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A RETROSPECTIVE ANALYSIS OF CALCINOSIS CUTIS: A COMMON ENTITY AT UNCOMMON ANATOMICAL SITES.

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Abstract

Background

Calcinosis cutis can be defined as a condition of calcium salts deposition on the surface of the skin including the deepest layer called hypodermis. Many interesting medical data about calcinosis cutis are available in pathological and clinical literature. This condition can be subdivided into five types, they are dystrophic, metastatic, idiopathic, iatrogenic, and calciphylaxis. Among these types, dystrophic calcification is the major cause and it is interlinked with the levels of phosphorus and calcium.

Objective

This study aims to spotlight the numerous clinical and pathological characteristics of calcinosis cutis from various lesions in medical history.

Methods

A complete investigation of the clinical and pathological characteristics of calcinosis cutis in all the selected cases was performed. The type of the study was retro-prospective where the data of seven years i.e. from July 2016 to June 2023 were collected from the Department of Pathology, PMCH, and Patna.

Results

A total of 17 cases with the condition of calcinosis cutis were selected for the study. Among these, the sites of the lesion were different (from 1 mm to 5 cm) in measurements and location in a few patients. The scrotum was the common location of the lesion. The selection of treatment was "wide surgical excision". The histopathological treatment was hardly challenging.

Conclusion

This study showcased various measurements and locations of the lesions site of the histopathological construction, and therefore this study spotlights the numerous clinical and pathological characteristics of calcinosis cutis from various lesions.

Keywords: Hypodermis, Calcinosis cutis, Histopathology, Calcium and phosphorus.
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Introduction

Calcinosis cutis can be defined as a condition of calcium salts deposition on the surface of the skin including the deepest layer called hypodermis. The symptoms of calcinosis cutis include mild to moderate pain, decreased movements or immobility, and prolonged infections. The condition of calcinosis cutis may vary depending on the type.

They are categorized into 4 major types, they are dystrophic, metastatic, iatrogenic, and idiopathic [1]. Many interesting medical data about calcinosis cutis are available in pathological and clinical literature [2, 3]. The idiopathic variety of calcinosis cutis is always congenial and is treated after associating conditions [4].

Even though the occurrence of calcinosis cutis is usually rare, the opportunity arose to treat a few cases affected by the condition, which was further correlated with histopathological findings of the subsequent cases. Therefore, the current study set out to illustrate the diverse

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clinicopathological features of lesions of calcinosis cutis at usual and unusual sites [5].

The primary objective of the study is to illustrate the diverse clinicopathological features of lesions of calcinosis cutis, with a focus on both usual and unusual sites of manifestation. By examining cases from medical history, the study aims to shed light on the various clinical and pathological characteristics associated with calcinosis cutis, thereby contributing to a better understanding of its presentation and aiding in the development of more effective management strategies for this condition.

Method

Study design

A retrospective study.

Study setting

The data for this study were obtained from the Pathology Department, Patna Medical College and Hospital (PMCH), Patna. India, where the data of seventeen cases were investigated for seven years (July 2016- June 2023).

Participants

A total of 17 cases with the condition of calcinosis cutis were selected for the study. Among these, the sites of the lesion were different in measurements and location in a few patients. Of the 17 selected patients, eight patients were males (47.05 %) and nine patients were females (52.94%). Differences in measurement and location of the lesions vary from 1 mm to 5 cm.

Inclusion criteria

For the study on calcinosis cutis, inclusion criteria were focused on patients with a confirmed diagnosis through clinical examination and histopathological analysis, encompassing cases with lesions in various anatomical sites, regardless of age or gender, documented between July 2016 and June 2023.

Exclusion criteria

Exclusion criteria included cases with incomplete medical records, calcinosis secondary to other systemic diseases, patients previously treated for calcinosis cutis, and those without consent for their data to be used, ensuring a comprehensive and ethical review of calcinosis cutis manifestations.

Data collection

A total of 17 cases with the condition of calcinosis cutis were selected for the study. A thorough examination of the patient's age, gender, associated conditions, swelling period, pain duration, and radiological investigations were all noted.

Procedure

Further investigations were performed post-surgery and retained tissues were cut sectionally, and fixated, the tissues were embedded in paraffin, stained with eosin and hematoxylin, and Van Kossa stains and finally these sections were seen under a microscope, and then allowed for histopathological investigation

Bias

The study is a retrospective design that introduces potential recall and documentation biases while the exclusion criteria and the reliance on a single tertiary center may lead to selection and institutional biases, impacting the generalizability of the findings. Awareness of these potential biases is essential for interpreting and applying the study's results accurately.

Ethical considerations

The study was approved by the Institutional Ethics Committee.

Results

A total of 17 cases with the condition of calcinosis cutis were selected for the study. Among these, the sites of the lesion were different in measurements and location in a few patients. The scrotum was the common location of the lesion (Table 1). The selected patients were examined clinically. In case of emergency, the procedure of fine needle aspiration was done and the obtained samples biopsies were investigated histopathologically. The number of cases was high in the age group of 35-45 years. Hence the average age is 40.11 years. Among the 17 patients, Eight patients were males (47.05 %) and nine patients were females (52.94%). The difference in measurement and location of the lesions varies from a few mm to 5 cm.

The scrotum was the common location of the lesion in this study, and then secondly the lesion was found in the fingers and toes. Four cases showed multiple lesions and 13 cases showed solitary lesions. Among the 17 patients, 7 patients underwent FNAC (41.17%). The results of FNAC showed the accumulation of calcium salts as chalky white substances. General anesthesia was used for the procedure of biopsy. The tissues were stained using H&E staining and Von Kossa stains were used.

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Table 1: Distribution of cases based on age, sex, clinical features, FNAC, size, and presentation of lesion.

S.no.	Site	Age in years	Sex	Clinical features	FNAC	Size	Solitary/Multiple
1	Hip joint	70	Female	Swelling for 6 months	Done	2cm	Solitary
2	Toe	34	Female	Swelling Since 6 months	Not Done	1.5x1x1c m	Solitary
3	Scrotum	35	Male	Swelling with pain	Not done	2.5cm multiple	Multiple
4	Gluteal region	65	Female	Swelling with ulceration	Done	3x2cm	Solitary
5	4th toe	35	Female	Swelling And it itching	Not Done	1.5x1.5cm	Solitary
6	Dorsum of foot	28	Female	Swelling	Not done	3x2cm	Solitary
7	Ankle	45	Female	Swelling and ulceration N	Done	5x4cm	Solitary
8	Scrotum	40	Male	Nodular growth	Not Done	4x3cm	Multiple
9	Groin	55	Female	Ulceration and pain	Not done	3x2cm	Solitary
10	Pinna	28	Female	Swelling And cosmetics	Not Done	1.5x1x1c m	Solitary
11	Scalp	25	Male	Nodular growth	Done	2x2cm	Solitary
12	Pinna	15	Male	Nodular growth	Not Done	1.5x1.5cm	Solitary
13	PaThe palmar surface of the hand	22	Male	Swelling	Done	3x2cm	Solitary
14	Chest wall	30	Male	Swelling	Not Done	1.5x1x1cm	Solitary
15	Fingers of hand	55	Female	Nodular lesions	Done	Multiple 1-2cm lesions	Multiple
16	Scalp	45	Male	Nodule	Done	2x2cm	Solitary
17	Scrotum	44	Male	Nodular growth	Not Done	3x4cm	Multiple

A few of the cases of calcinosis cutis are discussed below in pictures/cases 1 to 7.

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Fig no. 1 A female patient of about 65 years old with a history of swelling and ulceration B) X-ray showed hyperintense area C) In FNAC aspirated chalky white material D) FNAC showed pink amorphous material flakes E) Gross shows 3x 2 cm mass, cut surface shows chalky white areas F) sections shows areas of calcification hence diagnosed as calcinosis cutis.

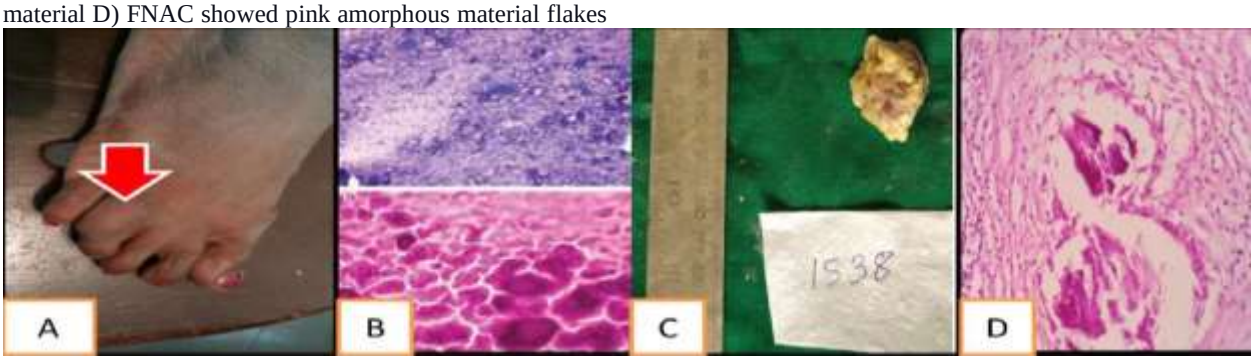

Fig no. 2: A) Patient 35 yrs. presents with swelling on the finger and was clinically suspected as GCT but on B)FNAC showed pink amorphous material C) After surgery gross was sent for histopathological examination which showed a grayish white lesion measuring 1.5x1.5cm. D) HPE showed calcium deposition at places.

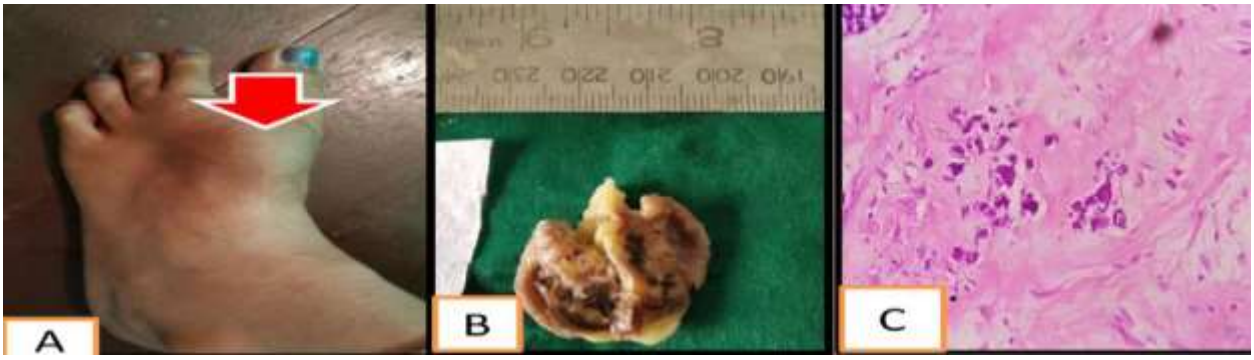

Fig no.3: A) 28 yr female presents with swelling on the dorsum of the foot B) Gross showed a grayish white lesion measuring 3x2x1cm C) Sections showed calcium deposition at places.

Fig no.4: A) 55YR female presents with a nodular swelling in the groin region with a focal area of ulceration B) showed areas of hyperintense areas at the lesion C) cut surface showed grayish-white areas D) Sections correlated with the findings of calcinosis cutis.

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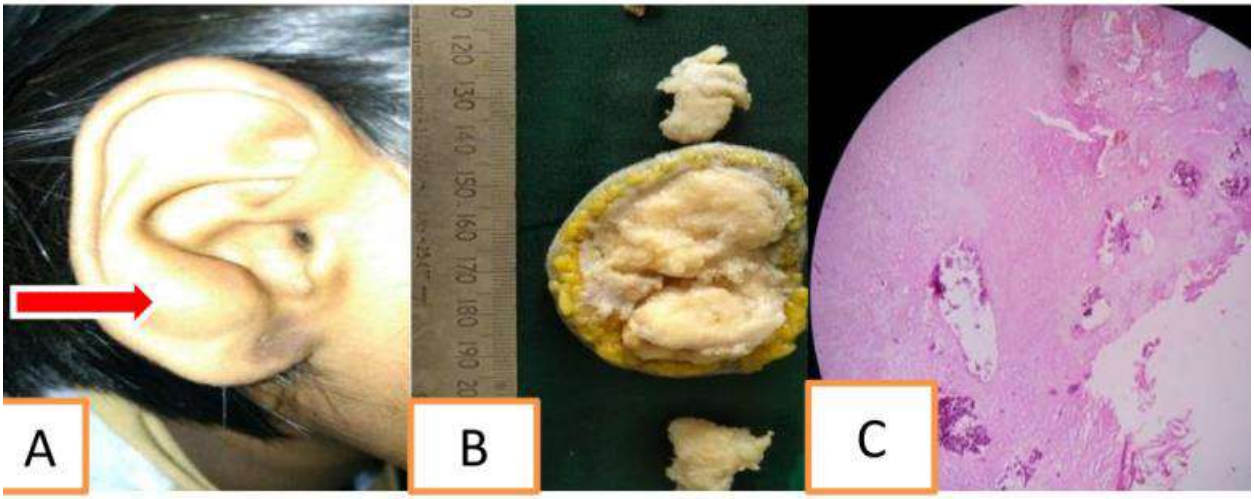

Fig no.5: A)Patients present with swelling in the ear lobule, Clinically suspected as an epidermal inclusion cyst FNAC yielded chalky white aspirate B) cut surface showed grayish-white areas C) section showed calcium deposition at places.

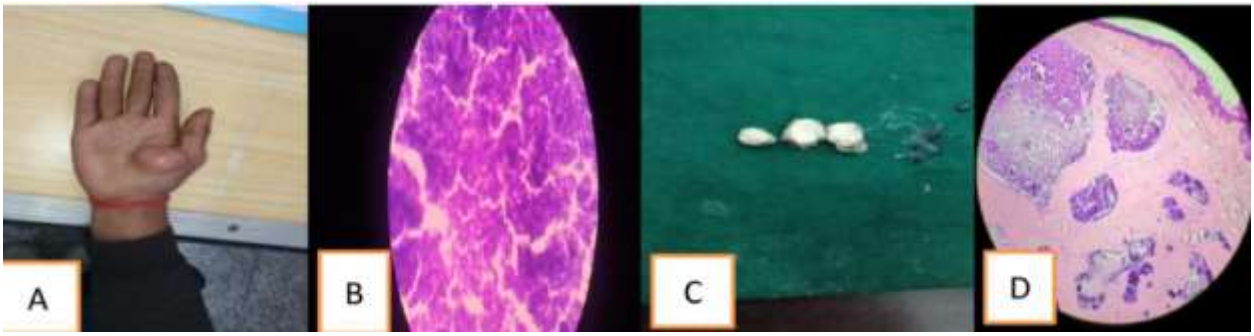

Fig no. 6: A) A 22-year-old male presented with a nodular lesion on the palmar surface of the hand. B) Aspirated chalky white material and cytology showed pink homogenous material C) single circumscribed lesion received cut surface showed a grayish white area D) HPE correlated with the findings of calcinosis cutis.

Fig no. 7: A female patient came with complaints of swelling in the ankle. Receiving a gross of 5x4x2 cm cut

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surface showed focal grayish white hard areas, HPE correlated with calcinosis cutis showing deposition of calcium below the epidermis.

Discussion

The entity known as calcinosis cutis can manifest at different ages, sizes, and locations, and with different pathophysiologies that may even exist from birth. The condition of calcinosis cutis is categorized into 5 types. They are dystrophic, metastatic, idiopathic, iatrogenic, and calciphylaxis.

1. Dystrophic calcinosis cutis
2. Metastatic calcinosis cutis
3. Idiopathic calcinosis cutis
4. iatrogenic calcinosis cutis
5. calciphylaxis

Table 2: Describes different types of calcinosis cutis / calcification.

Type	Description	Examples
Dystrophic	- Tissue damage - Release of phosphate binding protein (PBP) - PBP binds phosphate leading to calcification	• Systemic sclerosis • Dermatomyositis • Rheumatoid Arthritis (RA) • Systemic Lupus Erythematosus (SLE)
Metastatic	- Abnormal calcium & phosphorus level - Precipitate as calcium salts	• Hypervitaminosis • Sarcoidosis • Hyperparathyroidism • Malignant
Idiopathic	- Absence of any known tissue injury or systemic metabolic defect - Calcification localized to one general area	• Tumoral calcinosis • Subepidermal calcific nodule • Scrotal calcinosis
Iatrogenic	- Secondary to treatment or any procedure - Calcium salt precipitation	• Tumor lysis syndrome • After organ transplant
Calciphylaxis	- Use of phosphate binders and vitamin D supplementation + calcimimetics - Excessive calcium & phosphate deposits in small blood vessels	• Chronic renal failure • Dialysis

A few of the rare forms of calcinosis cutis as described in Table 3.

Table No. 3: Describes the rare forms of calcinosis cutis

Tumoral Calcinosis	- Caused by an error in renal phosphate metabolism resulting in hyperphosphatemia. - Characterized by large, calcified nodules. - Juxta particular location. - Progressive enlargement. - Tendency to recur after surgical removal. - Most common locations: hip, elbow, scapula, foot, leg, knee, and hand. - If familial, shows an autosomal recessive pattern.
Calcinosis Cutis Circumscripta / Calcinosis Universalis	- Caused due to altered ground substance. - Calcinosis cutis circumscripta occurs earlier and involves extremities. - Calcinosis universalis occurs later and is more widespread.
Transplant Associated Calcinosis Cutis	- Most common after renal transplant but is also described in liver, heart, and lung transplants.
Subepidermal Calcified Nodule	- Also known as cutaneous stone. - Presents as hard nodular swelling with calcification in the dermis.

Out of 17 cases, the mean age of presentation was 40.11 which was almost similar to the study by Alok Mohan et al [1] who studied on 18cases, and the mean age of presentation was 46.16 years. A study by Mohammad et al. involved 59 cases of calcinosis cutis [2]. Their mean age upon diagnosis was 50.7 years, which is similar to the

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findings. In the study, eight cases were males (47.05 %) and 09 cases were females (52.94%). There was a significant variation in the size of lesions ranging from a few millimeters up to 5 centimeters. However, a study by Alok Mohan et al stated, that of all the cases, 05 (27.78%) were female and 13 (72.22%) were male [1]. The size of the lesions varied significantly, ranging from a few millimeters to 4.8 centimeters.

The most common site involved in the study was the scrotum, followed by lesions in the fingers and toes. Three (17%) cases of idiopathic scrotal calcinosis were seen which was almost similar to the study by Alok Mohan et. al who stated 27% of scrotal calcinosis [10,11]. FNAC was performed in seven out of seventeen cases (41.17%) and aspirated chalky white material which was conclusive of calcinosis cutis. Cytological findings were of great importance in the diagnosis [12,13].

The incidence of calcinosis cutis in rare sites is described in Table 4 which was published between 1998 to 2021. The uncommon sites where calcinosis cutis is seen in the study are the hip, toe, gluteus region, dorsum of foot, ankle, groin, pinna, scalp, palmer surface of hand, chest wall, and fingers.

Table 4: Showing incidence of calcinosis cutis at different sites reported from 1999 to 2021

Unusual Sites	**Authors**
Hip	Alok Mohan et al [1]
Back	Alok Mohan et al[1]
Lateral Aspect Of Thigh	Koromilli Ramesh Kumar et al [3]
Arm	Alok Mohan et al [1]
Face	Patra S et al[4] Alok Mohan et al [1] Nestal-Zibo H et al [5]
Scalp	Alok Mohan et al [1]
Vulva	Biswas A et al[6]
Eyelid	Jun I et al [7] Samaka Rm et al [8]
Nasal Dorsum	Marsh Hr et al [9]

Generalization

This study on calcinosis cutis reveals a broad range of lesion sizes and occurrences across standard and unusual locations, suggesting the condition's variability may be underrecognized. Examining 17 patients highlights the need for healthcare professionals to anticipate calcinosis cutis beyond traditional sites, advocating for customized care approaches. The findings imply that greater awareness and documentation could unveil its more widespread prevalence, guiding improved management for affected individuals and underscoring the condition's potentially overlooked impact on public health.

Conclusion

Due to a lack of medical checkups, Calcinosis cutis is not recognized in many cases. To diagnose the condition of calcinosis cutis medical knowledge about the condition is essential. FNAC is an important procedure in the laboratory investigations continued by histopathological examinations and essential staining procedures are needed.

To find out the cause of calcinosis cutis, A thorough examination of the levels of calcium and phosphorus salts, malignant processes, collagen vascular diseases, renal insufficiency, excessive milk ingestion, and vitamin D poisoning are to be done. This study showcased various measurements and locations of the lesions site of the histopathological construction, and therefore this study spotlights the numerous clinical and pathological characteristics of calcinosis cutis from various lesions.

Limitations

A pertinent limitation of the study on calcinosis cutis is its reliance on a retrospective analysis from a single tertiary care center, which may not fully capture the diversity of manifestations and treatment outcomes of calcinosis cutis across different populations and healthcare settings. This limitation could restrict the generalizability of the findings, as the study sample may not represent the broader demographic variations or account for differences in clinical practices outside the studied institution. Furthermore, the retrospective nature of the study might lead to potential biases in case selection and data interpretation, limiting the ability to establish causal relationships between clinical presentations and treatment effectiveness.

Recommendations

To address the diverse manifestations of calcinosis cutis revealed by this study, it is recommended to develop

comprehensive diagnostic guidelines that include a wide range of anatomical sites, adopt a multidisciplinary approach for tailored treatment plans, and conduct further research to evaluate treatment efficacy. Initiating awareness programs for healthcare professionals and establishing a registry for calcinosis cutis cases are also advised. These steps aim to enhance early detection, improve management strategies, and gather detailed data on the condition's epidemiology and treatment outcomes, thereby improving care for patients affected by calcinosis cutis across varied clinical settings.

Acknowledgments
To all the participants for their patience and cooperation.

List of abbreviations
FNAC - Fine needle aspiration cytology
HPE - Histopathological examination
H&E - Hematoxylin and Eosin
PBP - Phosphate binding protein

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No source of funding

Conflict of interests
No conflict of interests.

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