized systemic scleroderma, and it is