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Clinical Spectrum of Calcinosis Cutis From Common to Rare Presentations: A Prospective Study

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Abstract
Calcinosis cutis is an aberrant calcium deposition in skin and subcutaneous tissues. In view of pathogenesis, there are four types: dystrophic, idiopathic, metastatic and iatrogenic. To explore common and rare presentations across clinical spectrum of calcinosis cutis. A prospective study of 20 suspected cases of calcinosis cutis that visited outpatient clinic at our tertiary care center over a period of one year are studied to know about the spectrum of clinical presentations. Dystrophic, idiopathic, metastatic and iatrogenic calcinosis cutis occurred in 45%, 50%, 5% and 0% of total 20 cases respectively. Of dystrophic calcifications, Calcinosis cutis owing to trauma, multiple scrotal sebaceous cysts, systemic sclerosis, secondary to hidradenitis suppurativa and carbuncle occurred in 22.22%, 33.33%, 22.22%, 11.11% and 11.11% respectively. Among three types of idiopathic calcinosis, scrotal calcinosis, subepidermal calcified nodule and tumoral calcinosis occurred in 50%, 30% and 20% of cases respectively. A Chronic kidney failure patient had metastatic calcification. Scrotum and extremities (35% each) are the most common sites involved. Most patients are middle-aged, youngest being one-month-old male baby and oldest is 78 year male. All relevant investigations done and diagnosis confirmed by histopathology. Though dystrophic calcifications are most common while idiopathic being rarest, our study showed slightly higher incidence of idiopathic cases even after thorough investigations. Additionally, study demonstrated atypical clinical presentations of calcinosis cutis in relation to age, location and resemblance to other dermatome posing diagnostic challenge and subsequently impacting treatment strategies.

INTRODUCTION

Calcinosis cutis is an aberrant deposition of calcium and phosphate salts in skin and subcutaneous tissues. They are categorized into four main types based on the aetiology and histopathology[1]:

- Dystrophic
- Metastatic
- Idiopathic
- Iatrogenic

Calcinosis cutis most often results from dystrophic calcification, which has normal laboratory values for phosphorus and calcium. A nidus for calcification is formed by tissue damage caused by an underlying disease, such as lupus erythematosus, systemic sclerosis, dermatomyositis, or mixed connective tissue disease. Metastatic calcification occurs when there are abnormal serum levels of calcium and phosphorus. Idiopathic calcification doesn't have both underlying tissue damage and aberrant laboratory results. Subepidermal calcified nodules, scrotal calcinosis and tumoral calcinosis are among them[1,3]. Taking high amounts of calcium or phosphate supplements can result in Iatrogenic calcification. Calciphylaxis is considered to be a specific form of Metastatic calcification. Dialysis and chronic renal failure are linked to calciphylaxis, which is the calcification of small and medium-sized vessels[2,3].

To assess the disease's state, severity and potential cause, laboratory tests and imaging should be performed. A routine haematological investigation should be taken, to rule out malignant neoplasms, lupus erythematosus, chronic kidney failure etc. To rule out hyperparathyroidism and hypervitaminosis D, tests for parathyroid hormone and vitamin D levels are performed. For metastatic calcification, measurements of serum calcium, phosphate, total proteins, albumin and 24-hour urine excretion of calcium/inorganic phosphate should be made. For lupus erythematosus and systemic sclerosis, antinuclear antibodies (ANA) and its immunofluorescence patterns have to be evaluated[2,3].

MATERIALS AND METHODS

The present study is a prospective one conducted in our Outpatient department of DVL, Government General hospital, Anantapur over a period of one year from July 2022 to July 2023. Informed consent was obtained from all the study patients. Patients who didn't consent to get enrolled in the study are excluded. All the patients suspected of having calcinosis cutis are studied to know about the spectrum of clinical presentations. The relevant clinical history, general clinical examination and cutaneous examination is recorded. The diagnosis of calcinosis cutis is made by doing all the relevant haematological, biochemical especially serum calcium and phosphorous levels, serum uric acid levels, serum parathyroid hormone, serum vit D levels etc, radiological investigations, extensive hormonal workup and sending the skin punch biopsies and excisional biopsies of the lesions for Histopathological confirmation.

RESULTS AND DISCUSSIONS

The present study has included a total of 20 cases. Majority of the patients are middle aged i.e. 45-59 years with 7 cases (35%), followed by 6 cases (30%) in the age group of 26-44 years (adults), 6 cases (30%) above age group of ≥60 years (elderly) and a single case of a neonate (Chart 1). The mean age is 47.80 years. The youngest patient in our study is a one-month-old baby and oldest is of 78years. Out of the total 20 cases, 12 cases (60%) are males and 8 cases (40%) are females. (Chart 2).

The presentations of the lesions in each case were different in number, site, size and appearance with some mimicking various other dermatoses. They were solitary to multiple in number forming a confluent mass. We have seen 4 solitary calcinosis cutis cases (20%) and 16 cases had multiple lesions of calcinosis cutis (80%). The commonest site involved was scrotum and extremities with 7 cases each (35%), followed by hip region and lower back with 2 cases each (10%) and least noted site of involvement was buttocks and scalp with one case (5%) each. The lesions presented as firm to hard, white to hyper pigmented nodule(s) of various sizes. (Table 1).

Out of the four types of calcifications, majority of the cases are idiopathic calcifications with a total of 10 cases (50%) followed by dystrophic calcifications with 9 cases (45%) and lastly a single case of metastatic calcification (5%). (Chart 3).

Among the three types of idiopathic calcifications, idiopathic scrotal calcinosis (fig 1), subepidermal calcified nodule(s) (fig. 2) and tumoral calcinosis [fig 3 and 4] occurred in 4 cases (40%), 4 cases (40%) and 2 cases (20%) respectively. Majority of the idiopathic calcifications are seen in elderly age group (60%) and male patients (80%). Apart from scrotum (40%), extremities (40%) are commonly involved, followed by scalp (5%) and buttocks (5%). (Table 2).

Dystrophic calcifications as seen in 9 of our cases, mostly occurred due to calcification of multiple scrotal sebaceous cysts. Three such cases of multiple calcified sebaceous cysts (33.33%) (fig 5) occurred in our study, followed by 2 cases of dystrophic calcifications owing to trauma (22.22%), 2 cases owing to calcinosis cutis in systemic sclerosis (22.22%) (fig 6), one case due to calcification in carbuncle (11.11%) (fig 7a) and one because of calcifications which occurred in Hidradenitis suppurativa (11.11%) (fig 7b). Dystrophic calcifications were majorly noticed in middle-aged patients (44.44%) and females (55.55%). Scrotum was commonly

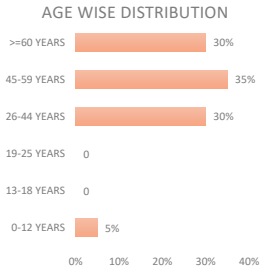

Chart. 1: Age wise distribution of the calcinosis cutis

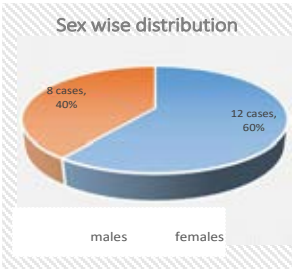

Chart. 2: Sex wise distribution of calcinosis cutis

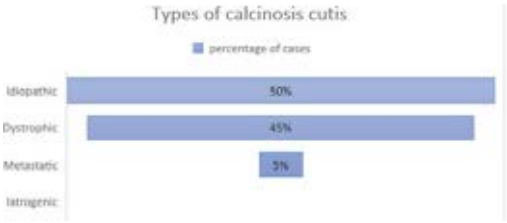

Chart. 3: Different types of calcinosis cutis

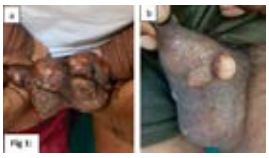

Fig. 1: a and b) Idiopathic scrotal calcinosis cutis

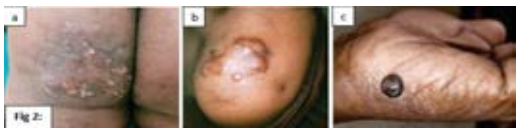

Fig. 2: Subepidermal calcified nodules

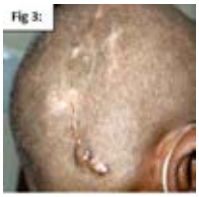

Fig. 3: Tumoral calcinosis

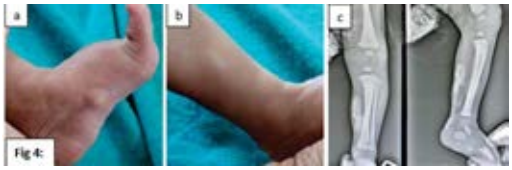

Fig. 4: a and b) Tumoral calcinosis

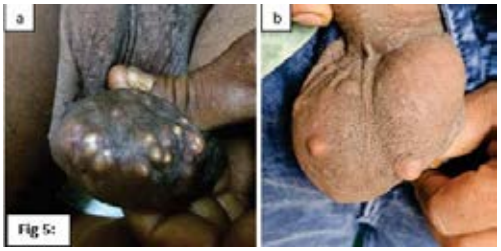

Fig. 5: a) Multiple Calcified sebaceous cysts of scrotum

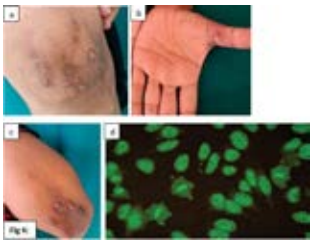

Fig. 6: Calcinosis cutis in systemic sclerosis: a)

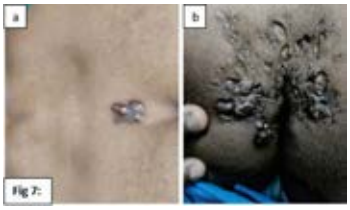

Fig. 7: Calcinosis cutis secondary to a)

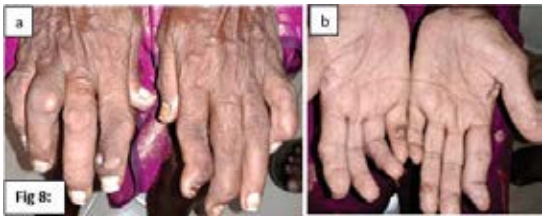

Fig. 8: Calcinosis cutis in chronic renal failure: a)

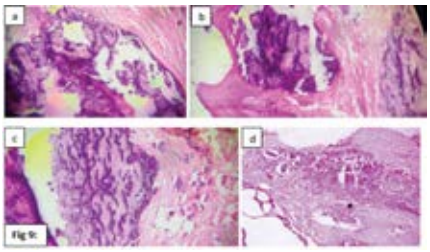

Fig. 9: Histopathology of Calcinosis cutis (a-d)

involved with 3 cases (33.33%), followed by 2 cases each (22.22%) involving lower back, hip region and limbs respectively. (Table 2).

A single case of metastatic calcinosis cutis over both the palms is recorded in a 72-year-old female patient having chronic renal failure. (fig 8) She also had elevated serum calcium and phosphorous levels along with deranged renal function tests. (Table 2).

In our study, most of the lesions are punch biopsies and some are accessional biopsies and sent to Department of Pathology for histopathological confirmation. (Fig 9).

Table 1: Distribution of cases on basis of age, sex, site, number, size and investigations

Age/Sex	Site	Solitary/multiple	Size (cm)	Biopsy done/not	Se. Ca^{2+}	Se. PO^{4-}	Se. Uric acid
65y/M	Scrotum	multiple	0.2-0.9	done	Normal	Normal	Not done
55y/M	Scrotum	Multiple	0.3-1.5	done	Normal	Normal	Not done
28y/M	Scrotum	Multiple	0.2-1	done	Normal	Normal	Not done
50y/M	Scrotum	Multiple	0.5-1.5	done	Normal	Normal	Not done
40y/M	Buttocks	Multiple	0.3-1	done	Normal	Normal	Normal
55y/F	Thigh	Solitary	3×2	done	Normal	Normal	Not done
78y/M	Hand	Solitary	2×2	done	Normal	Normal	Normal
38y/M	Shoulder	Multiple	0.5-1	done	Normal	Normal	Normal
60y/F	Scalp	Multiple	0.3-0.9	Not done	Normal	Normal	Normal
1mon/M	Legs	Multiple	1-2	Not done	Normal	raised	Normal
45y/M	Scrotum	Multiple	0.2-1	done	Not done	Not done	Not done
30y/M	Scrotum	Multiple	0.3-1.5	done	Not done	Not done	Not done
55y/M	Scrotum	Multiple	0.2-1	done	Not done	Not done	Not done
45y/F	Sacrum	Multiple	0.2-1	done	Normal	Normal	Normal
60y/F	Hip	Solitary	2×3	done	Normal	Normal	Normal
55y/F	Hip	Solitary	2×2	done	Normal	Normal	Normal
60y/M	Natal cleft	Multiple	0.2-0.7	done	Normal	Normal	Normal
35y/F	Elbows and knees	Multiple	0.3-0.7	Not done	Normal	Normal	Normal
30y/F	Fingers	Multiple	0.5-1	Not done	Normal	Normal	Normal
72y/F	Palms and fingers	Multiple	0.2-1.2	Not done	raised	raised	Normal

Table 2: Different types of calcinosis cutis and frequency of their subtypes

Type of calcinosis	Subtypes	No of cases	Percentage
Idiopathic	Scrotal calcinosis	4	40
	Subepidermal calcified nodules	4	40
	Tumoral calcinosis	2	20
Dystrophic	Multiple calcified sebaceous cysts	3	33.33
	Calcinosis cutis secondary to trauma	2	22.22
	Calcinosis cutis in systemic sclerosis	2	22.22
	Calcinosis secondary to hidradenitis suppurative	1	11.11
	Calcified carbuncle	1	11.11
Metastatic	Metastatic calcifications in Chronic renal failure	1	5

Table 3: Comparison of different parameters with studies of Alok *et al.*[2] Kotian *et al.*[3] and Robert L *et al.*[6]

	Alok *et al.*[2]	Kotian *et al.*[3]	Robert L *et al.*[6]	Present study
Number of cases	18	6	34	20
Mean Age and sex distribution	42 years	46.16 years	48.6 years	47.80 years
	13 male, 5 female	3 male, 3 female	22 male, 12 female	12 male, 8 female
Site	Scrotum, Hip, scalp	Scrotum	extremities	Scrotum, extremities
Size	0.5-4.8cm	0.3cm-3cm		0.2-3cm
Biochemical values (serum calcium phosphate, uric acid)	within normal limits	within normal limits	five cases had deranged values	Two cases had deranged values
Type of calcinosis cutis	11cases of dystrophic	Idiopathic calcinosis	24 cases of dystrophic	10 cases of idiopathic
	6 cases of idiopathic	only (all 6 cases)	4 cases of idiopathic	9 cases of dystrophic
	1 case of metastatic		2 case metastatic	1 case of metastatic
Evidence of calcification elsewhere in body	No	No	No	No

Subepidermal Calcified Nodules: Over left buttock with confluent multiple whitish hard nodules mimicking cutaneous myeloma b) Subepidermal calcified nodules over left shoulder joint with confluent multiple white hard nodules c) Solitary subepidermal calcified nodule over medial aspect of left palm showing hyper pigmented firm to hard nodule measuring 1×1cm.

Tumoral Calcinosis: Over scalp with multiple white hard nodules of calcifications over an uninvolved area of scalp along with a scar of previously excised calcinosis nodules.

Tumoral Calcinosis: of both feet and legs with subcutaneous hard nodules c) X-ray AP and Lateral view of left leg showing multiple white homogenous opacities.

Multiple Calcified Sebaceous Cysts of Scrotum: Showing many white hard papulo-nodules along with punctum b) Multiple Calcified sebaceous cysts of scrotum showing skin colored to erythematous hard nodules.

Calcinosis Cutis in Systemic Sclerosis: a): Multiple white hard nodules over left knee b) white hard nodule over the palmar surface of thumb c) multiple hard white nodules over left elbow d) strongly positive immunofluorescence for CENP-B and ANA Hep-2 autoantibodies.

Calcinosis Cutis Secondary to a): Carbuncle over sacral region in midline b) healed hidradenitis suppurativa scars and sinuses over natal cleft.

Calcinosis Cutis in Chronic Renal Failure: a): Two nodules of white hard morphology over DIP NAD PIP joints of 2nd and 4th right hand digits along with flexor contractors b) multiple hard white nodules over both palms and digits.

Histopathology of Calcinosis Cutis (a-d): Showing large amorphous calcifications in epidermis, dermis and subcutis along with dense dermal inflammatory infiltrate and thick fibro-collagenous stroma (Hand ×100).

The present study had results in concordance to Alok *et al.*[4] and Kotian *et al.*[5] in view of mean age, sex

distribution, common site of involvement and size of the nodules. But this study differs from the other two, in reporting majority of the cases as idiopathic calcifications (50%) and two of the cases having deranged values. (Table 3).

Idiopathic scrotal calcinosis is seen in 20% of the study group with normal biochemical values comparable to Alok *et al.*[4] who reported a percentage of 27.77%. Four cases of subepidermal calcified nodules, with one over buttocks was reported in an adult patient similar to the study done by *et al.*[6].

Massive spontaneous deposits of calcium salts are often seen over large joints in otherwise healthy individuals. The disease is usually familial, associated with hyperphosphatemia[4]. A one-month-old male child was brought with hard subcutaneous nodules in both legs for 15 days. Serum calcium, PTH and uric acids were normal with elevated serum phosphates and low levels of Vit D. Mother was normal. A diagnosis of Hyperphosphatemic tumoral calcinosis is made[8]. A 60years female who presented with recurrent calcinosis cutis over scalp since her 6 years of age, normal laboratory investigations and with similar history in her granddaughter was diagnosed of having familial tumoral calcinosis[9].

Dystrophic calcification manifests in dead, degenerated, diseased tissues. The main reason of calcium deposition was local injury at the site, followed by chronic inflammatory process and lastly by ischemic injury. We have reported three cases of multiple calcified scrotal sebaceous cysts comparable to Kotian *et al.* who reported 4 cases[5] and two cases of dystrophic calcification over hip owing to trauma from weight bearing water containers alike Alok *et al.*[4]. Two cases of calcinosis cutis over extremities in systemic sclerosis was observed in our study whereas Alok *et al.*[4] reported calcinosis cutis over hip in dermatomyositis. Alok *et al.*[4] reported a case of dystrophic calcification in facial acne similar to our study which also observed two cases of dystrophic calcification in inflammatory processes like carbuncle and Hidradenitis suppurativa.

Metastatic calcification develops as a result of metabolic disorders resulting in hypercalcemia or Hyperphosphatemic. Instances of cutaneous metastatic calcinosis are rare. Most patients are related to renal hyperparathyroidism and osteodystrophy. We have reported a case of 72-year-old female with diabetes mellitus, chronic renal failure, osteodystrophy of digits, largely elevated serum blood urea and creatinine, slightly elevated calcium and phosphate was diagnosed to have metastatic calcification alike a case reported by Shiu-Dong Chung[11].

CONCLUSION

Though dystrophic calcifications are most common while idiopathic being the rarest, our study showed slightly higher incidence of idiopathic cases even after thorough investigations. Additionally, study demonstrated atypical clinical presentations of calcinosis cutis in relation to age, location and resemblance to other dermatome posing diagnostic challenge and subsequently impacting treatment strategies.

REFERENCES

1. Fairley, J.A. and A.B. Aronson, 2024. Calcium and other mineral deposition disorders. In: Fitzpatrick's Dermatology,, Kang, S., M. Amagai, A.L. Bruckner, A.H. Enk, D.J. Margolis, A.J. McMichael and J.S. Orringer, (Eds.)., McGraw-Hill Education,, New York, USA., ISBN-13: 9780071837835,
2. Le, C. and P.M. Bedocs, 2023. Calcinosis Cutis. StatPearls Publishing,, Treasure Island, Florida,
3. Bourke, J., 2024. Calcification of the skin and subcutaneous tissues. In: Rook's Textbook of Dermatology., Griffiths, C., J. Barker, T. Bleiker and R. Chalmers and Daniel Creamer (Eds.)., John Wiley and Sons, Inc., Hoboken, New Jersey, USA.,
4. Mohan, A., S. Singh, V.K. Sharma, P. Sharma and S. Kaur, 2017. Calcinosis cutis of usual and unusual sites: An eight year retro-prospective study in a tertiary teaching hospital in Western Uttar Pradesh, India. Indian J. Pathol. Oncol., 4: 161-165.
5. Kotian, T., P. Gaddam, S. Cherian, R. Naidu, U. Chaturvedi and Sruthimayura, 2021. Clinicopathological study of 6 cases of idiopathic calcinosis cutis: A case series. Indian J. Pathol. Oncol., 8: 302-305.
6. Tian-Yu, E., X.J. Yang, C. Bi, F. Xue and Y.Q. Cao, 2023. Idiopathic calcinosis cutis of the buttocks: A case report and review of the literature. Medicine, Vol. 102 .10.1097/md.0000000000031129.
7. Evans, M.J., K. Blessing and E.S. Gray, 1995. Subepidermal calcified nodule in children: A clinicopathologic study of 21 cases. Pediatr. Dermatol., 12: 307-310.
8. Tiwari, V. and F. Zahra, 2023. Hyperphosphatemic Tumoral Calcinosis. StatPearls Publishing LLC., Treasure Island, Florida,
9. Gutch, M., S. Kumar, S. Razi and K. Gupta, 2014. Tumoral calcinosis of scalp: A rare phenomenon. CHRISMED J. Health Res., 1: 198-200.
10. Róbert, L., N. Kiss, M. Medvecz, E. Kuroli, M. Sárdy and B. Hidvégi, 2020. Epidemiology and treatment of calcinosis cutis: 13 Years of experience. Indian J. Dermatol., 65: 105-111.
11. Chung, S.D., C.W. Lu, V.C. Wu, Y.S. Chen, K.C. Chang and S.H. Chu, 2008. Metastatic calcinosis cutis. QJM, Int. J. Med., 102: 359-359.