



## Idiopathic tumoral calcinosis

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**Idiopathic tumoral calcinosis is an unusual benign condition characterized by the presence of calcified soft tissue masses of varying size around the joints. In this retrospective study, clinical data and radiological features of nine cases of idiopathic tumoral calcinosis are reviewed. Imaging features, particularly magnetic resonance imaging findings are detailed.**

**Keywords :** idiopathic tumoral calcinosis ; diagnosis ; imaging.

### INTRODUCTION

Idiopathic tumoral calcinosis is an unusual benign condition characterized by the presence of calcified soft tissue masses of varying size around the joints. It was previously described by Giard in 1898, Duret in 1899 and Teutschländer in 1935 but the term "tumoral calcinosis" was used for the very first time by Inclan in 1943 (3,5,8,9,14,17,19,20).

Idiopathic tumoral calcinosis should be diagnosed by eliminating other conditions in which similar calcified masses are seen, such as chronic renal failure, hypervitaminosis D, milk-alkali syndrome, sarcoidosis, primary hyperparathyroidism, calcinosis universalis, calcinosis circumscripta, collagen vascular diseases and paraneoplastic syndromes (8,9,12,15,24,26,28).

These latter diseases are associated with a high serum calcium level while normocalcaemia is seen in idiopathic tumoral calcinosis (4,7,11,27). Hence, the diagnosis of tumoral calcinosis has to be

refuted if an elevation of the blood levels of urea, calcium or non-protein nitrogen is found (14).

There are very few studies presenting the magnetic resonance (MR) imaging characteristics of this disorder (28). The purpose of this study is to describe the imaging findings in idiopathic tumoral calcinosis with emphasis on MR imaging.

### PATIENTS AND METHODS

We retrospectively reviewed nine patients with histopathologically proven tumoral calcinosis explored at two institutions over a ten-year period. Data pertaining to age, sex, location, clinical presentation, radiological features, histological findings and follow-up are reviewed.

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All patients had radiographs and MR scans. MR imaging was performed with a 1 Tesla MRI system (Magnetom Impact Expert, Siemens, Erlangen, Germany). All lesions were evaluated in the axial plane and at least another orthogonal plane. Both T1 and T2 weighted spin echo sequences were obtained. Intravenous gadolinium chelate was administered in 8 patients. Three patients underwent ultrasound studies. Computed tomography (CT) scans were performed in five patients. An additional Tc-99m-labelled phosphate bone scintigraphy was performed in two patients.

## RESULTS

Patients ranged in age from 2 to 53 years. All were Caucasian. There were 6 males and 3 females. All patients had neither familial antecedents nor biological abnormalities. A history of trauma was found in 2 cases. The lesion presented clinically as a slow growing swelling in all cases and size varied from 4 to 20 centimetres. Pain was reported in 5 patients. Joint range of motion was limited in one patient. One patient experienced recurrent tenderness and swelling of the legs. Infection and ulcerations

were seen in one case. No patient had any dental abnormality. Age, sex, location and clinical presentation are summarized in table I.

Radiographs showed well-demarcated, lobulated and calcified soft tissue masses, located in the peri-articular areas, unattached to bone in all cases. The masses consisted of conglomeration of multiple small and round opacities with different size and density separated by radiolucent septa. Fluid-calcium levels were noted in 2 cases (fig 1).

Radiographs also showed periosteal reaction associated to ill-defined patchy areas of osteocondensation within the medullary cavity of the tibias in one patient. On scintigrams, increased radionuclide uptake was seen in the tibial diaphysis. These lesions resolved completely on follow-up.

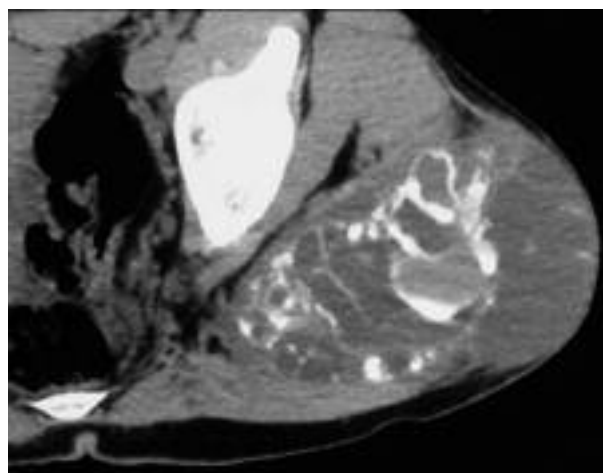
Ultrasound studies showed well-defined lobulated soft tissue masses demonstrating heterogeneous echogenicity, mainly multicystic in all cases, associated with irregular and calcified areas in two cases. The cysts contained anechoic or hypoechoic liquid. Fluid-fluid levels were noted in two cases (fig 2). Cysts were separated by hyperechoic thin

Table I

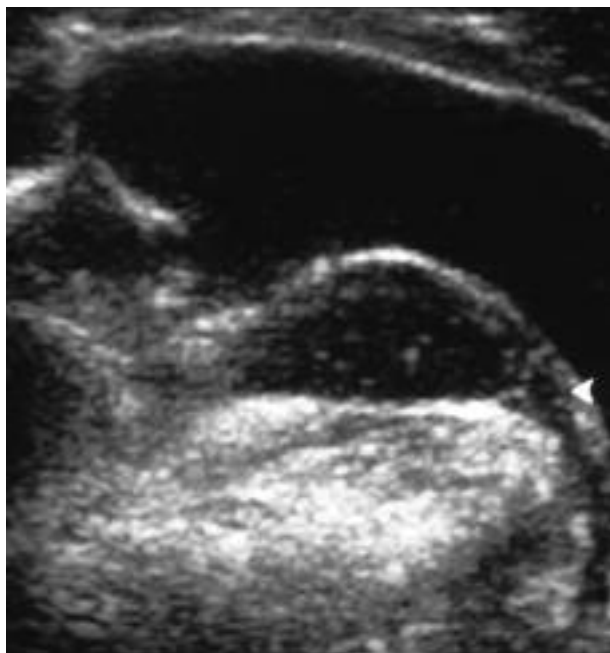
Case	Age/gender	First localization	Recurrence	Other localization	Clinical presentation
1	9Y/Male	Elbow R			Swelling Pain Limited range of motion
2	10Y/Female	Elbow R		Elbow L	Swelling Pain
3	3Y4M/Male	Hip L	+	Elbow L Foot R	Swelling Pain
4	2Y/Male	Foot L	+	Elbows L and R	Diaphysitis Swelling
5	8Y/Male	Elbow L		Elbow R Hips L and R	Swelling
6	53Y/Female	Foot R			Swelling Pain
7	12Y/Male	Hip R		Hip L	Swelling Pain Infection
8	9Y/Female	Elbow R			Swelling
9	13Y/Male	Hip L	+		Swelling



**Fig. 1.** — Anteroposterior radiograph of the left hip in a 12-year-old boy shows well-demarcated lobulated calcified mass with fluid-calcium levels also known as the “sedimentation sign” (case # 7).



**Fig. 3.** — Same patient. CT image of the left hip : the mass shows a mainly cystic component with low attenuation centres and thin calcified walls. Fluid-calcium levels are noted.



**Fig. 2.** — Same patient. Ultrasound study shows multicystic mass. Cysts contain hypoechoic liquid and are separated by hyperechoic thin septa. Fluid-fluid levels are noted.

septa, sometimes partially calcified. Colour Doppler detected blood flow within the septa in 2 cases.

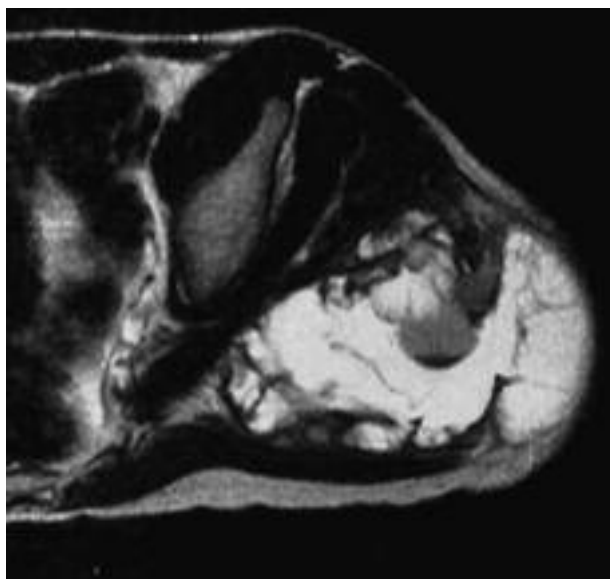
On CT scans, one lesion showed a nodular calcified component separated by low-attenuation septa, another lesion consisted of mainly large cystic components with low attenuation centres and thin calcified walls. Three lesions showed both patterns. Fluid-calcium levels were seen in 4 patients (fig 3). Septal enhancement after contrast injection was seen in one case.

On T1-weighted MR images, all lesions showed intermediate to low signal with more hypointense round or semi-lunar foci. On T2-weighted images, all lesions were heterogeneous and almost all presented mainly hyperintense multiloculated cystic structure associated with hypointense foci.

In one case, the lesion presented with low signal on both T1- and T2-weighted images.

The septa separating the cysts were thin, showing low signal on T1-weighted images and variable signal on T2-weighted images. Some cysts (n = 5) contained fluid-fluid levels, upper layers being hyperintense and inferior ones hypointense (fig 4).

Peripheral and septal enhancements were noticed in all cases after Gadolinium administration.



**Fig. 4.** — Same patient. Transverse T2-weighted MR image demonstrates heterogeneous and mainly hyperintense multi-lobulated cystic structure associated to fluid-fluid level.

Pseudo-tumoral areas were seen in 4 lesions showing low signal intensity on T1-weighted images, heterogeneous and variable intensity on T2-weighted images with heterogeneous and marked enhancement after contrast injection. These areas corresponded to mainly calcified zones on CT scans in 2 cases (figs 5a, 5b, 5c & 5d). No bone or joint involvement was seen on imaging.

All patients underwent surgical resection. The follow-up period ranged from 3 months to 3 years.

On gross pathological examinations, the masses were multiloculated and exuded yellowish creamy to chalky fluid.

Microscopic analysis showed large calcified central areas surrounded by several layers of histiocytes mixed with some multinucleated giant cells and lymphocytes. These granulomas were separated by large fibrous walls.

## DISCUSSION

Idiopathic tumoral calcinosis is characterized by the presence of progressively enlarging juxta-articular calcified soft tissue masses. Chemical analysis of these deposits shows a mixture of

amorphous calcium carbonate, calcium phosphate and hydroxyapatite crystals (18,24).

An inborn error of phosphorus and vitamin D metabolism is the most probable hypothesis in the pathogenesis of idiopathic tumoral calcinosis, however the reasons behind it remain unclear (1,3,8,9,10,12,17,19,25,32). Literature reports of families in which several siblings were affected (17) and hyperphosphatemia found in some patients support this theory (8,19).

The question on whether the transmission is autosomal recessive or dominant with variable clinical expressivity remains open (4,5,8,15,19,24,26,27,29). Recent studies illustrate the extent of genetic and phenotypic heterogeneity in familial tumoral calcinosis (6,22).

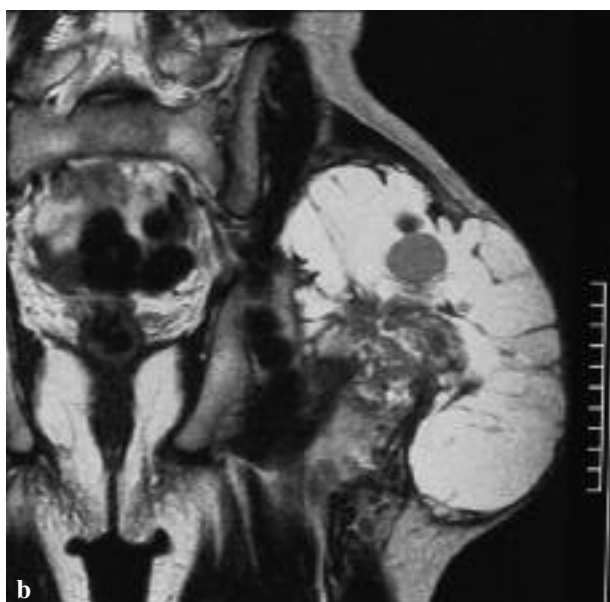
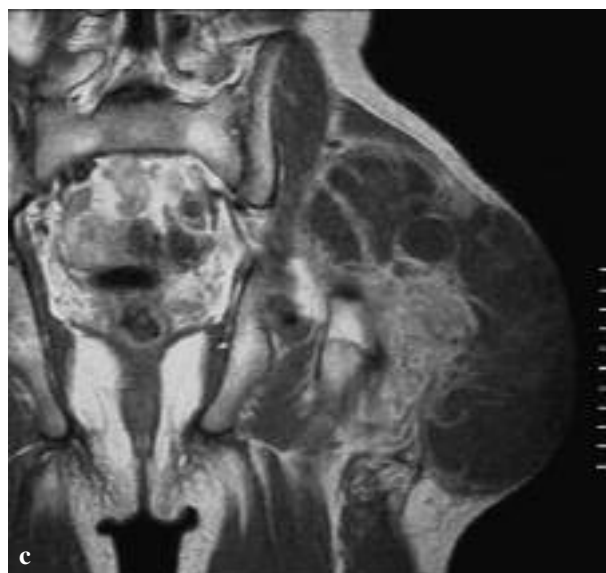
However, familial occurrence and hyperphosphatemia are not an invariable finding in tumoral calcinosis and are observed in only one third of the reported cases (3,10,32). “Hyperphosphataemic tumoral calcinosis” can be considered as a subgroup characterized by a comparatively high familial incidence, onset before 20, black race and multiple lesions (19,27).

In its idiopathic form, tumoral calcinosis usually occurs in the first three decades of life (3,12,26,27,29). There is apparently no sex predominance (3,17,22).

Predilection for black people and people from tropical climates has been reported (4,9,10,17,19,22).

Grossly, tumoral calcinosis is well circumscribed and has a multinodular growth pattern with yellow-grey pasty cut surface. A milky heterogeneous material can be washed out revealing cystic spaces delineated by fibrous walls.

Two histological types are distinguished on microscopic level, corresponding to the so-called active and inactive stages. The former is more frequent and is easily identified. It is characterized by the presence of a large central calcified granular area bordered by an inflammatory infiltrate with predominant epithelioid histiocytes mixed with several lymphocytes and scattered giant multinuclear macrophages. The cellular infiltrate is limited by thick fibrous septa. In the inactive phase, the inflammatory infiltrate is absent. Only calcified deposits and dense collagenous tissue are observed. Histologically, all our cases were in active phase.



**Fig. 5.** — Same patient. Pseudo-tumoral area showing low signal intensity on T1-weighted MR images (5a), heterogeneous variable intensity T2-weighted MR images (5b) and marked heterogeneous enhancement after intravenous contrast injection (5c).

On clinical evaluation, it presents as a slow growing soft tissue mass, painless in most cases, arising in the vicinity of large joints, with the hip joint being the most common site in the reported series (19,20). The other sites are the elbow, shoulder, knee, wrist, hand and foot (5,8,9,12,20,26,27,32). In our series, the most affected site was the elbow (n = 9), with the hip coming in second position (n = 6).

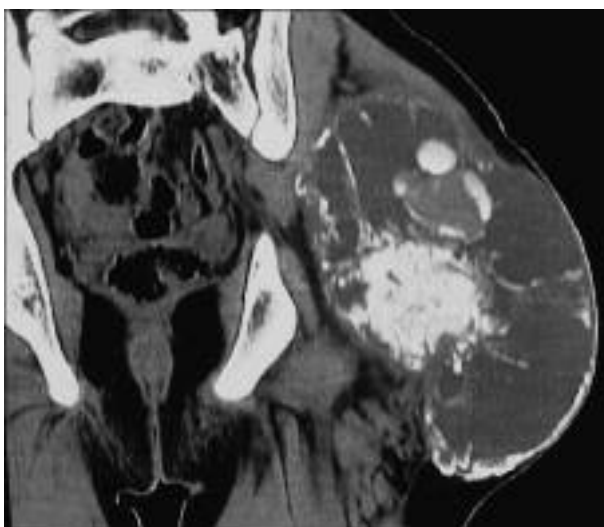
The mass has variable size with firm or soft consistence.

The disease is more often multiple than solitary, and two thirds of patients have multiple lesions (8).

When growing, the tumour may interfere with joint motion or cause pain by nerve compression (3,5,17). The overlying skin is usually intact, although ulcerations or sinuses occasionally appear, draining chalky white or yellow milk-like fluid usually sterile. However, the mass can become a site of secondary infection (17).

Laboratory analysis usually indicates normal calcaemia, parathyroid hormone level, renal function, alkaline phosphatase and uremia. Phosphataemia and Vitamin D levels are normal or slightly elevated (26).

On radiographs, the characteristic appearance of tumoral calcinosis is a well-demarcated lobulated calcified mass located in the periarticular soft tissue, commonly on the extensor side of the articulation. It is a conglomeration of multiple round or oval opacities with different size and density (14,20). The lobules are separated by radiolucent lines



**Fig. 5d.** — This area corresponds to a mainly calcified zone on CT scans.

which correlate histologically to the fibrous septa (5,30). Fluid-calcium levels may be seen on upright radiographs (5).

The size of the tumour varies considerably depending on the location of the lesion : in general, lesions in the buttock tend to be larger than those at the elbow (11,14).

Generally, the mass is unattached to bones and there are no osseous anomalies, although periosteal reaction or erosion of the adjacent bone (from pressure by the mass) rarely occur (16).

Associated diaphysitis and periostitis of tubular bones has been described ; it is characterized by recurrent pain and swelling of the legs (7,17). Some investigators suggest that it is related to inflammatory changes in the shaft bone marrow as a response to calcium deposit (17). It is important to be sure that there are no osseous anomalies suggesting other diseases which may be associated with tumoral calcinosis (2).

Radionuclide bone scans show increased uptake of Tc-99m-labelled phosphate compound in the mass and help to detect and quantify all lesions especially asymptomatic ones (1,3,17).

Tumoral calcinosis can be explored by ultrasound, especially when the lesion is not very calcified. Typically, the lesion appears as a multi-



**Fig. 5e.** — Gross examination of this area shows multiple small and empty cysts. We speculate that the particular pattern of collapsed cysts walls accounts for the pseudo-tumoral feature on MRI.

loculated mass with multiple cavities limited by echogenic thin septa. Some of these septa may be vascularised as shown by Colour Doppler. Cavities are filled with anechoic or echogenic fluid. In some cases fluid-fluid levels can be seen.

When the lesions are entirely calcified, they appear as a hyperechogenic mass with an acoustic shadow (4).

Computed tomography appearances vary. The lesion may consist mainly of large cystic components with low attenuation centres and thin layers of calcium outlining the walls. More commonly, there is a more nodular calcified component separated by low-attenuation septations. Fluid-calcium levels may be seen (4). Some of the septa may enhance after contrast injection.

CT clearly demonstrates that the lesion is separated from the bone and shows associated osseous anomalies when present.

On MRI, tumoral calcosinosis is seen as a well-circumscribed multicystic mass. On T1-weighted images, the mass appears inhomogeneous and has intermediate to low signal intensity. Interestingly, the lesion displays heterogeneous and relatively high signal intensity on T2-weighted images, despite the large calcium component. Some authors suggest that it is due to the granulomatous foreign-body reaction (17) or to the hypervascularity of the lesion (18).

We think that it can also be due to the semi fluid nature of the calcium material, like the "milk of calcium".

Multiple intralocular fluid-fluid levels are seen. Fluid-calcium levels (also known as the sedimentation sign) have been described on upright radiographs, ultrasound, CT and MR images, and it is admitted that this feature is due to the calcium deposit (23,28,30). On MRI, the calcium deposit has low intensity on T1 and T2 weighted images; the supernatant fluid floating above the calcium has high signal intensity on T2 images and low signal intensity on T1 weighted images (23).

A low signal intensity of the entire lesion in all sequences has been described (21). We think it is due to the lesion's high calcium concentration.

The septa separating the cysts have low signal on T1-weighted images, variable signal on T2-weighted images and enhance after Gadolinium injection. The inner layers of the septa can hold calcified incrustations, which explain the low signal on both T1 and T2 weighted images. The outer layers are composed of connective tissue associated to a variable degree of vascularisation and inflammatory reaction, accounting for the high intensity present on T2-weighted and on post-contrast T1-weighted images.

It can also explain the peripheral pseudo-capsule bordering the lesions.

No prior description of pseudo-tumoral areas upon MRI was performed to our knowledge. These areas show low signal intensity on T1-weighted images, heterogeneous variable intensity T2-weighted images and marked heterogeneous

enhancement after intravenous contrast injection. In one patient, gross examination of these areas showed multiple small and empty cysts. We suppose that the pattern of the collapsed cysts walls is responsible for the pseudo-tumoral feature on MRI (figs 5a, 5b, 5c and 5e). In two of our cases, these areas corresponded to mainly calcified zones on CT scans (fig 5d).

MRI, with its high contrast resolution, is superior to CT to detect septal enhancement and pseudo-tumoral areas. It also provides accurate information about the location, extent and relation with adjacent structures. Although MR imaging provides only additional information, it does not affect treatment or prognosis.

The diagnosis of idiopathic tumoral calcosinosis is one of exclusion. The differential diagnosis includes chronic renal failure, primary hyperparathyroidism, calcosinosis universalis, calcosinosis circumscripta, chronic vitamin D intoxication, milk-alkali syndrome and collagen vascular diseases (2,28). Such diseases are excluded by history and laboratory findings in our patients.

Idiopathic tumoral calcosinosis can be confused with calcium pyrophosphate dihydrate crystal deposition disease and particularly with its pseudo-tumoral form, also known as 'tophaceous pseudogout'. The latter disease occurs in elderly patients in association with degenerative joint disease. It is most often observed in the knee, the temporomandibular joint, the cervical spine and the hand. On radiographs, the calcified masses of calcium pyrophosphate dihydrate crystal deposition disease have a granular and more delicate appearance (5,8,31).

The treatment is naturally symptomatic since the cause of the disease is unknown. To our knowledge, only one case of spontaneous regression has been described (19).

Medical treatment using calcitonin, diphosphonates, steroids, phenylbutazone and radiation therapy has proved unsuccessful (3,5,20,27).

Calcium and phosphorus restricted diets with phosphate-binding antacids have been used in some cases with variable results (3,8,19,32). This alternative treatment could be successful in the hyperphosphataemic subgroup (25,32). However, such regimes

may be potentially detrimental to children (3,12,19, 29). A prospective study evaluating the effect of pharmacological treatment in adults is suggested.

Complete surgical excision of tumoral calcinosis is the optimum treatment (3,5,8,13,19,20). Inadequate excision leads to a high level of recurrence in patients with and without metabolic disturbances (5, 19) and growth of recurrent masses is frequently more rapid than that of the initial lesions (20,27,29).

Some lesions are surrounded by a pseudocapsule but others extend as finger-like projections into adjacent tissues, making complete excision extremely difficult (29).

Slavin *et al* postulated that surgical intervention during the active phase of tumoral calcinosis can be difficult, incomplete, and complicated by recurrences, because such lesions tend to be poorly circumscribed and progressive (29).

In some patients, masses tend to recur easily despite repeated complete surgical resections (11,32).

It is thought that recurrences are quite common in cases with hyperphosphatemia (24) or with predisposing genetic abnormality (13).

Management will be easier once all mechanisms of the disease are elucidated.

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