RadioGraphics

Tumoral Calcinosis: Pearls, Polemics, and Alternative Possibilities[1]

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ONLINE-ONLY CME

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LEARNING OBJECTIVES

After reading this article and taking the test, the reader will be able to:

- Discuss the entity known as tumoral calcinosis and the debate about this term.
- Identify the characteristic features of tumoral calcinosis at multimodality imaging.
- Describe the imaging features of common mimics of tumoral calcinosis.

TEACHING POINTS

See last page

Massive periarticular calcinosis of the soft tissues is a unique but not rare radiographic finding. On the contrary, tumoral calcinosis is a rare familial disease. Unfortunately, the term *tumoral calcinosis* has been liberally and imprecisely used to describe any massive collection of periarticular calcification, although this term actually refers to a hereditary condition associated with massive periarticular calcification. The inconsistent use of this term has created confusion throughout the literature. More important, if the radiologist is unfamiliar with tumoral calcinosis or disease processes that mimic this condition, then diagnosis could be impeded, treatment could be delayed, and undue alarm could be raised, possibly leading to unwarranted surgical procedures. The soft-tissue lesions of tumoral calcinosis are typically lobulated, well-demarcated calcifications that are most often distributed along the extensor surfaces of large joints. There are many conditions with similar appearances, including the calcinosis of chronic renal failure, calcinosis universalis, calcinosis circumscripta, calcific tendonitis, synovial osteochondromatosis, synovial sarcoma, osteosarcoma, myositis ossificans, tophaceous gout, and calcific myonecrosis. The radiologist plays a critical role in avoiding unnecessary invasive procedures and in guiding the selection of appropriate tests that can result in a conclusive diagnosis of tumoral calcinosis.

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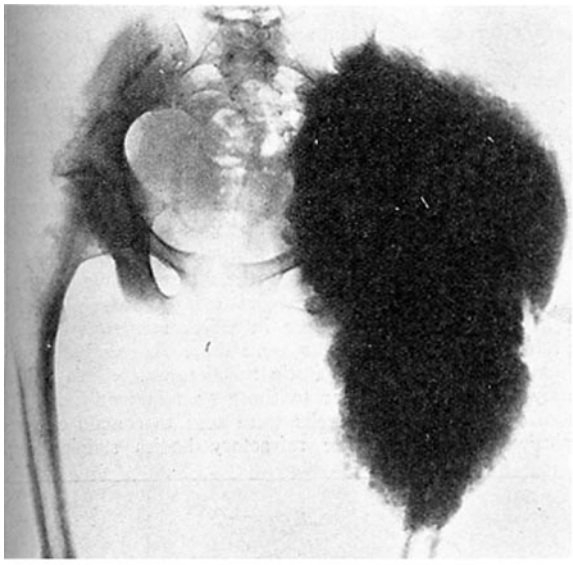

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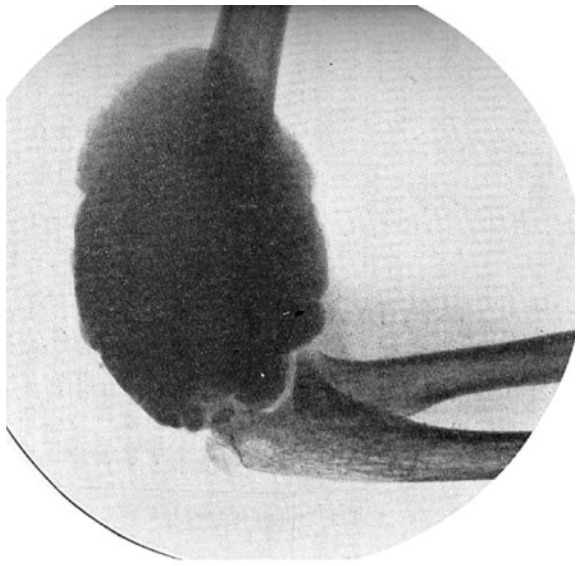

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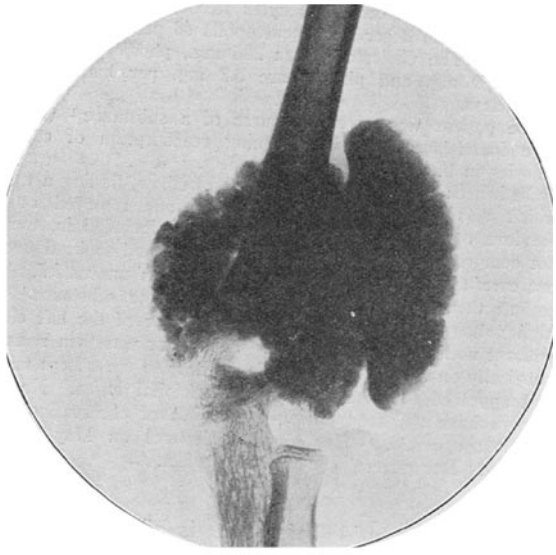


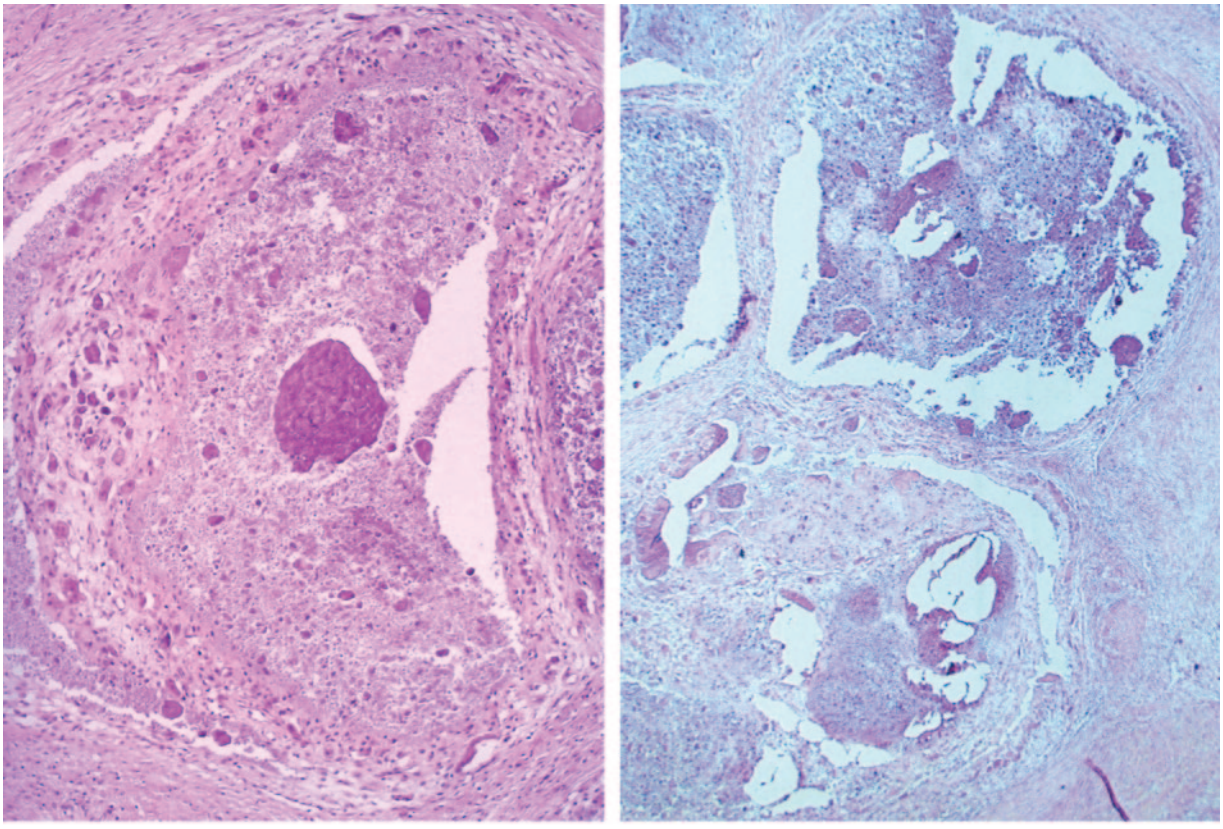
c.

Figure 1. First published radiographs of tumoral calcinosis lesions. **(a)** Tumoral calcinosis of the hip. **(b, c)** Lateral **(b)** and anteroposterior **(c)** views show tumoral calcinosis of the elbow. (Reprinted, with permission, from reference 6.)

Introduction

Tumoral calcinosis is a familial condition characterized by solitary or multiple painless, periarticular masses. Giard (1) and Duret (2) described this entity in the medical literature in 1898 and 1899, respectively. Teutschlaender (3,4) studied this disease process from 1930 to 1950, at which time it became known as *Teutschlaender disease* in the European literature (5). Unaware of these publications, Inclan et al (6) described this condition in the American literature in 1943; this publication became the pivotal article in developing a standard by which to diagnose the disorder and in coining the term *tumoral calcinosis*. Inclan et al (6) differentiated tumoral calcinosis from the dystrophic and metabolic (also known as "metastatic") calcifications previously described in the literature, specifically calcifications associated with renal osteodystrophy, connective tissue disease, and hormonal imbalance. In addition to outlining the metabolic features of tumoral calcinosis, namely normal serum calcium levels with elevated serum phosphate levels, Inclan et al (6) were the first to publish radiographs of the condition (Fig 1).

Many case reports followed. In the mid-1960s, reviews established that tumoral calcinosis had a familial tendency without sex predominance but with a significantly higher incidence in patients of African descent (7–9). Lesions primarily proliferate during the first 2 decades of life. Although all of the patients had normal serum calcium levels, a minority of patients had mild hyperphosphatemia, thereby expanding the metabolic standards of strict hyperphosphatemia of Inclan et al (6). The classic tumoral calcinosis lesions were characterized as lobular, densely calcified masses confined to the soft tissue, generally at the extensor surface of the joint in the anatomic distribution of a bursa. The most common locations of tumoral calcinosis in descending order are the hip, elbow, shoulder, foot, and wrist. At surgery, these lesions are commonly cystic and contain a white to pale yellow chalky material identified as calcium hydroxyapatite crystals with amorphous calcium carbonate and calcium phosphate. At histopathologic examination, epithelioid elements and multinucleated giant cells surround calcium granules (Fig 2).



a. b.

Figure 2. Histopathologic features of tumoral calcinosis. **(a)** High-power photomicrograph shows a calcified mass in the center of the field with foreign body inflammatory reaction, giant cells, and surrounding fibrosis. **(b)** Low-power photomicrograph shows several calcified masses with chronic inflammatory and fibrotic encapsulation. (Reprinted, with permission, from reference 10.)

Martinez et al (11) published a hallmark article on the radiologic features of tumoral calcinosis in 1990, further characterizing this entity. They studied five new cases that adhered to the metabolic and descriptive criteria of Inclan et al (6) and described additional characteristics using bone scintigraphy, computed tomography (CT), and magnetic resonance (MR) imaging. They are also credited with being the first to recognize its association with calcific myelitis. Additional selective case reports in the literature have included characteristic dental abnormalities (12,13) and other locations of the calcinosis masses: temporomandibular joint, scalp, larynx, spine, sacrum, hand, and knee (14–19). Ocular involvement can range from angioid streaks to corneal calcification deposits (20). The associations of tumoral calcinosis with hyperostosis and diaphysitis have also become well established (21–24), as has that with pseudoxanthoma elasticum (25).

In light of these well-documented cases, the definition of tumoral calcinosis seems straightforward; however, the term has inconsistently been used as a descriptive diagnosis, at times referring to any calcified mass regardless of the presence of a known metabolic or inflammatory condition or in the absence of biochemical abnormalities characteristic of tumoral calcinosis. This progression can be traced back to the middle of the 20th century, when several case reports were published that did not meet the criteria of Inclan et al (6), as noted by Harkess and Peters (7). The extrapolation was perhaps the result of an increasing presence of radiology in the diagnosis of soft-tissue calcifications. For example, advanced chronic renal failure, now managed with hemodialysis, subsequently increased in prevalence, which in combination with the ease of using a single term to identify lesions of similar appearance, readily contributed to the nomenclature confusion.

By the 1980s, a dichotomy arose between a faction composed mainly of clinicians who became increasingly lax about defining the disorder through metabolic standards and another faction consisting largely of authors further investigating the underlying metabolic disturbances of tumoral calcinosis (26–28). The flurry of metabolic studies of the disease demonstrated that patients with

tumoral calcinosis had reduced fractional phosphate excretion, increased 1,25-dihydroxy–vitamin D formation, and a normal dynamic response to parathyroid hormone in the proximal renal tubule (26–28). Although the pattern of inheritance is still debated, the generally accepted mode of transmission is autosomal dominant with variable expressivity. However, recent discoveries in the field of genetics have identified autosomal recessive mutations, specifically to genes *GALNT3* (29) and *FGF23* (30), which induce metabolic dysregulation of phosphate (31), suggesting a posttranslational defect. Against the background of this metabolic abnormality, the three most prominent theories of the pathogenesis of the tumoral calcinosis lesions are as follows: *(a)* repetitive trauma leading to reparative dysfunction, *(b)* periarticular forces dissecting histiocytic aggregates that initiate osteoclastic activity, and *(c)* hemorrhage from microtrauma causing an exaggerated reparative response (32). A definitive explanation remains elusive, and studies continue to attempt to delineate the underlying process that leads to the radiologic manifestations of tumoral calcinosis.

Despite these scientific advancements in understanding tumoral calcinosis, this catchy term became increasingly prevalent in the clinical literature. The term became incorporated in texts as *primary tumoral calcinosis* (also known as *idiopathic tumoral calcinosis* or *familial tumoral calcinosis*), which referred to the original disease reported by Inclan et al (6), and as *secondary tumoral calcinosis*, which referred to calcified masses associated with an identifiable condition. The most common of these identifiable conditions was chronic renal failure, which was much less prevalent when Teutschlaender (3,4) and Inclan et al (6) described their cases. The problem, however, is twofold: *(a)* this categorization refrains from being universal and *(b)* this descriptive diagnosis creates a subsequent dissociation of the finding from its cause.

In an attempt to rectify this discrepancy, Smack et al (33) recently reviewed the literature on tumoral calcinosis and proposed a pathogenesis-based classification: *(a)* primary normophosphatemic tumoral calcinosis, *(b)* primary hyperphosphatemic tumoral calcinosis, and *(c)* secondary tumoral calcinosis. Although this new standard would bring clarity to the definition, it is not practical for the clinician for several reasons. First, radiologists are usually the first clinicians to report the character of this lesion, and serum phosphate levels are rarely measured at the time of imaging. Second, a normal serum phosphate level should raise suspicion—rather than permitting satisfaction with a descriptive diagnosis—that there is likely an underlying connective tissue disease causing a dystrophic lesion. Third, there is little utility in distinguishing phosphate levels in "primary tumoral calcinosis" because phosphate extraction is employed for both. Finally, use of the term "secondary tumoral calcinosis," unlike use of "primary tumoral calcinosis," would still be a descriptive diagnosis, creating a disconnection between the lesion and its etiology.

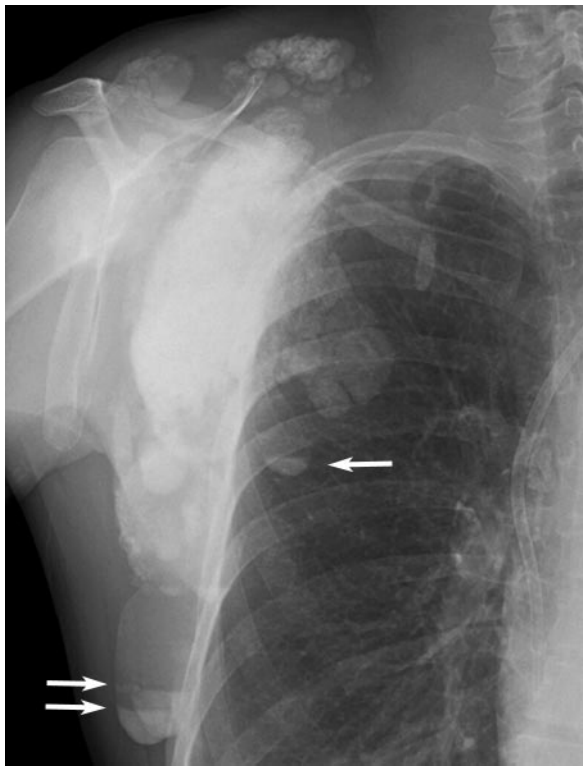
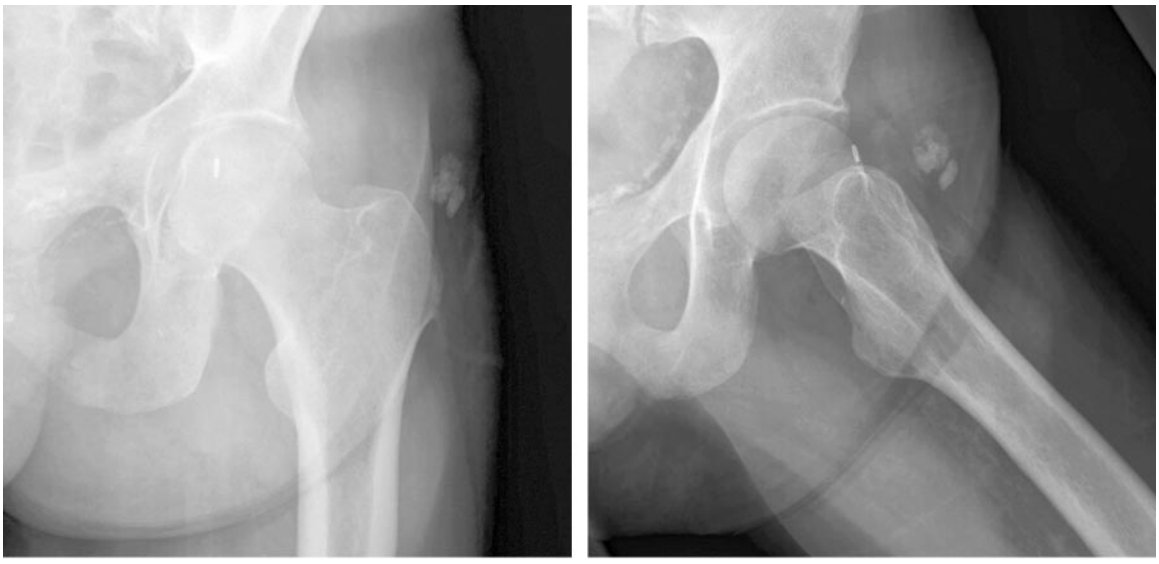


Figure 3. Tumoral calcinosis of the shoulder girdle. Anteroposterior radiograph shows multiple rounded calcified masses, some of which demonstrate sedimentation (arrows).

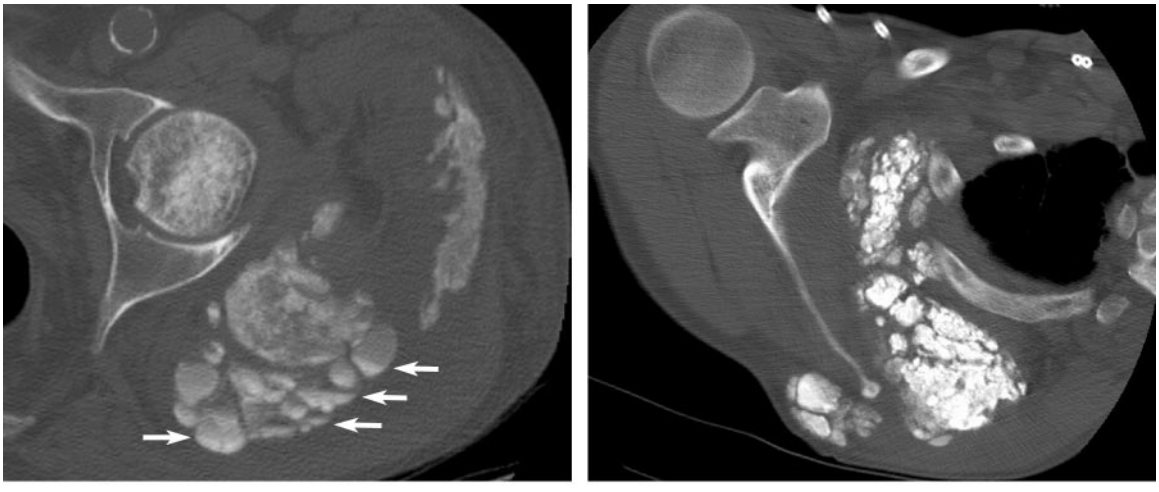
Therefore, we propose that our community stay true to the historical definition and use the term *tumoral calcinosis* strictly in reference to a disease caused by a hereditary metabolic dysfunction of phosphate regulation associated with massive periarticular calcinosis. In doing so, we need to collectively identify underlying diseases that are associated with these soft-tissue calcifications to facilitate its diagnosis. In this article, we present the classic findings of tumoral calcinosis using a multimodality approach and review additional associated radiologic features described in the current literature. Second, we compare tumoral calcinosis with its common mimics and provide terminology to reference those lesions. We conclude by outlining treatments for the diseases causing the periarticular soft-tissue calcifications.

Teaching Point



a. b.

Figure 4. Tumoral calcinosis of the greater trochanteric bursa. Anteroposterior **(a)** and frog lateral **(b)** radiographs show a multilobulated, rounded, calcified mass in the soft tissues.



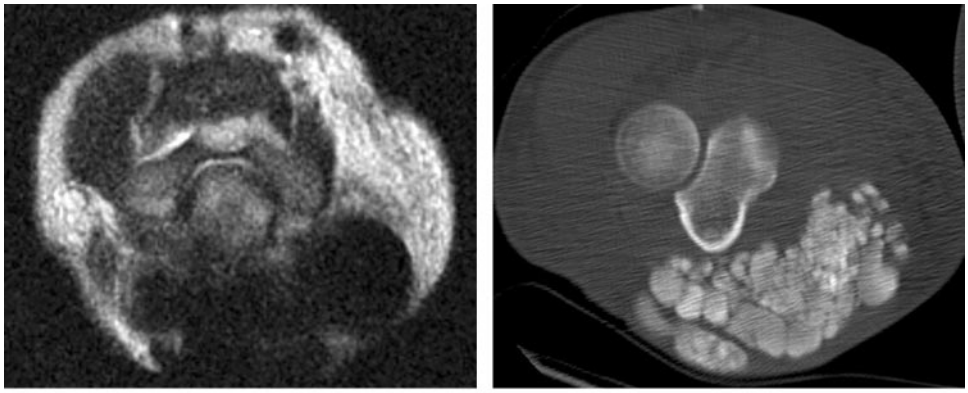
a. b.

Figure 5. CT appearance of tumoral calcinosis. **(a)** CT scan shows tumoral calcinosis of the greater trochanteric bursa. The tumoral calcinosis appears as cystic calcified lesions, some of which demonstrate sedimentation (arrows). **(b)** CT scan of another patient shows tumoral calcinosis lesions between the scapula and chest wall. The lesions appear predominantly homogeneous rather than cystic, an appearance suggestive of lower metabolic activity than that associated with the more cystic lesions in **a**.

Radiologic Features of Tumoral Calcinosis

Teaching Point

Tumoral calcinosis has a typical appearance on radiographs: amorphous, cystic, and multilobulated calcification located in a periarticular distribution (Fig 3). Axial CT better delineates the calcific mass. Figure 4 demonstrates these characteristics at the greater trochanteric bursa, the most common site of involvement (7–9). The cystic appearance shows fluid-fluid levels caused by calcium layering and commonly termed the *sedimentation sign* (34). However, the lesion may appear homogeneous, suggesting a reduced metabolic activity and lower likelihood of growth (7,11) (Fig 5). Erosion or osseous destruction by adjacent soft-tissue masses is absent, another distinguishing finding of tumoral calcinosis. MR imaging with T2-weighted sequences generally shows inhomogeneous high signal intensity even though there is a large amount of calcification.



a. b.

Figure 6. MR imaging appearance of tumoral calcinosis. **(a)** Axial T1-weighted MR image shows tumoral calcinosis at the extensor surface of the elbow. The tumoral calcinosis appears as multiple rounded masses with low signal intensity. **(b)** Correlative CT scan shows the distribution and morphology of the lesions.

Two patterns are generally observed: *(a)* a diffuse, lower-signal-intensity pattern or *(b)* a bright, nodular pattern with alternating areas of high signal intensity and signal void. T1-weighted sequences usually show inhomogeneous lesions with low signal intensity (11) (Fig 6).

Martinez et al (11) discovered additional radiologic features, primarily bone marrow involvement, which demonstrates a periosteal reaction on radiographs and increased radionuclide uptake at bone scintigraphy. CT shows patchy increased attenuation of affected areas. MR imaging demonstrates focal increased signal intensity with multiple small foci of decreased T2 signal intensity surrounded by a high-signal-intensity ring in the periosseous subcutaneous tissue. As expected, T1-weighted images of the marrow abnormality show decreased signal intensity. Martinez et al (11) identified varying presentations of calciphylaxis, dural calcification, and arthropathy resembling calcium pyrophosphate dihydrate crystal deposition disease. In their study cases, Martinez et al (11) also identified prominent dental abnormalities and features that resemble pseudoxanthoma elasticum, consistent with previous case reports. More recently, cerebral and peripheral aneurysms have been identified in patients with tumoral calcinosis (35).

Therefore, tumoral calcinosis has extensive variation in appearance (Table 1) and can be confused with other soft-tissue calcifications if the clinician does not consider the broad differential diagnosis.

Mimics of Tumoral Calcinosis

Teaching Point

Many of the mimics discussed in the following sections share the radiologic features of tumoral calcinosis, including similar distribution, size, and morphology. Therefore, one approach to differentiating tumoral calcinosis from its mimics is by categorizing soft-tissue calcification in terms of serum chemistry levels (36). Metabolic calcification usually results in generalized mineral deposition, including visceral organs. It is associated with abnormal calcium and/or phosphate levels. Dystrophic calcification, occurring in either a localized or generalized pattern, results from an underlying inflammatory process and is found in patients with normal serum chemistry levels. With normal serum levels, antibody screening for an underlying rheumatic disease is prudent. Finally, idiopathic calcification, the category in which tumoral calcinosis resides alone, is associated with normal calcium and elevated phosphate concentrations; infrequently, normal serum phosphate levels occur (9). Suggested markers for tumoral calcinosis include elevated 1,25-dihydroxy–vitamin D levels and dental abnormalities on orthopantographic radiographs (37); however, they are not universally observed in patients with tumoral calcinosis.

Table 1
Clinical, Radiologic, and Laboratory Features of Tumoral Calcinosis

Clinical features
Patients most commonly of African descent
Progression commonly in the 1st and 2nd decades of life
Periarticular tumors that reduce the range of motion
Lesions not painful unless impinging on a local nerve
Late-stage ulcers extruding chalky white matter
Radiologic features
Radiography: a lobulated calcific mass within soft tissues, which is typically cystic, has a bursal distribution, and usually affects extensor surfaces
CT: lobulated cystic calcifications, which communicate with the bursa in many cases
T1-weighted MR imaging: inhomogeneous lesions with low signal intensity
T2-weighted MR imaging: *(a)* a diffuse lower-signal-intensity pattern or *(b)* a bright nodular pattern with alternating areas of high signal intensity and signal void
Laboratory features
Hyperphosphatemia, less frequently normophosphatemia
Normocalcemia
Normal or elevated serum 1,25-dihydroxy–vitamin D level
Normal parathyroid hormone level
Normal glomerular filtration
Negative results for antinuclear, anti-Smith, anticentromere, and antiscleroderma antibodies

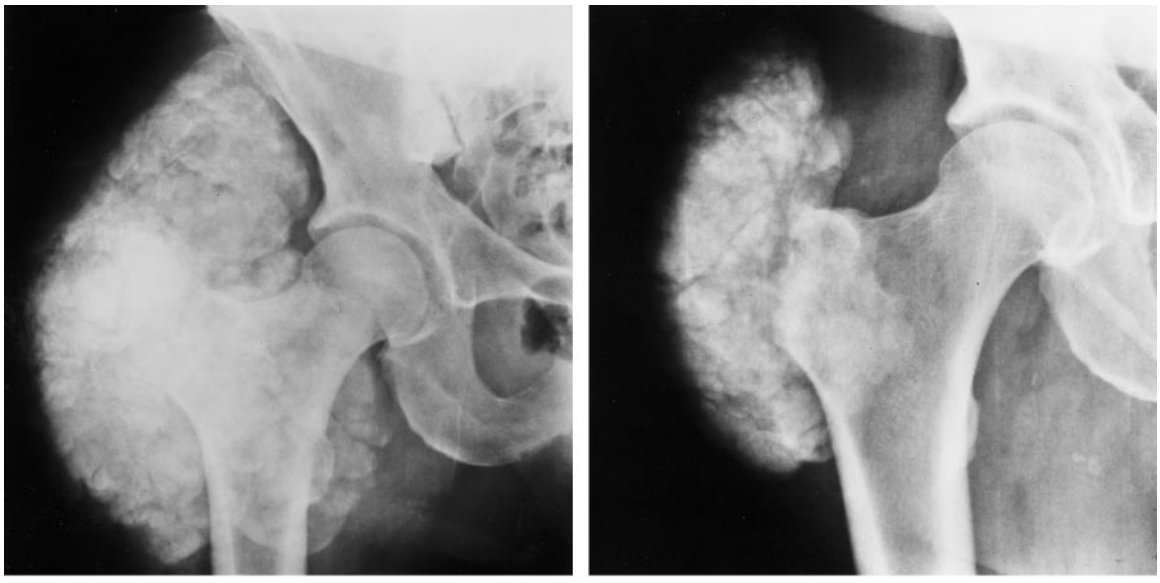
Table 2
Differential Diagnoses for Tumoral Calcinosis

Causes of dystrophic calcification
Connective tissue diseases
Progressive systemic sclerosis
Mixed connective tissue disease
Dermatomyositis
Polymyositis
Systemic lupus erythematosus
Neoplastic diseases
Synovial sarcoma
Osteosarcoma
Chondrosarcoma
Metaplasia
Synovial osteochondromatosis
Degenerative diseases
Calcium pyrophosphate deposition disease
Calcific tendonitis
Calcific bursitis
Causes of metabolic calcification
Hyperphosphatemia
Chronic renal failure
Hypercalcemia
Primary hyperparathyroidism
Milk alkali syndrome
Hypervitaminosis D
Sarcoidosis
Hydroxyapatite deposition disease
Hyperuricemia
Tophaceous gout

There are numerous causes of metabolic and dystrophic calcification (Table 2). The entities discussed in the following sections are a selection of tumoral calcinosis mimics most commonly misdiagnosed as tumoral calcinosis. A brief review of each mimic and its differentiating radiologic features from tumoral calcinosis are also included.

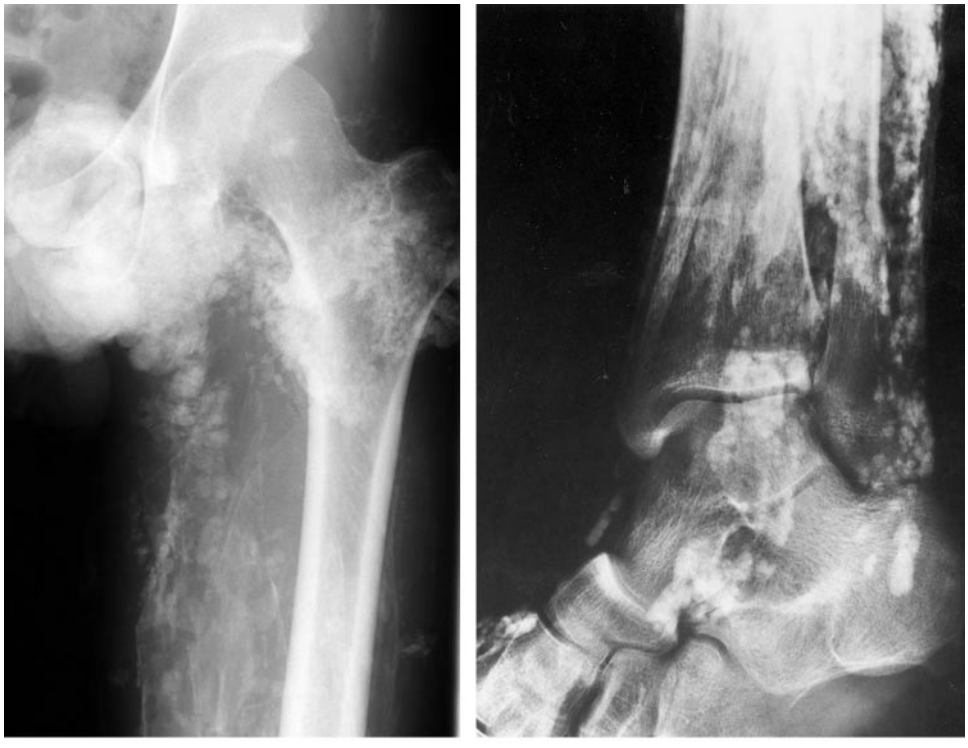
Calcinosis of Chronic Renal Failure

The most frequent cause of a periarticular calcified mass is chronic renal failure. This lesion is identified by many names in the literature, including *uremic tumoral calcinosis*, *secondary tumoral calcinosis*, *tumoral calcinosis–like lesion*, *pseudotumor calcinosis*, *nonfamilial tumoral calcinosis*, and *tumoral calcification*. Although soft-tissue calcification in hemodialysis patients is common, the prevalence of periarticular masses in this population is 0.5%–1.2% (38,39). The specific cause underlying the development of massive periarticular calcification as opposed to visceral calcification or calciphylaxis remains unknown. Although it is most frequently attributed to hyperparathyroidism, there is evidence that it may occur independently of concomitant hyperparathyroidism (38). Interestingly, there are no radiologic or histologic differences between these



a. b.

Figure 7. Massive periarticular calcinosis in an adult woman with chronic renal disease. **(a)** Radiograph obtained at presentation shows an appearance indistinguishable from that of tumoral calcinosis. **(b)** Radiograph obtained 2 weeks after initiation of hemodialysis shows that the size of the calcification has diminished considerably. (Reprinted, with permission, from reference 41.)



8. 9.

Figures 8, 9. **(8)** Calcinosis universalis in a 19-year-old man with proximal muscle weakness and a diagnosis of mixed connective tissue disease. Anteroposterior radiograph shows rounded, dense, amorphous calcifications around the left hip and thigh. Some calcifications are distributed in a sheetlike manner along the medial thigh muscles. (Artifacts were removed by using Photoshop [Adobe Systems, San Jose, Calif].) (Reprinted, with permission, from reference 42.) **(9)** Calcinosis universalis in a 26-year-old woman with dermatomyositis. Radiograph of the ankle shows amorphous, dense soft-tissue calcification distributed in vertical sheets following the fascial planes of the lower leg. No underlying bone or joint abnormality is present. (Reprinted, with permission, from reference 43.)

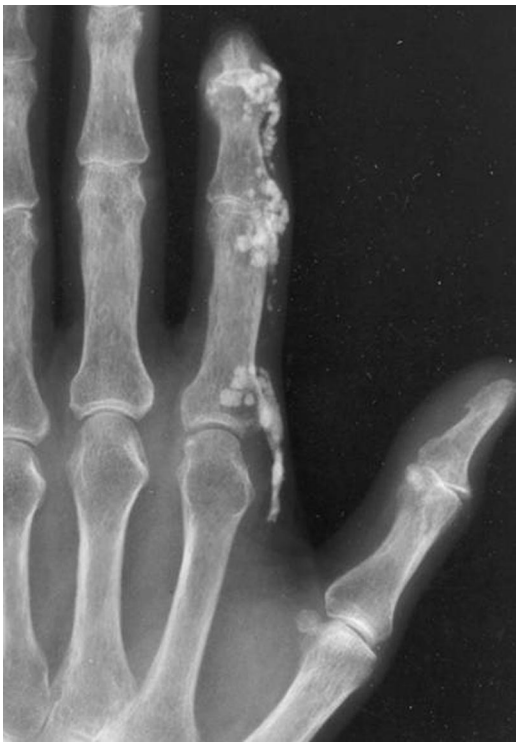


Figure 10. Calcinosis circumscripta in a 74-year-old woman with a long-standing history of CREST syndrome. Radiograph of the hand shows focal, dense, well-defined calcifications in the soft tissues of the distal thumb and index finger.

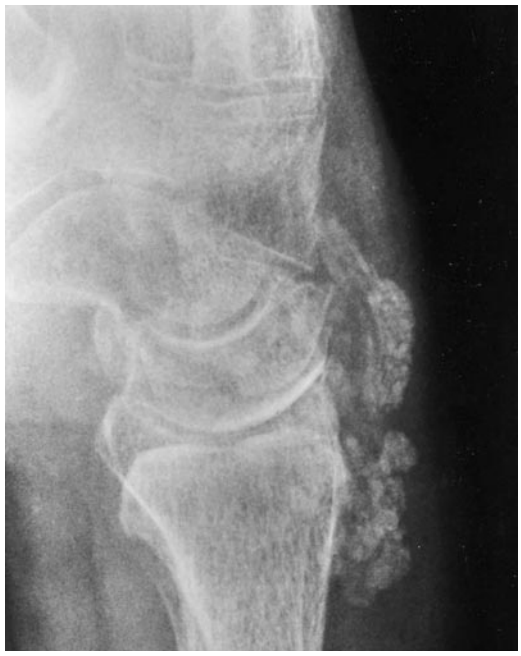


Figure 11. Calcific tendonitis in a 70-year-old man with acute pain and swelling over the dorsal aspect of the wrist. Lateral radiograph shows amorphous calcifications overlying the expected location of the extensor tendons of the wrist. (Reprinted, with permission, from reference 44.)

lesions and the lesions of tumoral calcinosis (40) (Fig 7); therefore, diagnosis is based solely on history, serum chemistry levels including vitamin D, and glomerular filtration rate.

Calcinosis Universalis

The term *calcinosis universalis* refers to diffuse, sheetlike deposition of calcium involving the muscles, subcutaneous tissues, and fascial planes. Calcinosis universalis is most commonly associated with connective tissue disease (Fig 8), primarily polymyositis and dermatomyositis. Systemic lupus erythematosus is infrequently associated with this lesion, but when it is, it typically involves the lower extremity (as in Fig 9). The characteristic sheetlike distribution of calcinosis universalis and its involvement of muscle and fascial planes usually makes this condition distinct from tumoral calcinosis at imaging.

Calcinosis Circumscripta

Clinically, calcinosis circumscripta is described as firm, white dermal papules, plaques, or subcutaneous nodules found in a variety of distributions. They commonly ulcerate, extruding a chalky white material most frequently identified as hydroxyapatite. As in calcinosis universalis, these calcifications occur in connective tissue disease, most prevalently seen in the early stages of polymyositis but also in dermatomyositis, systemic lupus erythematosus, progressive systemic sclerosis, and CREST syndrome (Fig 10). There are conflicting reports associating this lesion with disease severity.

Other causes include localized trauma, insect bites, tumors, and inherited disorders (Ehlers-Danlos syndrome, Werner syndrome, Rothmund-Thomson syndrome, and pseudoxanthoma elasticum.) Any cause of metabolic calcification can theoretically cause calcinosis circumscripta, but it has been most commonly associated with renal failure. Adjacent bone may become eroded if there is an underlying rheumatic disorder. Calcinosis circumscripta tends to be much less extensive than the lesions of tumoral calcinosis, and calcinosis circumscripta lesions are typically located in the subcutaneous tissues rather than in bursal regions.

Calcific Tendonitis

Hydroxyapatite deposition within tendons and tendon sheaths is termed *calcific tendonitis* (Fig 11). It occurs in up to 3% of adults and is the

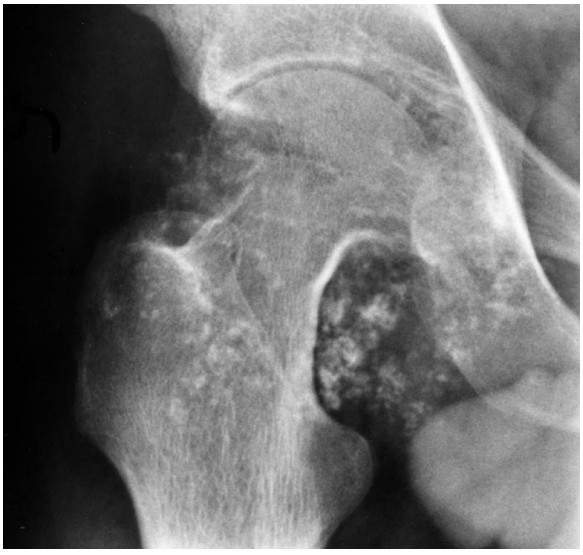


Figure 12. Synovial osteochondromatosis in a 24-year-old man with hip pain. Radiograph shows multiple small, dense, punctate calcifications involving the hip joint with secondary shallow erosions of the underlying femoral neck. (Reprinted, with permission, from reference 46.)

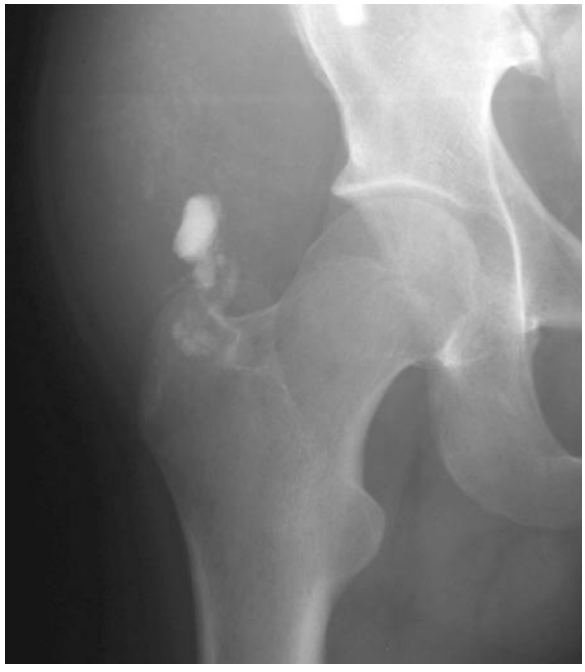


Figure 13. Synovial sarcoma in a young adult with a right buttock mass. Radiograph of the hip shows several dense, rounded calcifications overlying the greater trochanter. The noncalcified portion of the lesion extends superiorly from the femur to the lateral aspect of the iliac wing.

cause in up to 40% of painful shoulder syndromes. The locations affected in decreasing order of frequency include the shoulder, hip, elbow, wrist, and knee. The primary theory of pathogenesis is degeneration of the tendon with an abnormal reparative response, leading to crystal deposition. Rarely, adjacent osseous destruction and marrow involvement occur, in which case calcific tendonitis may be readily confused with a neoplasm (45). The location within a tendon, the lack of sedimentation, and the clinical presentation make calcific tendonitis distinct from tumoral calcinosis.

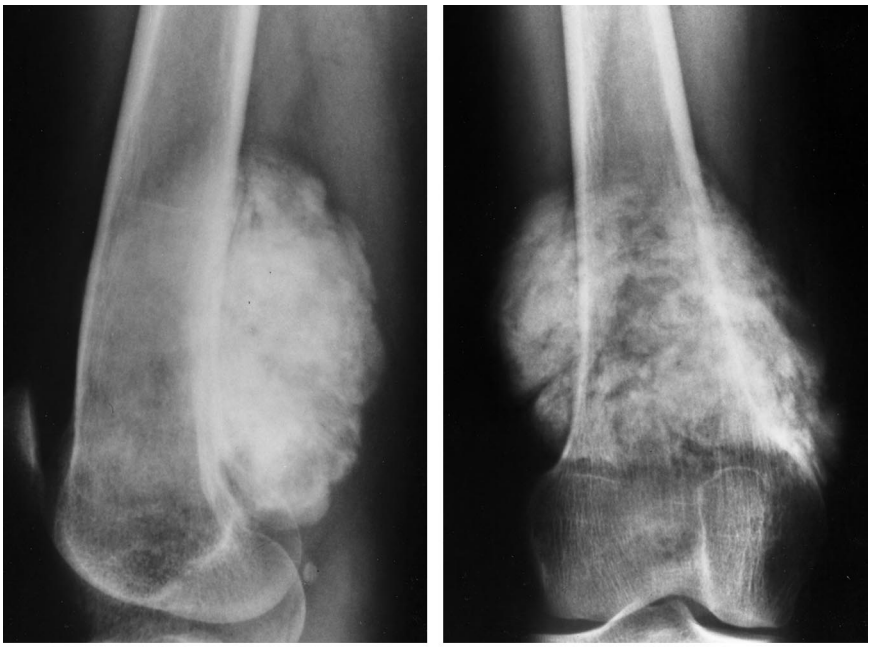
Synovial Osteochondromatosis

Synovial osteochondromatosis is a proliferation of intrasynovial nodules of cartilage or of bone and cartilage caused by metaplastic, rather than neoplastic, changes of the synovium. It usually occurs within a joint or a tendon sheath, although when periarticular, it can mimic the calcinosis of tumoral calcinosis (Fig 12). At radiography, individual lesions appear as multiple calcifications with a rings-and-arcs morphology characteristic of cartilage, and in mature lesions, ossified loose bodies (47). Erosion, if present, provides a primary clue to the intraarticular location of the calcifications. Similar in radiographic appearance to synovial osteochondromatosis, soft-tissue osteochondroma rarely calcifies and is unifocal rather than multifocal. Identification of the rings-and-arcs morphology of the calcifications and of the intraarticular location makes synovial osteochondromatosis distinct from tumoral calcinosis at imaging.

Synovial Sarcoma

Synovial sarcoma is defined as a malignant mesenchymal neoplasm with epithelial and spindle cell components. Areas of hyalinization within the spindle cell components may form punctate calcifications and ossify in up to one-third of cases (48). Two-thirds of synovial sarcomas are located in the lower extremities and occur primarily in periarticular regions. Bone involvement ranges in severity from osteoporosis, superficial erosions, and periosteal reaction to invasion by the neoplasm. The radiographic appearance of synovial sarcomas is variable, but they may show dense, lobulated calcification involving only a portion of the tumor (Fig 13).

At MR imaging, most synovial sarcomas are poorly defined and infiltrative (49). Similar to other soft-tissue sarcomas, large synovial sarcomas appear septated with areas of high signal



a. b.

Figure 14. Parosteal osteosarcoma in a 24-year-old woman with a posterior knee mass. Lateral **(a)** and anteroposterior **(b)** radiographs of the thigh show a densely ossified mass arising from the posterior cortex of the distal femur. (Reprinted, with permission, from reference 51.)

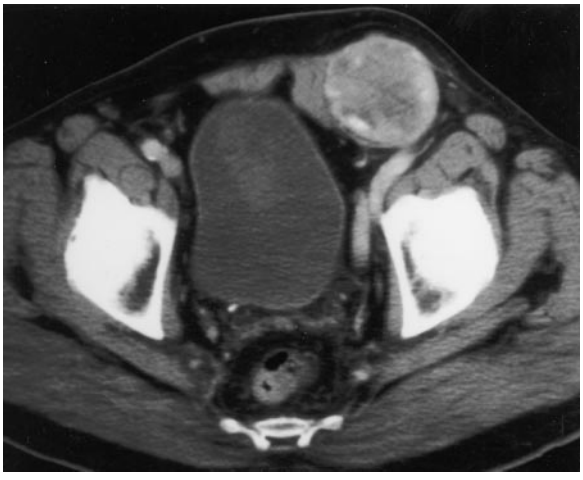


Figure 15. Extraskeletal osteosarcoma in a 24-year-old man with a hard inguinal mass. CT scan shows a well-demarcated ossified mass in the left rectus sheath. (Reprinted, with permission, from reference 52.)

intensity on T1-weighted MR images, which represent hemorrhage. One-third of the tumors appear hyper-, iso-, and hypointense on T2-weighted MR images, representing solid, cystic, and fibrous elements with areas of hemorrhage (50). Calcification in other types of soft-tissue connective tissue sarcomas is uncommon. The presence of a noncalcified soft-tissue mass makes synovial sarcoma different from tumoral calcinosis at imaging.

Osteosarcoma

Osteosarcoma variants that arise on the cortical surface without destroying the underlying bone or that arise primarily in the soft tissues may mimic tumoral calcinosis when they manifest as mineralized soft-tissue masses. Parosteal osteosarcomas typically arise on the cortical surface and expand into the adjacent soft tissues as a densely mineralized mass (Fig 14). If the stalk that connects the lesion to the underlying bone is not apparent, the radiographic appearance may suggest tumoral calcinosis or another cause of massive periarticular calcinosis. Cross-sectional images should demonstrate the relationship with the underlying bone, and the clinical history should be very different, allowing differentiation of a parosteal osteosarcoma lesion from tumoral calcinosis. Extraskeletal osteosarcomas may manifest as calcified soft-tissue masses (Fig 15), and biopsy is generally required to establish the diagnosis. Involvement of bone or the presence of a noncalcified soft-tissue mass should make osteosarcoma distinct from tumoral calcinosis at imaging.

Myositis Ossificans

Myositis ossificans is a mass composed of heterotopic bone and cartilage formation that is typically located within muscle. The localized form of myositis ossificans circumscripta is usually secondary to injury, a cerebrospinal disorder, or burns. It primarily occurs in muscles but may also form around ligaments, tendons, fasciae, aponeuroses, and joint capsules. Plain radiography reveals faint calcifications as early as in 2 weeks

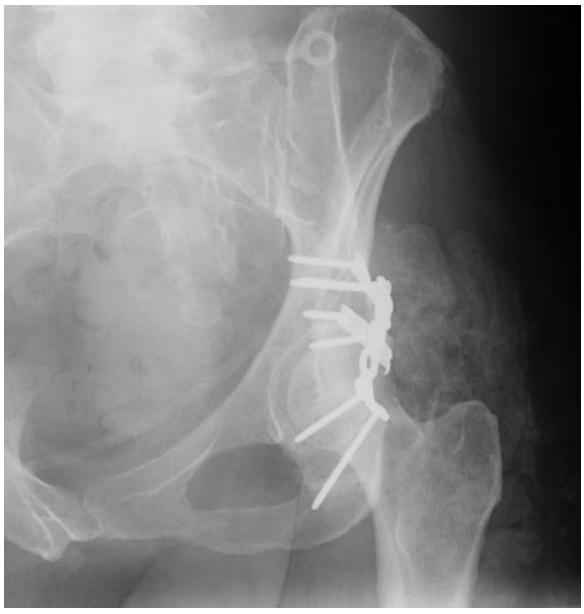


Figure 16. Heterotopic ossification in a woman with an internally fixed fracture of the posterior acetabular wall after reduction of a traumatic fracture-dislocation of the posterior hip. Radiograph of the hip obtained 9 weeks after the trauma shows a mass of maturing bone in the posterior soft tissues. Note the emerging cortical and trabecular structure of the bone.

(Fig 16) and a well-circumscribed osseous mass after 6 weeks or more (47). This lesion can be radiographically distinguished from calcinosis in tumoral calcinosis by its rapid evolution from faint calcification to organized cartilage and bone and lack of lobular morphology. Late lesions, also called heterotopic ossification, are clearly different from tumoral calcinosis because of their organization into bone with a distinct cortex and medullary space.

Tophaceous Gout

Tophaceous gout may result from hyperuricemia that is sustained over many years, if not decades. Deposits of urate crystals form periarticular masses and may cause focal erosions of the underlying bone. When large, deposits may appear as calcified periarticular masses (Fig 17). Calcified tophi are typically less radiopaque than tumoral calcinosis and will not demonstrate sedimentation. Hyperuricemia is not present in patients with tumoral calcinosis unless they also have gout.

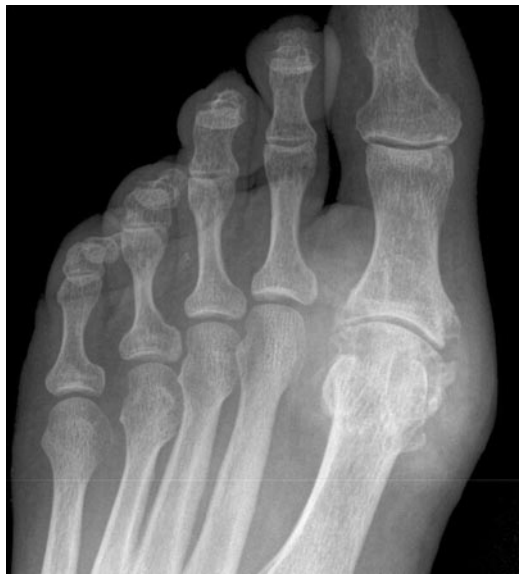


Figure 17. Tophaceous gout in a man with long-standing hyperuricemia. Radiograph of the foot shows radiopaque soft-tissue swelling at the great toe with underlying erosive changes of the adjacent osseous structures.

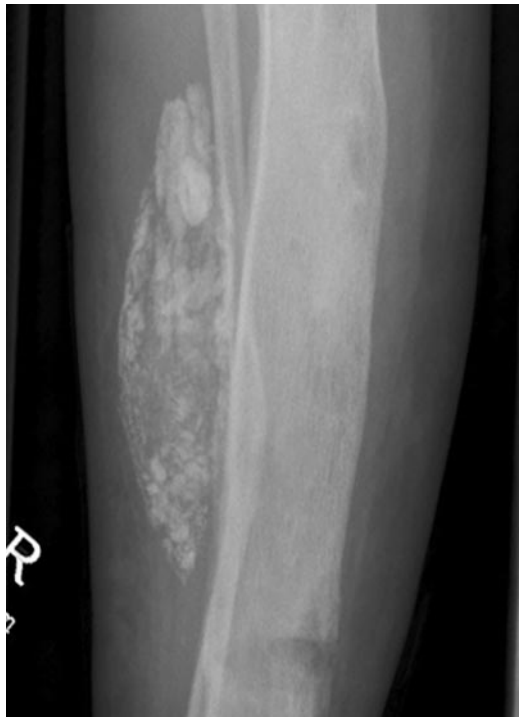


Figure 18. Calcific myonecrosis in a 62-year-old man with a remote history of leg trauma. Anteroposterior radiograph of the lower leg shows a large, well-marginated, ovoid calcification overlying the expected location of the anterior compartment. The bone changes are the result of chronic osteomyelitis, which also dates back to the initial episode of trauma.

Calcific Myonecrosis

Calcific myonecrosis occurs most often following ischemic necrosis of muscle, typically the result of a compartment syndrome in an extremity. A common location is the anterior compartment of the leg (53) (Fig 18). At radiography and CT, calcific myonecrosis may be evident as a peripherally calcified lesion that replaces the necrotic muscle. Because the lesion replaces the necrotic muscle, there should be no mass effect. This intramuscular location is the key point of distinction from tumoral calcinosis.

Treatment of Tumoral Calcinosis

The treatment of massive periarticular calcinosis depends largely on its underlying cause. Surgical excision of the tumoral calcinosis lesion is a well-documented treatment, but recurrences due to poor circumscription are common, particularly when it is actively progressing. Phosphate depletion in both normo- and hyperphosphatemia has proved to have variable success (54–56). Resistant cases are thought to be related to a late-stage tumoral calcinosis lesion surrounded by an impeding fibrous layer that prevents ion exchange (32). However, surgical excision combined with phosphate deprivation (using aluminum hydroxide) in conjunction with acetazolamide synergistically lowers hyperphosphatemia and has proved to be the most effective therapy (57,58). Other therapies, including systemic steroid therapy and radiation therapy, have not been proved to be effective (6,9,59).

Teaching Point

In treatment of dystrophic calcifications like calcinosis universalis, there has been limited success with intralesion steroid injection, etidronate disodium, or aluminum hydroxide (60). Low-dose oral anticoagulant therapy many times prevents or reverses subcutaneous lesions (61). Calcific tendonitis, on the other hand, has demonstrated proved benefits in randomized trials of ultrasound therapy (62). More recently, modified fine-needle aspiration performed with ultrasonographic guidance by using a double small-gauge needle technique, one for saline lavage and the other for percutaneous fragmentation and aspiration of the calcific deposits, relieved pain and disability by clinically significant margins of 30% and 24%, respectively (63).

Therapy for metabolic calcification is rooted in treating the underlying cause of the metabolic dysfunction (eg, dialysis for patients with renal osteodystrophy, hormonal regulation in primary hyperparathyroidism). If extensive soft-tissue calcification is symptomatic, surgical excision should be considered.

Conclusions

Tumoral calcinosis is a hereditary disease of phosphate metabolic dysfunction but is commonly mistaken for a lesion. This dysregulation, yet to be completely understood, leads to the formation of characteristic soft-tissue lesions described as lobulated, well-demarcated calcification distributed most commonly around the extensor surface of large joints. Because there are many conditions with similar-appearing lesions, diagnosis is difficult with diagnostic imaging alone. However, the radiologist plays a critical role in decision making to avoid unnecessary, invasive procedures and provides the consultant with direction in selecting appropriate tests that can then result in a conclusive diagnosis.

Teaching Point

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Tumoral Calcinosis: Pearls, Polemics, and Alternative Possibilities

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Therefore, we propose that our community stay true to the historical definition and use the term *tumoral calcinosis* strictly in reference to a disease caused by a hereditary metabolic dysfunction of phosphate regulation associated with massive periarticular calcinosis.

Page 875
Tumoral calcinosis has a typical appearance on radiographs: amorphous, cystic, and multilobulated calcification located in a periarticular distribution (Fig 3).

Page 876
Many of the mimics discussed in the following sections share the radiologic features of tumoral calcinosis, including similar distribution, size, and morphology. Therefore, one approach to differentiating tumoral calcinosis from its mimics is by categorizing soft-tissue calcification in terms of serum chemistry levels (36).

Page 883
However, surgical excision combined with phosphate deprivation (using aluminum hydroxide) in conjunction with acetazolamide synergistically lowers hyperphosphatemia and has proved to be the most effective therapy (57,58).

Page 883
Because there are many conditions with similar-appearing lesions, diagnosis is difficult with diagnostic imaging alone. However, the radiologist plays a critical role in decision making to avoid unnecessary, invasive procedures and provides the consultant with direction in selecting appropriate tests that can then result in a conclusive diagnosis.