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WHAT'S YOUR DIAGNOSIS?

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FIGURE 1.

History

A 15-year-old Saudi male presented to his clinician with multiple masses in the right shoulder, left ankle and left hip. The masses had started one-and-a-half years earlier, and were becoming progressively larger (Figure 1). The patient had a past surgical history of removal of a right subcapsular mass three years earlier. There was no history of a similar condition in relatives, and the patient did not recall episodes of trauma to the affected areas. He had a family history of sickle cell anemia (mother) and thalassemia (brother). On examination, the patient looked healthy, apart from pallor and multiple irregular firm, partially cystic masses in the left ankle, left hip and right subcapsular region. The shoulder mass measured 13 cm in maximum dimension, with two ulcerated nodules on the

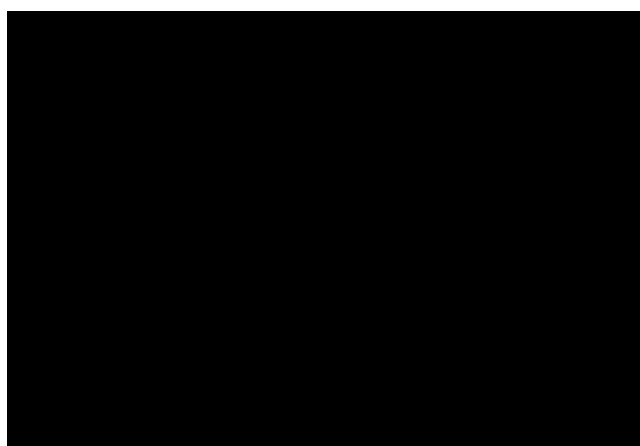


FIGURE 2.

surface. This mass was tender, limiting his right shoulder movement. The other two masses were smaller and not tender. The patient had normal serum calcium and high serum phosphorus of 2.10 mmol/L (normal 1-1.6 mmol/L). His renal profile was within normal limits, and hemoglobin was 86 g/L (normal range 132-172 g/L), with hypochromia and microcytosis. The masses were resected. Figure 2 shows the resected shoulder mass. Parathyroid tests were not performed.

1. What abnormality can be seen?
2. What is the differential diagnosis?
3. How is the diagnosis confirmed?

ANSWER TO WHAT'S YOUR DIAGNOSIS? (PREVIOUS PAGE)

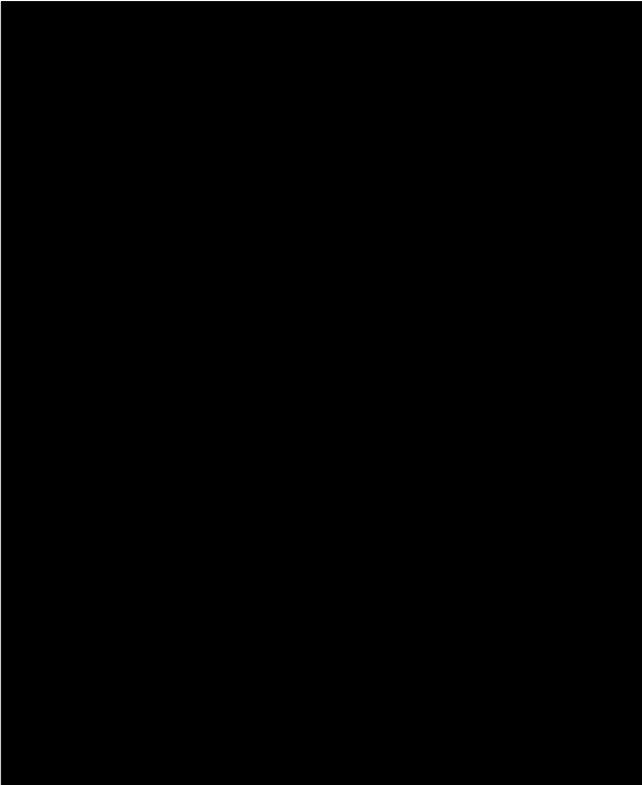


FIGURE 1. Plain film of the right shoulder demonstrates a large irregular calcified mass.

Radiologic Findings: In Figure 1, a plain film of the right shoulder demonstrates a large irregular calcified mass, with some relatively lucent areas seen interposed between ribs and scapula, which appear displaced posterolaterally by the mass. Several of the lucent areas contain both high- and low-density fluid components, with a straight line in between, consistent with calcium-fluid levels.

Histopathologic Findings: Three irregular masses from the shoulder, ankle and hip regions were received. The sizes of the masses varied between 5 cm to 13 cm in maximum dimension. The largest one was covered by skin,

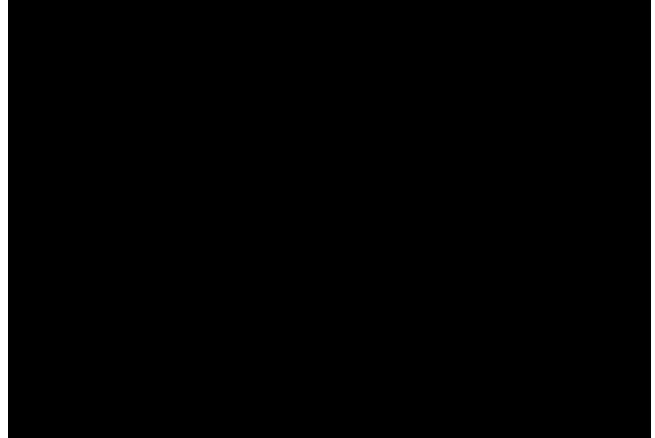


FIGURE 2. Microscopic appearance of tumoral calcinosis, showing palisading giant cells with histiocytes and lymphocytes (200x).

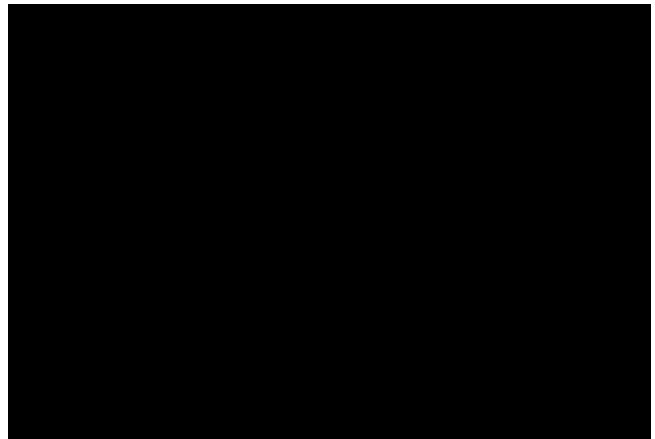


FIGURE 3. This photomicrograph shows the amorphous basophilic calcified material filling the cystic spaces.

which had two ulcerated nodules. The masses were solid and partially cystic, with yellow to gray hard cut surface. The cysts were filled with milky, chalk-like material. The microscopic examination revealed subcutaneous cystic spaces lined by granulation tissue, foamy and hemosiderin-laden macrophages and osteoclast-like giant cells (Figure 2). The cysts contained amorphous basophilic material (Figure 3). The two nodules described grossly on the skin were formed by ulcerated granulation tissue.

Diagnosis: Tumoral calcinosis.

Discussion: Tumoral calcinosis (TC) is a well-known entity characterized by periarticular soft tissue calcified masses. There are two types of TC, the idiopathic and the secondary type. Most of the idiopathic TC are familial, and the mode of transmission in these families is thought to be autosomal dominant.¹ Most of the patients are young, with normocalcemia and hyperphosphatemia. Few reported cases have normocalcemia and normophosphatemia.² The non-familial secondary type can be the result of chronic renal failure with secondary hyperparathyroidism, hypervitaminosis D, milk alkali syndrome and bone destruction caused by neoplastic or infectious lesions.^{1,3} The most frequent sites of involvement by TC are the hip, elbow, ankle areas and, to a lesser degree, the hands and feet.² The association of TC with calcified skin lesions,^{2,4} dental abnormalities¹ and arterial calcification⁵ has been reported.

The pathogenesis of TC remains obscure. Some authors have suggested that TC is possibly initiated by repeated minor trauma, which act as a triggering mechanism in patients with an inborn error of calcium metabolism. The trauma causes bleeding in the periarticular connective tissues, which provokes a histiocytic response with secondary deposition of calcium. This is supported by the high incidence of TC in pressure areas.⁶ TC may infiltrate muscle, tendons or fascia, but does not involve the bone.⁴ The disease is common in blacks, especially in Southeast and Central Africa, but is rare in North America and Europe. There have only been four previously reported cases in Saudi Arabia, one from Jeddah,⁵ and the other three at King Faisal Specialist Hospital and Research Centre, including this case.

Radiological studies usually reveal soft tissue masses of multiple rounded opacities. No bone abnormality is associated with the disease. The electron microscope examination mainly shows intramitochondrial calcification within the cytoplasm of the osteoclast-like giant cells. The foamy histiocytes show accumulation of cholesterol crystals and lipids in the form of vacuoles. The cystic cavities contain calcium spherules.

TC is divided into three stages:^{1,4} Stage 1: The lesion is cellular without calcification, but shows aggregating foamy macrophages. Stage 2: The lesion becomes cystic with calcification and infiltration by foamy macrophages, which are seen surrounding osteoclast-like giant cells. The calcified particles aggregate into large masses or form laminated calcospherites. Stage 3: The inactive calcifying lesions are characteristically filled with calcified material and surrounded by hyalinized fibrous tissue. No accompanied cellular reaction is seen. The biochemical analysis shows that the calcium deposition is in the form of

calcium oxalate or hydroxyapatite crystal.¹

Complete surgical resection is the primary approach to management of tumoral calcinosis. A high rate of recurrence has been reported with incomplete surgical removal, ranging from 84% in primary to 79% in secondary tumoral calcinosis.² In primary tumoral calcinosis, some benefits have been reported from dietary treatment, using oral aluminum hydroxide in combination with a low-calcium, low-phosphate diet. In secondary tumoral calcinosis, successful treatment of the underlying calcification-promoting disorder resulted in the resolution of the calcifications. Enzanger and Weiss reported an attempt at treatment with corticosteroids and radiation, but with an unsatisfactory response.⁴ Well-known complications of TC are skin ulceration, repeated wound infection and abscess formation. However, the most important complication is the frequent recurrence of the mass.

No association between tumoral calcinosis and anemia has been described. Our patient had microcytic hypochromic anemia, which could be unrelated to his condition. In view of his family history of thalassemia, it was likely he had a trait. However, no further investigations were carried out to resolve the underlying cause.

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