Calcinosis cutis in a background of chronic viral infection: Report of 2 cases: Diagnosed by fine needle aspiration cytology

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Abstract
Calcinosis cutis is an uncommon entity which develops due to the deposition of hydroxyapatite crystals of calcium phosphate in the skin. As the calcific deposits can clinically mimic a tumor, it is feasible to investigate them by fine-needle aspiration cytology (FNAC).
In this study, we describe two cases of calcinosis cutis that were diagnosed by fine needle aspiration (FNA). Both the patients presented with nodular lesions in hand and sacrococcygeal region respectively. Aspiration yielded chalky white material. FNA smears showed flakes of amorphous material indicating calcium along with few macrophages. The presence of amorphous calcium salts along with histiocytes in the appropriate clinical settings is diagnostic of calcinosis cutis. The cases are interesting, since both the patients have positive viral markers and are suffering from debilitating diseases.

Keywords: Calcinosis cutis, Viral infection, Cytology, Calcium.

Introduction
Calcinosis cutis commonly called as calciphylaxis is one of the uncommon manifestations of systemic calcinosis characterised by precipitation and deposition of calcium and phosphate salts in the dermis and subcutaneous tissues.[1] The pathogenesis of calcinosis cutis is not completely understood and a variety of factors can contribute for varied clinical presentations to occur.[2] We report two different cases of calcinosis cutis co-existing with viral hepatitis and diagnosed on fine needle aspiration(FNAC). These were reported as association of this condition with viral hepatitis hasn't been documented yet and it being rare to be diagnosed on FNAC.

Case Report I
A 70 year old male with unexplained renal failure, on hemodialysis (serum creatinine- 4.2) and HBSAg positive presented in the Nephrology outpatient department, Dayanand Medical College and Hospital, Ludhiana with complaint of multiple, slow growing subcutaneous nodular swellings over the dorsum of both hands and the right scapular region. The swellings were firm in consistency, non-tender, immobile and ranged from 4- 7cm in diameter. Fine needle aspiration cytology (FNAC) of the nodule on the hand was advised and the patient was referred to the Pathology department. The FNAC was done using a 22-gauge needle. On multiple aspirations, 10 ml of white chalky material was aspirated. Air-dried smears were stained with Giemsa stain and methanol-fixed smears were stained with Hematoxylin-Eosin (H&E).

Cytomorphology: The smears showed mainly flakes of amorphous granular material that stained deep blue on Giemsa stain and basophilic on H&E stain along with presence of occasional histiocytes. This material was interpreted as calcium. The presence of amorphous calcium salts along with histiocytes in this appropriate clinical setting was diagnostic of calcinosis cutis.

Few months later, the patient expired because of chronic renal failure.

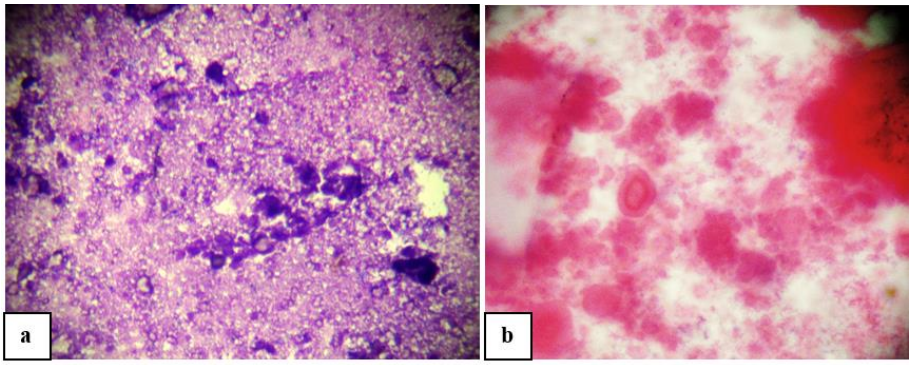

Fig. 1: Case I a) Photomicrograph showing calcium seen as amorphous material on Giemsa on fine needle aspiration (100X) b) H& E showing calcium crystals

Case Report II

A 47 year old HCV positive male presented in the Surgery Outpatient department of the same hospital with chief complaints of a big swelling in the sacrococcygeal region since 2 months which was associated with a whitish discharge since 10 days. The patient had a previous history of duodeno-jejunal stenting which was done for perforation along with colostomy for anastomotic leak and was thereafter bed ridden with bed sores. Serum calcium and phosphate done on two different occasions were within normal limits. Serum uric acid, electrolytes and alkaline phosphatase were within normal limits. Serum parathyroid hormone level was normal. The patient was advised an FNAC before going any further and was referred to Pathology department. On examination, the swelling was seen in the sacrococcygeal region, was subcutaneous, 8x6 cms, firm, non tender and overlying skin was ulcerated. FNAC from the swelling yielded whitish chalky material. Microscopic examination revealed presence of many multinucleated giant cells present against a dirty granular background containing crystalline material-calcification. A suggestive diagnosis of calcinosis cutis was given on FNAC and biopsy was advised. The specimen of the excised sacrococcygeal mass was received in the histopathology section of our Pathology department. On gross examination,the mass was greyish brown in colour with overlying skin flap measuring 11x11x4 cm. Two ulcerated areas were noted on the skin each measuring 1cm and 2cm respectively and had eroded edges with a necrotic base. On cut section, the mass was soft to firm with multiple nodules and loculi filled with chalky white material and many gritty areas noted. Sections taken from the mass showed extensive areas of dystrophic calcification which were surrounded by histiocytes and accompanied by foreign body giant cell reaction in the dermis and subcutis. Thus, a diagnosis of Calcinosis cutis was given which was confirmed on histopathology. The patient was discharged in good condition and no recurrence has been reported yet.

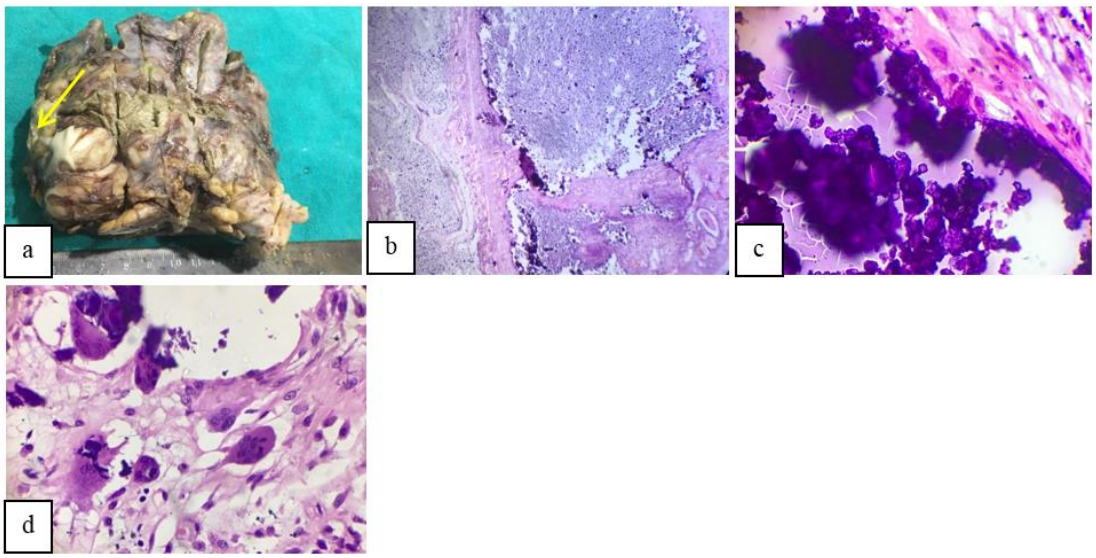

Fig. 2: Case II a): Gross examination of the sacrococcygeal mass with whitish material oozing from it; b): Histopathological examination showing pools of basophilic material (100X); c): Crystals of calcium seen with foreign body giant cells around (400X); d): Extensive foreign body giant cell reaction along with histiocytes seen. (400X)

Discussion

Calcinosis cutis as described by Virchow in 1855 is the deposition of calcium phosphate in subcutaneous tissue of the body and various types and subtypes have been recognised.[3] Calcinosis cutis is of four main types: metastatic, dystrophic, idiopathic and iatrogenic.[4] Metastatic calcification results due to the raised serum levels of calcium or phosphorus. Dystrophic calcinosis is calcification which is associated with infection, inflammatory processes, cutaneous neoplasm or connective tissue diseases. However, if the calcium levels are normal and no cause is known, then it is Idiopathic calcinosis cutis. Subepidermal calcified nodule and tumoral calcinosis are idiopathic forms of calcification. Iatrogenic and traumatic calcinosis are those types which are associated with medical procedures.[5] The various subtypes include: subepidermal calcified nodule, tumoral calcinosis, auricular calcinosis, milia like calcinosis, idiopathic scrotal calcinosis, calciphylaxis, calcification of blood vessels of skin, calcification of cysts and neoplasm.[3]

Calcinosis cutis is an uncommon condition, and is a severe complication of end-stage renal disease, seen in only 1% of patients undergoing chronic dialysis.[6] A number of cases of calcinosis cutis have been reported, but only a few have been documented involving areas of the hand. The most common sites affected are the superior and lateral shoulder, posterior elbows, and lateral hip and gluteal regions, though it has been noted in hands, feet, spine, temporomandibular joint, and knee.[7] The first patient had involvement of the usual shoulder regions, but also the rare involvement of the hand. Metabolic and physical factors are pivotal in the development of most cases of calcinosis.

Chronic renal failure affects many factors in calcium metabolism due to primary or secondary hyperparathyroidism, vitamin D intoxication, and milk-alkali syndrome.[1] Palpable, hard nodules, occasionally of considerable size, are noted usually in the vicinity of large joints and become fluctuant with an increase in size.[8] This is the most common setting in which metastatic calcification occurs as seen in our patient in the first case. Hyperphosphatemia occurs in chronic renal failure due to a decrease in renal clearance of phosphorus and is associated with a compensatory drop in the serum calcium level.[9] The low level of ionized calcium in the serum stimulates parathyroid secretion, leading to secondary hyperparathyroidism and to resorption of calcium and phosphorus from bone. The demineralization of bone causes both osteodystrophy and metastatic calcification.[4]

Dystrophic calcification is more commonly seen and occurs in either a localized or a generalized pattern, resulting from an underlying inflammatory process, and it is found in patients with normal serum chemistry levels.[10] The damaged tissues allow the influx of calcium ions causing an increase in intra-cellular calcium levels and subsequent crystalline precipitation.[3] The cutaneous lesions are usually found on the abdomen, buttocks, or thighs and present as firm, tender papules, nodules, or plaques that may periodically discharge chalky material.[1] This was similar to the second case as the patient was in a chronic debilitating state and had underwent a surgery too.

Calcification can be noticed in different conditions but etiology can be made out only by proper history. Co-infection with HBV or HCV as in both the above cases further led to a decrease in immunity resulting in debilitating state of the patient making him prone to getting calcinosis cutis. The presence of calcifications in cytologic material has been associated with entities like, pilomatrixoma, calcified epidermal cyst, tubercular lymph node, lymphoepithelial lesion of parotid, sarcoidosis involving parotid, and osteitis fibrosa cystica.[11] Tuberculosis and sarcoidosis would show a granulomatous response, whereas a calcified epidermal cyst shows anucleate and nucleate squames. Pilomatricoma on the other hand is composed of basaloid cells, ghost cells, and multinucleated giant cells in addition to calcification. A calcified fibrous pseudotumor shows abundant hyalinised collagen, fat, and neurovascular bundles along with calcification. Lymphoepithelial lesions are comprised of a polymorphous population of lymphoid cells along with histiocytes and calcification. However, absence of any tumor cells rules out the possibility of an extraskeletal osteosarcoma. The clinical evaluation helps in the exclusion of osteitis fibrosa cystica.[4] The treatment for small calcified deposits and large localized lesions is surgical excision which is curative and also allows histopathological examination that is required for confirmation of the diagnosis, whereas systemic therapy is required for disseminated and extended calcinosis.[12] Thus, FNAC is a simple, rapid and cost effective method of diagnosing this rare entity.

Conclusion

A complete laboratory workup is advised to rule out the abnormalities of calcium and phosphorus metabolism, any malignant tumor, collagen vascular diseases, renal insufficiency, excessive milk ingestion, vitamin D poisoning before giving the final diagnosis. The pathologist should be aware of the cytomorphology of calcinosis cutis and a proper knowledge of patient's clinical history can help in reaching the correct diagnosis.

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