# Localized papulonodular lesions on the leg

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## CLINICAL FINDINGS

A male patient 26 years old, complaining of asymptomatic skin lesions of 7 years duration. The lesions were characterized by gradual onset and slowly progressive course. The lesions were initially treated with potent topical steroid for 2 months duration, but without any significant improvement. Intralesional injection with triamcinolone acetonide also failed to achieve a good response while, cryotherapy showed improvement of some lesions. There was no previous history of similar condition and family history for similar disease was negative.

Cutaneous examination showed unilateral, multiple, firm papules and nodules that were localized on the inner aspect of the left leg (Fig. 1). The lesions were discrete, variable-sized and non-tender. Some lesions showed intact surface while few showed superficial erosion (Fig. 2). Radiological examination (plain X-ray) showed no abnormalities. General examination was irrelevant while routine investigations showed no significant abnormalities.

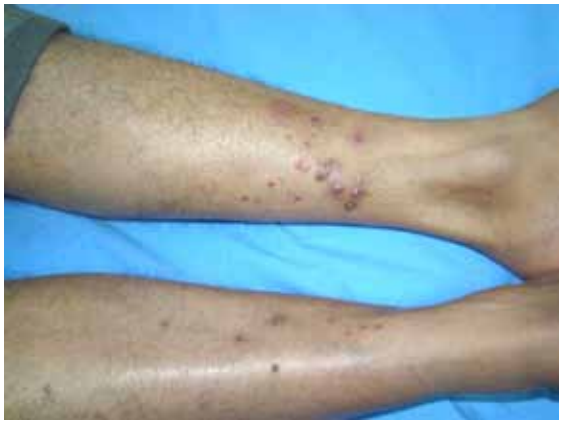

**Fig. 1** A male patient presenting with multiple darkly-pigmented papules and nodules on the left leg.

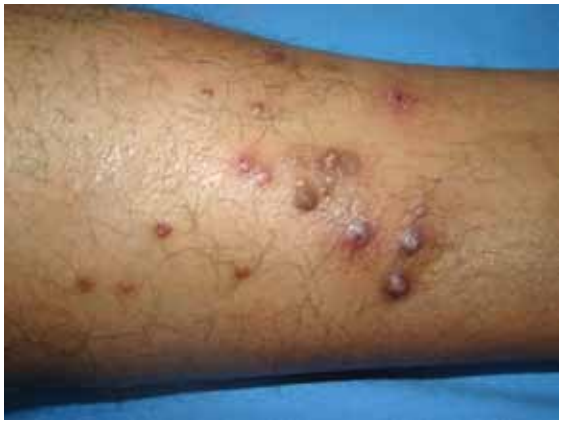

**Fig. 2** Some lesions show intact skin while few lesions are eroded.

**What is your clinical differential diagnosis?**

Kaposi's sarcoma, papular sarcoidosis, angiokeratoma of Mibelli, multiple dermatofibroma, and tufted angioma.

## PATHOLOGICAL FINDINGS

A skin biopsy from a well-developed lesion showed dermal masses containing large deposits of amorphous material (Fig. 3) that stained purple with routine H&E (Fig. 4). Special staining with Von Kossa stain showed blackish discoloration of

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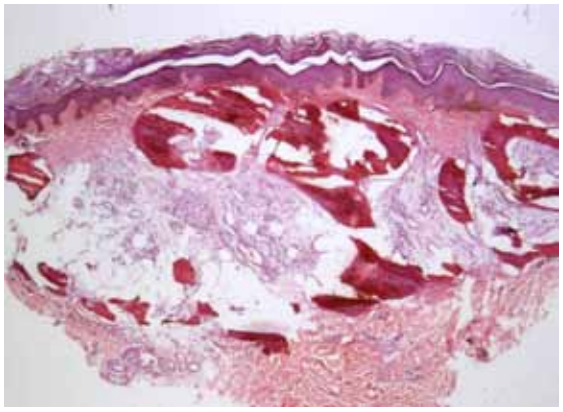

**Fig. 3** The dermis shows calcium deposits in the upper and mid dermis (H&E, x40).

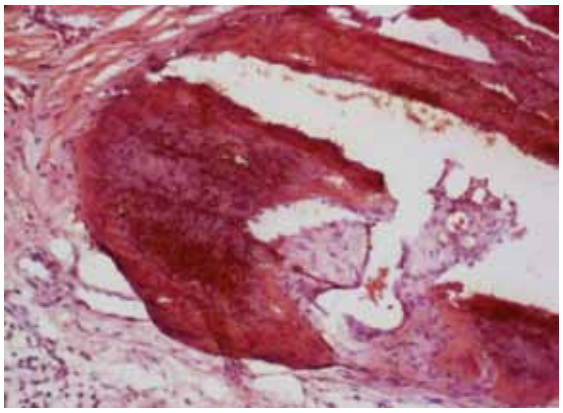

**Fig. 4** The calcium deposits are purplish in color with H&E stain (x400).

the deposits indicating calcium deposits. The surrounding stroma showed mild inflammatory infiltrate with increased vascularity. The epidermis showed moderate acanthosis and hyperkeratosis.

## DIAGNOSIS

Idiopathic Calcinosis Cutis (ICC).

## COMMENT

There are various forms of calcinosis cutis, mostly reported are idiopathic, dystrophic, metastatic, and iatrogenic. Dystrophic calcinosis is calcification associated with infection, inflammatory processes, cutaneous neoplasm, or connective tissue diseases. Metastatic calcification results from elevated serum levels of calcium or phosphorus. Iatrogenic and traumatic calcinosis are those types which are associated with medical procedures. A few rare types have been variably classified as dystrophic or idiopathic. These include calcinosis cutis circumscripta, calcinosis cutis universalis, tumoral calcinosis, and transplant-associated calcinosis cutis.[1-3]

The term idiopathic calcinosis cutis (ICC) is used when no obvious underlying cause can be identified for tissue calcification. ICC is characterized by lack of history of trauma, no preceding pathologic lesions at the sites of the papulo-nodular lesions, normal serum calcium and phosphorus levels, and absence of history of parenteral therapy. ICC can be wide-spread or localized. Distinct anatomical areas, vulva, scrotum, penis, neck, and breast have been reported to develop idiopathic CC. Skin ulceration may occasionally be seen in some cases.[4,5]

Calcinosis cutis is characterized by deposition of insoluble compounds of calcium (hydroxyapatite crystals or amorphous calcium phosphate) within the skin. This could be due to local, systemic, metabolic or physical factors.[6] High levels of gamma carboxy glutamic acid, a unique amino acid, have been found in the calcified tissue and urine of patients with calcinosis cutis. This amino acid is normally found in bones and teeth but ectopic soft tissue calcification can be triggered if it is produced de novo at these sites.[7]

Very few cases of idiopathic calcinosis cutis are reported in early childhood in the literature. Calcinosis cutis with Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly, and telangiectasia is referred to as CREST syndrome.[8] Primary normophosphatemic or hyperphosphatemic tumoral calcinosis shows no evidence of disorders associated with soft-tissue calcification, although,

**The clinicopathological challenges of ICC.**

| Diagnosis | Clinical | Pathological |
|---|---|---|
| **Kaposi's sarcoma** | • Affects predominantly men in the fifth to seventh decades<br>• The lesions are commonly limited to the lower part of the legs<br>• Lymph nodes and other organs may be involved<br>• Lesions may have macular, papular, nodular, or plaque like appearances<br>• Lesions may assume a brown, pink, red, or violaceous color<br>• Mucous membrane involvement is common | • Proliferation of irregular, often jagged, vascular channels in the dermis (slit-like vessels)<br>• Dermal proliferation of interlacing bundles of spindle cells<br>• Positive promontory sign (proliferating vessels surround pre-existing blood vessels)<br>• Perivascular lymphocytes and plasma cells<br>• Extravasated erythrocytes<br>• Variable nuclear pleomorphism and mitotic Figures<br>• Dermal siderophage deposition |
| **Sarcoidosis** | • Multisystemic disease with common pulmonary impairment<br>• Described in all races, genders and age ranges<br>• Nonspecific symptoms such as fever, malaise, fatigue in 1/3 of cases<br>• Presented with erythematous-violet papules, some with central umbilication | • Nodular dermal granulomatous reaction<br>• Well formed granulomas containing histiocytes with broad and vacuolated cytoplasm<br>• Absence or minimal lymphocytes surrounding the tubercles<br>• Negative Ziehl-Nielsen and PAS stains |
| **Angiokeratoma** | • Presented as solitary or multiple keratotic papules or plaques<br>• Occurs on any part of the body, but the lower extremities are most commonly affected in multiple type<br>• Lesions appear deep red to blue-black in color | • Marked dilatation of papillary dermal vessels to form large cavernous channels<br>• Irregular acanthosis of the epidermis with elongation of the rete ridges<br>• Varying degrees of hyperkeratosis.<br>• Epithelial collarette could be seen at the margins of the lesions |
| **Dermatofibroma** | • Round or ovoid, firm dermal nodules, usually less than 1 cm in diameter<br>• Common on the extremities, particularly the lower, of young adults<br>• Usually dusky brown in color<br>• Aneurysmal variants may be red<br>• Tumors with abundant lipid are creamy or yellow in color<br>• Often solitary and rarely multiple | • Poorly demarcated dermal mass that may extend into the superficial subcutis<br>• The mass is composed of a variable admixture of fibroblast-like cells and histiocytes, xanthomatous and multinucleate giant cells<br>• Monster cells (large atypical cells )<br>• Epidermis usually shows acanthosis with basal hyperpigmentation |
| **Tufted angioma** | • Slowly spreading erythematous macules, plaques, and nodules<br>• Multiple lesions are rare<br>• May show pyogenic granulomas like appearance<br>• Predominant in children and young adults<br>• Commonly located on the neck and upper trunk<br>• Sometimes painful or large-sized | • Multiple separated cellular lobules within the dermis and subcutis<br>• Each lobule is composed of cells with spindle-shaped and oval nuclei<br>• Small capillary-sized vascular lumina are present<br>• The vessels may show semilunar profile<br>• Hemosiderin may be present<br>• Lack of inflammatory infiltrate |

secondary tumoral CC cases have a concurrent disease capable of dermal calcification.[9] Another soft-tissue calcification disorder is calciphylaxis or calcifying pannucilitis, which is defined as small vessel calcification mainly affecting blood vessels of dermis and sub-cutaneous fat. Obesity, liver disease and high-serum calcium (Ca), parathormone (P) levels, combined therapies of calcium salts with vitamin D and corticosteroids have been observed to increase the likelihood of this

disease.[10,11]

Histopathological detection of large calcium deposits within sub-cutaneous tissue with no other pathology is enough to make the diagnosis of CC. Histhopathologic findings include calcific deposits beneath epidermis without any inflammatory infiltration. There may be histopathologically vascular changes lead to fibrosis, intimal hyperplasia, and occasionally thrombosis of the vessel in severe cases of calciphlaxis.[12] Von Kossa and Alizain stain is used to confirm the presence of calcium encrusting degenerated collagen bundles throughout the reticular dermis. In early reports, some authors used immunohistochemical stain to demonstrate whether there was an increased number of mast cells in the infiltrate. Now, it is clear that mast cells have no role in the development of the lesions. H&E stain is usually enough to demonstrate calcific deposits within the dermis.[13]

Although, surgical excision is the main choice of treatment, electrodessication or CO2 laser ablation may be performed for small, multiple lesions. Indications for surgical treatment include painful masses, recurrent infection, ulcerations, functional impairment and cosmetic concerns. Medical line of treatment after excision is a recommended protocol. Intralesional corticosteroids may be beneficial. Probenecid and colchicine have been useful in some patients. Magnesium or aluminium antacids may be effective phosphate binders in patients with hyperphosphatemia.[14]

Sodium etidronate and bisphosphonates may be helpful in some individuals by reducing the bone turnover and inhibiting the growth of ectopic hydroxyapatite crystals. Warfarin has shown benefit in some cases. There have been variably beneficial effects with the use of calcium channel blocker, Diltiazem over the period of last five years. The therapeutic effect of this is believed to be antagonism of calcium-sodium ion pump. The above medical management, though beneficial in some cases, is not recommended for children as the risks outweigh the benefits, thereby posing a challenge to the medical fraternity in the treatment of ICC.[15]

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