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Is pathogenesis of calcinosis cutis related to epidermal cyst: A series of 12 cases with review of literature.

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Abstract

Introduction: Calcinosis cutis is the deposition of calcium in the skin and subcutaneous tissue. The presence of calcinosis cutis can be noted in any part of the body; more commonly in extremities, scrotum and head & neck region. Most importantly, it has a wide range of differentials, such as soft tissue and bony lesions, so it needs to be diagnosed accurately.

Aim: To describe the clinical, cytomorphological & histopathological features of calcinosis cutis at different locations with an idea to study its relationship with epidermal cyst.

Materials & methods: We reviewed a total of 12 cases of calcinosis cutis on fine needle aspiration cytology (FNAC) along with its clinical and histopathological findings, wherever available.

Results: A total of 12 cases of calcinosis cutis were reported on FNAC. We included both adult & pediatric patients, age ranging from 12-60 years. The common presentation was of gradually increasing, painless masses with most of the cases showing solitary nodules. In our study, the most common site noted was scrotum [5 cases] followed by neck [2 cases], thigh [2 cases], back [1 case], ear lobule [1 case] and gluteal region [1 case]. All these cases had an insidious onset with aspirate showing chalky white material in all cases. Cytomorphological evaluation showed presence of amorphous crystalline deposits of calcium in all cases with few cases also showing histiocytes, lymphocytes and giant cells in the smears examined. No epithelial cells or any abnormal cells were found in any case. Histopathological correlation was present in 06 of the 12 cases.

Conclusion: Calcinosis cutis is basically deposition of calcium in the skin layer and can be found anywhere in the body. FNAC is a very simple investigative modality which can help us in diagnosis of this not so common

entity and can also avoid the need of histopathological evaluation to a certain extent, considering the clinical picture of the patient. With this simple technique and cytomorphological features, we can differentiate it from other soft tissue or bony lesions at that site.

Keywords: Calcium metabolism, FNAC, calcification, scrotum, ear lobule, epidermal cyst, skin biopsy

Introduction

Calcinosis cutis is an uncommon benign lesion which is described as deposition of calcium in skin and sub-cutaneous layers.[1-3] Clinically, they present as firm to hard, solitary or multiple painless nodules.[2-4] Usually, in these benign lesions, there is no alteration of the calcium and phosphate metabolism, but can be due to tissue damage, some alteration in metabolism or idiopathic factors.[3-12] Few cases have also mentioned the presence of dystrophic calcification in pre-existing lesions like epidermal cyst, calcification eccrine sweat ducts, degenerated muscle, or calcified nodules.[3-10] These lesions can be seen anywhere in the body with common locations being scrotum, head & neck region, neck, back, thigh, arms, axilla.[5-12] In the current study, we aim at studying the detailed cytomorphological findings in calcinosis cutis at various sites and to discuss whether there is any association of these lesions with pre-existing cyst or history of any trauma.

Aims & objective

To study the detailed clinical & cytological features of calcinosis cutis on FNAC at varied location in the body.

To describe the histological features of calcinosis cutis, wherever available

To study if there is any link between the pathogenesis of calcinosis cutis with pre-existing lesions like epidermal inclusion cyst.

Materials & methods

All cases with a diagnosis of Calcinosis cutis on FNAC were collected from the Pathology Department for a period of one year. A total of 12 cases were retrieved from the archives of Cytopathology Department. A detailed clinical and cytomorphological data were collected from the pathology records and cytology slides were re-evaluated for those features. Histological data was available in 6 of the 12 cases. The sections were examined for confirmation of calcinosis cutis.

Results

We reviewed a total of 12 cases of Calcinosis cutis over a period of 2 year. The age of the patients ranged from 12-60 years, with median age being 35 years. Male preponderance was noted with male: female ratio of 2.5:1. The patients presented to hospital with slowly growing, painless, solitary to multiple, firm to hard, variably sized nodules. The swellings were mobile as well as slightly fixed, depending on different cases. In our study, the sizes of swelling ranged from 0.8 cm to 4 cm.

Scrotum was the most common location of calcinosis cutis in our study with 5 of the total 12 cases. Other regions noted in our study were neck, back, ear lobule, cheek, lower chest, arm, thigh region with one case each. All cases had unilateral presentation in our study. Of 12 cases, 7 cases showed solitary nodule, except for 5 cases of scrotal calcinosis, which presented with multiple subcutaneous nodules over the scrotal sac region.

The patients gave a long history of these evolving lesions, ranging from approximately 1-14 years with no history of trauma in any of our cases. On examination, swellings were firm to hard in majority of the cases.

Based on clinical examination and depending on the site of lesions, provisional diagnosis given in different cases were epidermal cyst, calcified nodule, post-traumatic

lesions, soft tissue lesion, neurofibroma, tumor calcinosis, etc.

Radiological findings were present in 5 of our 12 cases. Ultrasound findings in 2 cases of scrotal calcinosis ere there and suggested presence of discrete and aggregated echogenic nodule in subcutaneous region of scrotum with no involvement of deeper structures. X-ray was reported as calcified nodule in 3 of other cases.

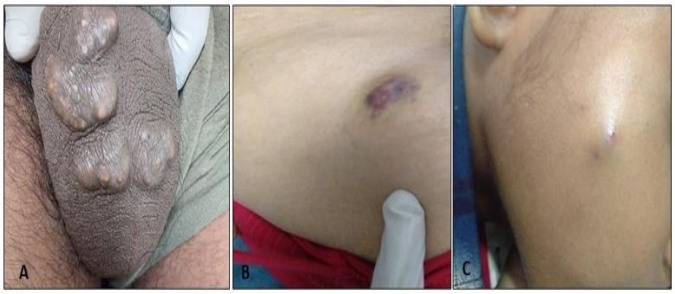

Figure 1 A-C: Clinical images showing calcific nodules, A- Multiple calcific nodules in scrotal skin. B- Right upper thigh. C- Left cheek.

FNAC was done in all these cases and a gritty sensation was noted in while needing in all cases. In few cases, it was difficult to pass the needle and needle got blocked by thick material. On FNA, chalky-white paste like material was obtained stained with Papanicolaou stain and Giemsa stain. Smears examined from different cases showed similar morphology with presence of bluish amorphous granular material and crystalline structures; confirming the presence of calcium deposits. There was no evidence of epithelial cells in all these cases. However, few cases showed presence of scattered histiocytes, lymphoid cells and multinucleated giant cells

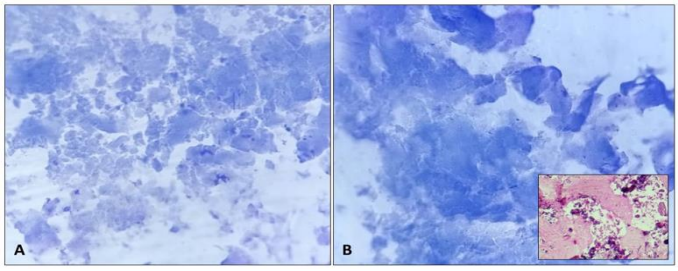

Figure 2A-B: Cytological smears showing presence of bluish amorphous granular material, suggestive of Calcinosis cutis [A&B- Pap stained, 40X]; Inset B- Section showing globular deposits of basophilic calcified material.

A diagnosis of Calcinosis cutis was given based on the presence of extensive calcium deposits on cytological smears. Along with calcium deposits, different cases showed presence of lymphocytes, macrophages, multi-nucleated giant cells. Surgical excision was done in 6 of the 12 cases. Sections were stained with hematoxylin & eosin stains. Sections examined showed extensive, globular deposits of basophilic calcified material. A detailed clinical, cytological & histological finding of all our 12 cases from the current study is described in Table No.1

Table 1: Clinical & detailed cytological findings in all 12 cases of Calcinosis cutis in current study:

Case No.	Age	Sex Male/Female (M/F)	Location	Solitary/Multiple (S/M)	Provisional Clinical Diagnosis	Cytomorphological feature	Cytological diagnosis
1	32	M	Scrotum	M	Epidermal cyst	Calcium deposits, macrophages, occasional multinucleated giant cells	Calcinosis cutis
2	35	M	Scrotum	M	-	Calcium deposits, lymphocytes,macrophages	Calcinosis cutis
3	40	F	Back	S	Epidermal cyst	Calcium deposits	Calcinosis cutis
4	12	M	Upper Cheek	S	Skin adnexal tumor	Calcium deposits, macrophages	Calcinosis cutis

5	39	F	Thigh	S	-	Calcium deposits & giant cells	Calcinosis cutis
6	51	M	Neck	S	-	Calcium deposits	Calcinosis cutis
7	42	F	Lower chest	S	? soft tissue tumor	Calcium deposits, occasional macrophages	Calcinosis cutis
8	30	M	Scrotum	M	Benign cyst	Crystalline & amorphous calcium deposits	Calcinosis cutis
9	27	F	Arm	S	Neurofibroma	Amorphous calcium deposits	Calcinosis cutis
10	34	M	Scrotum	M	Calcinosis	Crystalline calcium deposits	Calcinosis cutis
11	24	M	Ear Lobule	S	Epidermal cyst	Calcium deposits, lymphocytes	Calcinosis cutis
12	60	M	Scrotum	M	-	Calcium deposits, macrophages	Calcinosis cutis

Discussion

Calcinosis cutis is deposition of calcium in the skin & sub-cutaneous regions.[1-3] This entity was first described by Virchow in 1855. It is usually found in scrotum, head & neck region; however, it is ubiquitous and can be noted throughout the body.[2-5] Idiopathic scrotal calcinosis was first described by H.M. Lewinsky in 1883, a benign rare subtype of calcinosis cutis.[2-5] The common age group presenting this entity is 20-40 years, however extreme of age group has also been reported in literature.[3-7] We reported cases ranging from 12 years to 60 years, with mean age being 36 years. No gender predilection has been mentioned because it varies from study to study. In our series, we got a male preponderance with male: female ratio of 3:1. It results from idiopathic factors, tissue damage, abnormal calcium or phosphorus metabolism. Calcinosis can be described as dystrophic, metastatic, iatrogenic and idiopathic.[4-8] There is no exact consensus about the pathogenesis of calcinosis cutis. Few studies have attempted to explain its link with dystrophic calcification of pre-existing cystic lesions, eccrine ducts, eccrine epithelial cysts, degenerated dartos muscle in scrotal calcinosis. Association of this entity has also been explained with connective tissue disorders like systemic lupus erythematosus, scleroderma, dermatomyositis, and also with previous trauma, inflammation, impacted foreign material landing up in degeneration and resulting in formation of these calcium deposits.

Few cases have seen its presence with previous epidermal inclusion cyst with granulomatous reaction occurring when cysts rupture.[5-9] This also causes the presence of few inflammatory cells along with destruction of keratinous lining epithelium. Consequently, there is absence of any epithelial remnants in these calcified lesions. In one of our cases also, we found a case where patient had two lesions, on arm. On cytology, one lesion showed presence of sheets of anucleated squames, confirmed the diagnosis of epidermal inclusion cyst. The other lesion located almost in the same area showed calcium deposits, along with few giant cells and few lymphoid cells.

The presence of these two lesions in same region, points towards a similar epithelial abnormality; however, in second lesion may be because of rupture and long duration initially an inflammatory reaction had occurred followed by deposition of extensive calcium resulting a

firm to hard nodular lesion. This could be a type of dystrophic calcification. To generalize this pathogenesis, a greater number of cases are required to be published to at least prove the presence of some epithelial remnants in these calcified lesions.

In metastatic calcification, there is deposition of calcium with underlying abnormality in calcium metabolism and subsequently there is raised serum calcium & phosphorus; can be seen in renal failure patients.[5-9]

Iatrogenic calcification can sometimes occur due to subcutaneous injections of calcium-containing heparins, calcium containing electrode compounds for electromyographic or electroencephalographic examination or occupational exposures leading to tissue damage and causing local elevation of calcium.[6-12] Idiopathic calcinosis like we see in scrotal region have cutaneous calcification with normal serum calcium. Tumoral calcinosis is also a rare entity and is considered under idiopathic entity.

A term calciphylaxis has been given to a fifth type of calcinosis where there is deposition of calcium in the walls of small vessels of dermis and sub-cutaneous fat, ultimately causing infarction.[10-12]

Clinically, these lesions present as sub-cutaneous and cutaneous painless lesions/nodules with long standing history.[1-12] We noted similar presentation in all our cases. Mostly these lesions are solitary except for in scrotal region where variably sized calcified nodules are noted. FNAC reveal similar results with aspirate being chalky-white and granular. On examination, extensive calcium deposits were seen along with variable amounts of lymphocytes, macrophages and giant cells. We need to distinguish this entity from calcified epidermal cyst, calcified fibrous pseudo-tumor, pilomatricoma, tuberculosis, etc. These entities can be diagnosed by presence of their lining epithelial remnants and other specific features.

Histopathology is not often required to make a definitive diagnosis of calcinosis cutis. Radiology in conjunction with cytology should suffice in making a correct diagnosis.[9-12] FNAC is a simple, non-invasive and fast technique in identifying these calcific nodules and helping in management by simple excision of these localized lesions.

Conclusion

A lot has been discussed about the pathogenesis of calcinosis cutis but a definite etiopathology has not been defined. In our study, we can downline the underlying cause of calcinosis cutis to some tissue in preexisting cystic lesions, thereby leading to calcium deposition. In scrotal calcinosis per se, degeneration and destruction of dartos muscle in response to certain injury could be the underlying pathogenesis.

Additionally, our study highlights the importance of a simple investigative modality, i.e., FNAC in diagnosing these firm to hard cutaneous & sub-cutaneous lesions. In fact, to much extent, cytological evaluation can avoid the need of histology as well. In all our 12 cases, cytology helped us in giving an accurate diagnosis of calcinosis cutis and helping in management of these patients.

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