Acta Biomed 2019; Vol. 90, N. 4: 587-594 DOI: 10.23750/abm.v90i4.8251

Case report

Recurrence of tumoral calcinosis: a case report

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Summary. We describe radiographic, contrast-enhanced MDCT and MRI findings with pathologic correlations of an unusual recurrence of tumoral calcinosis, also called Teutschlander disease. The disease was silent in the first decade of life, when it appeared with elbows recurring lesions, until the seventh decade of life, when a left hip active growth lesion developed. A review about tumoral calcinosis pathogenesis, clinical course and imaging differential diagnosis is reported. (www.actabiomedica.it)

Key words: calcifications; tumoral calcinosis, Teutschlander disease, musculo-skeletal (MSK) imaging, magnetic resonance imaging

Introduction

Tumoral calcinosis (TC), also called Teutschlander disease, is a relative rare disorder characterized by calcium salts accumulation in iuxta-articular soft-tissues, producing solitary or multiple painless periarticular masses (1, 2). Large joints such as the hip, shoulder, and elbow are usually involved. This entity most commonly presents in the first 2 decades of life. Approximately one-third of patients with TC shows familial inheritance (3, 4).

TC has been generally presented as case reports and the plain radiography findings of the disease have been well documented. To date, there are few studies presenting computed tomography (CT) and magnetic resonance (MR) imaging characteristics of TC with radio-pathologic correlation (5).

We report the unusual case of an adult patient without familiar inheritance, who had undergone surgery for elbows TC during the first decade of life and presented left hip recurrence in the sixth decade. We describe CT and MR findings with histopatological correlation on surgical specimen.

Case report

A 64 years-old male patient was referred to our institution for swelling of the left gluteus and hip. He had a history of elbow recurring TC in the first decade of life that needed five surgical procedures. No other manifestations of calcinosis occurred during the following decades. He didn't referred TC in the other family members.

The patient had a mild hyperphosphatemia, without haematic value alterations of 1,25-dihydroxyvitamin D or parathyroid hormone. Renal function was normal.

Radiography showed a grossly periarticular calcified mass around the left hip joint and the upper thigh (Fig. 1). At contrast-enhanced (CE) multidetector computed-tomography (MDCT) a grossly calcified

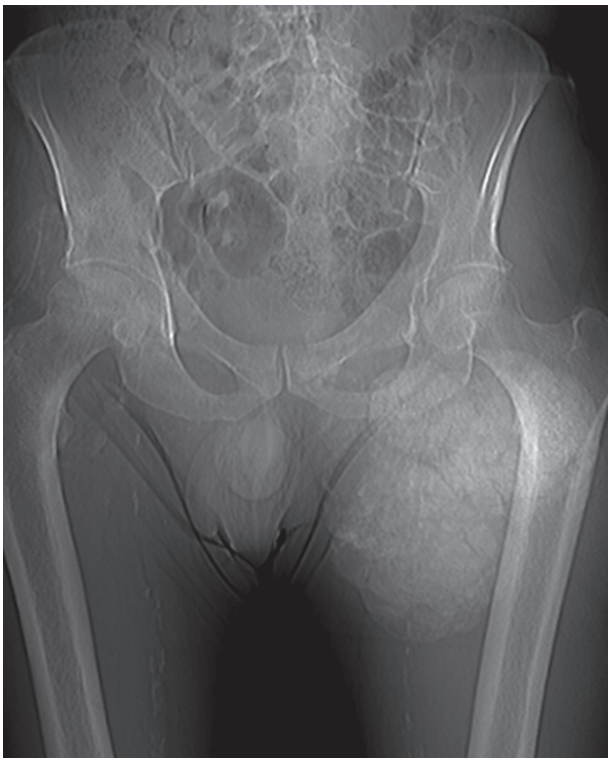


Figure 1. Radiography shows a grossly periarticular calcified mass around the left hip joint and the upper thigh

lobular mass was visible with large cystic areas and fluid-fluid levels inside (CT sedimentation sign) (Fig. 2a and 2b). A peripheral enhancement of cystic areas was observed after CE administration, without pathologic solid portions. The mass was localized in the region of the left greater trochanteric bursa, deeply to gluteal muscles, extending medially to the upper part of the ischio-pubic branch, and along the posterior compartment of the lower part of the thigh, as well demonstrated by CT multiplanar and tridimensional (3D) images (Fig. 3a-c).

At MRI the lesion had inhomogeneous diffuse low signal intensity on T1-weighted sequences, while it presented alternating signal patterns on T2-weighted sequences with low intensity areas and cystic components with fluid-fluid levels (MRI sedimentation sign) (Fig. 4a-f). After CE administration, fibrous septa surrounding cystic and calcified areas enhanced, producing a "web" or "cobblestone" pattern. No nodular enhancement was reported, neither involvement of surrounding muscolar and bone structures, vessels and nerves.

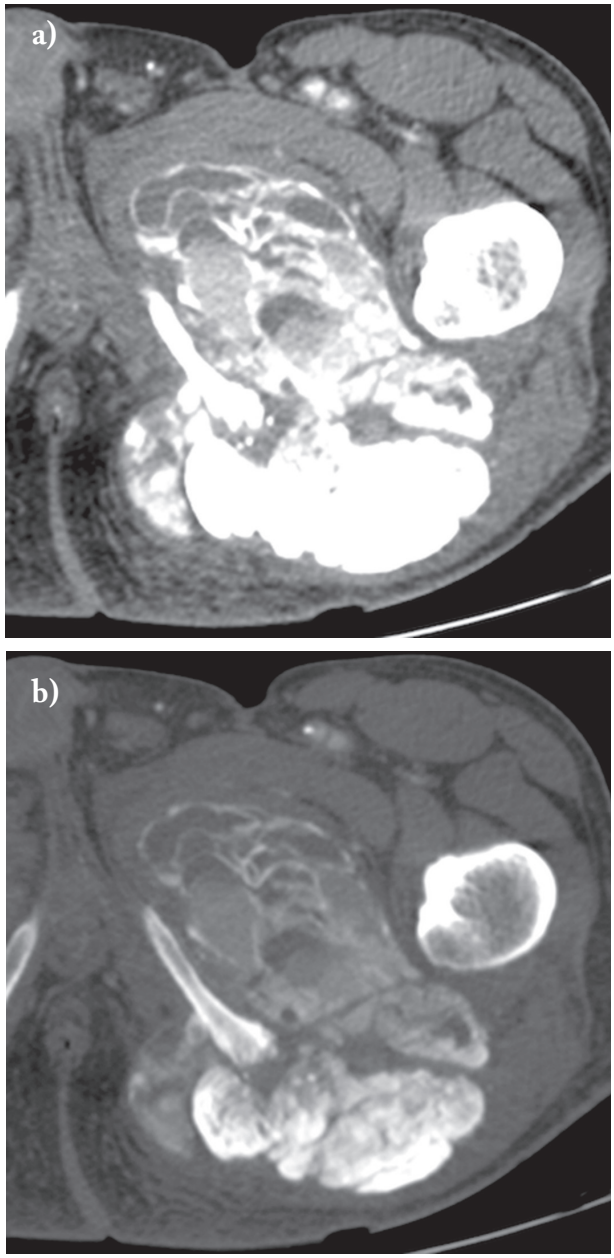
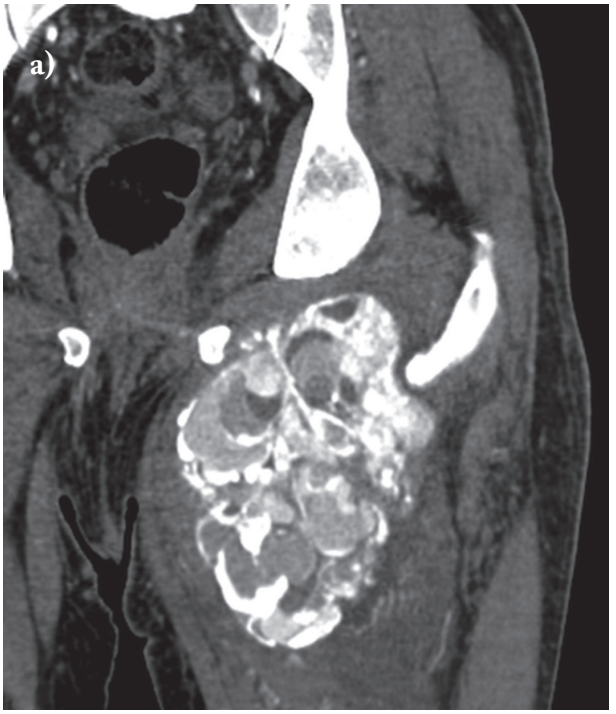


Figure 2. On MDCT, reported in soft-tisse (**a**) and bone (**b**) windows, the mass has large cystic areas, with gross and egg-shell calcifications and fluid-fluid levels inside ("sedimentation sign")

Patient underwent surgery. The mass was resected, measuring 62 cm in the largest diameter. Pathologic evaluation confirmed the diagnosis of TC, showing grossly calcifications and cysts with chalky material inside (precipitated calcium salt), surrounded by inflammatory reaction and fibrosis (Fig. 5a-c). No signs of



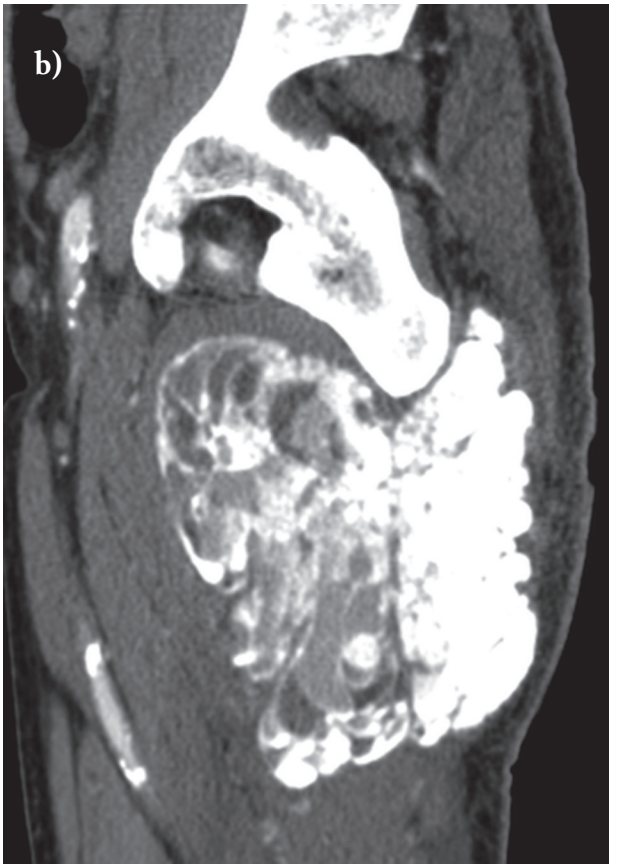


Figure 3. MPR reconstructions on coronal (**a**) and sagittal (**b**) planes and 3D reconstructions (**c**) CT scans better depict lesion localization and extension around the left hip joint and the upper thigh

malignancy were found and no part of the mass was seen to make direct contact with the underlying bone.

Discussion

TC was first described by Giard (7) and Duret (8) in 1898 and 1899 and then widely studied from 1930 to 1950 by a german pathologist, Otto Teutschlander and named it as "lipocalcinogranulomatosis" (9). The current term of TC was firstly used by Inclan in 1943 in American literature (10). During the following years the disease has been identified with different terms and criteria. To date, approximately 200 cases have been reported since Duret's first description in 1899 (11-14).

Pathogenesis of TC is not known, and similar lesions can be observed in metabolic disease with increased haematic levels of calcium and phosphate, such as chronic renal failure, primary hyperparathyroidism, hypervitaminosis D, sarcoidosis (15, 16). On the basis of 122 reviewing cases and their clinical and pathologic findings, Smack et al divided all TC in three groups (17). One group are primary normo-phosphatemic TC usually presenting in first two decades of life as solitary lesions. According to this group of authors these patients are without evident familial connection, although recent literature detected familial connection involving mutations in the gene encoding SAMD9 protein. The second group are primary hyperphosphatemic TC usually presenting during the first and second decades of life. This group of patients have genetic predisposition with reduced urinary phosphate excretion caused by recessive mutations in *GALNT3* and *KLOTHO*, that causes the inactivation of FGF23, a phosphaturic hormone. The third group encompasses secondary TC connected with chronic renal failure. Despite their different etiology and pathogenesis, histopathology is identical in all types suggesting possible common path-way which eventually results in the for-

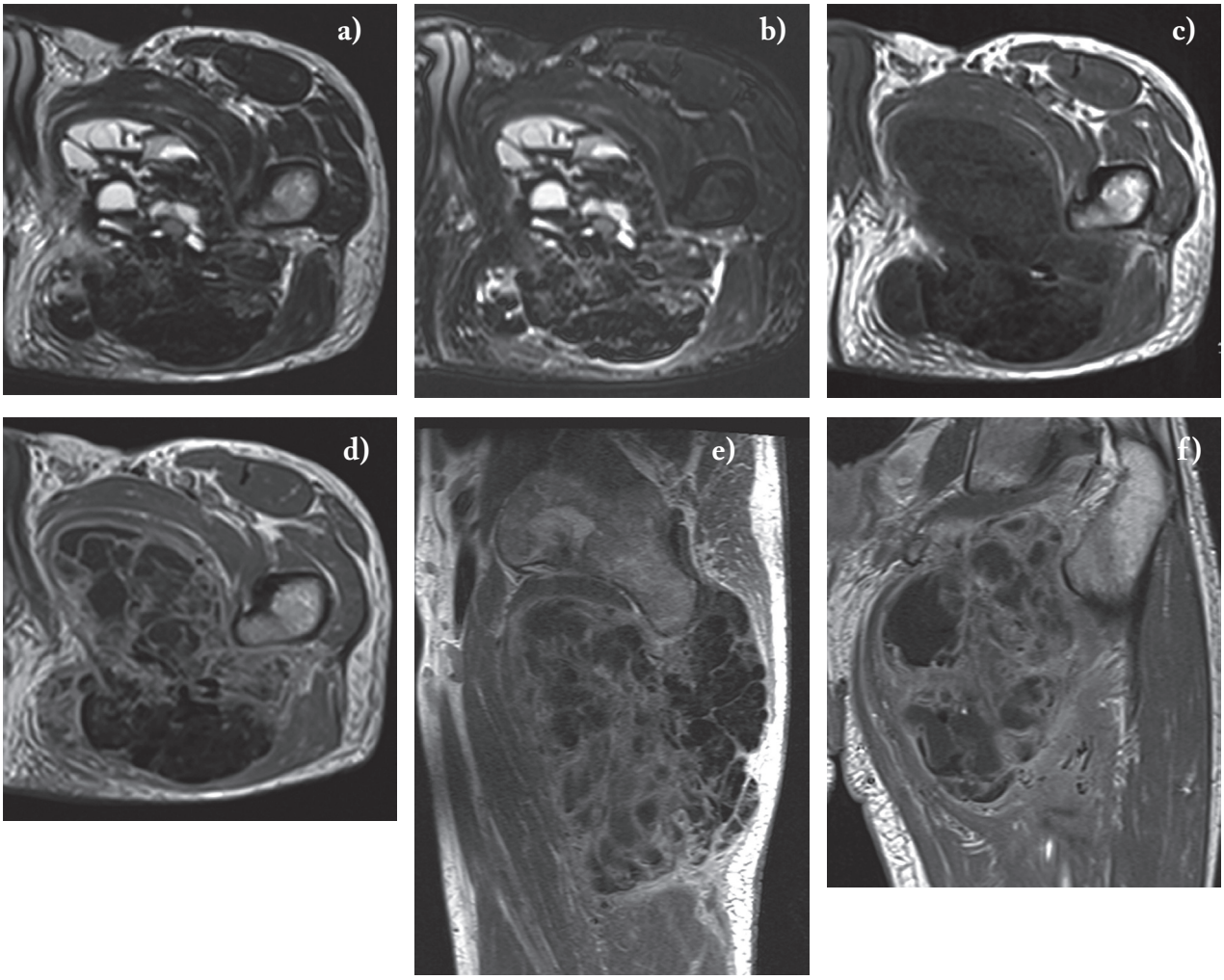


Figure. On MRI axial T2w (**a**) and fat-suppressed T2w (**b**) sequences the lesion present low intensity and bright nodular areas, with cystic components and fluid-fluid levels ("sedimentation sign"). On T1w sequences (**c**) lesion shows inhomogeneous diffuse low signal intensity. After CE injection, T1w axial, coronal and sagittal images show (**d, e** and **f**) fibrous septa surrounding cystic and calcified areas enhanced, producing a "web" or "cobblestone" pattern.

mation of the characteristic TC lesions and originates from minimal repetitive trauma and reparative inflammatory process (17-20).

Typical radiological findings in TC suggest a correct diagnosis in the majority of cases. Radiographs show lobulated calcifications on joints extensor surface. Calcifications are well defined, rounded, sometimes with a cystic appeareance and a fluid-fluid level inside (14). Fluid-fluid levels, producing the "sedimentation sign", derive by calcium crystals layering inside intracystic amorphous chalky material. Fibrous septa can produce linear or curved radiolucencies between gross calcifications, producing a "cobblestone" pattern (12).

CT shows calcified cystic lesions in fibrofatty planes, deeply to muscles. It clearly depicts lesion topography and extension, particularly using 2D Multiplanar Reconstruction (MPR), 3D Shaded Surface Display (SSD) and Volume Rendering (VR) reconstruction. Reconstructions help surgeons to correctly plan a complete surgical ablation (1).

At MRI lesions have variable signal intensity, with a low signal in largely calcified portions, and cystic areas with high signal in T2-weighted sequences. At MRI the typical "sedimentation sign" shows a greater

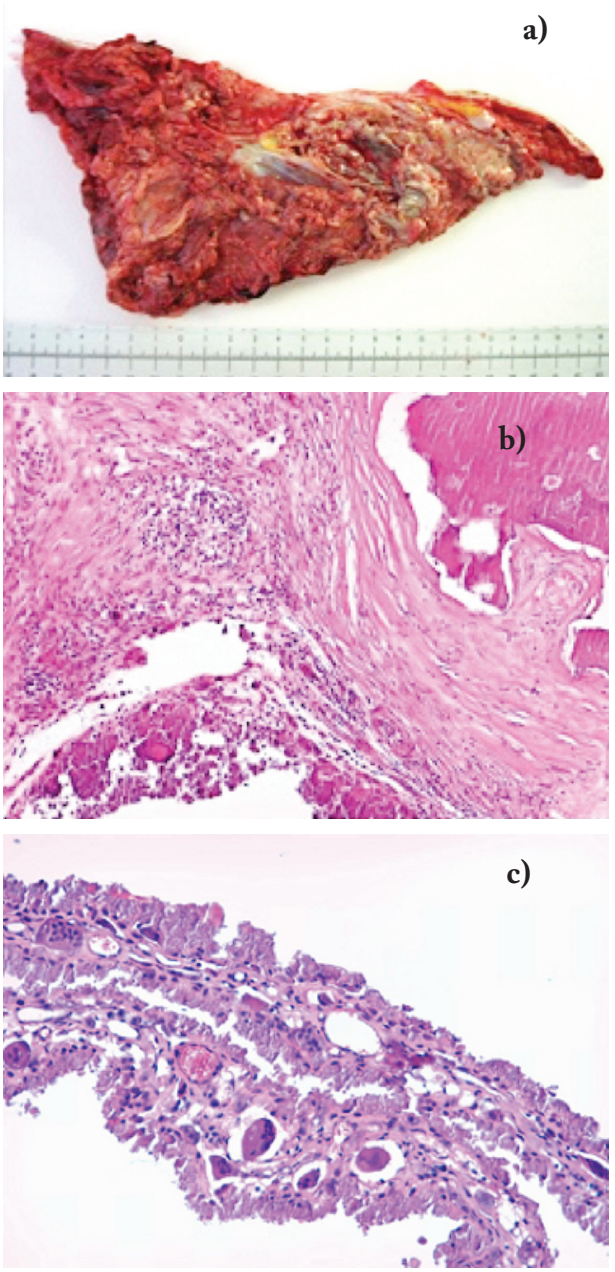


Figure 5. (**a**) The cut surface of the surgical specimen was yellow-white with a cystic appearance. (**b**, **c**) Low-power photomicrographs show calcific debris with chronic inflammatory reaction and surrounding fibrosis.

conspicuity (5). According to some authors (1), an alternating high and absent signal MRI pattern is associated to metabolically active lesions, with a prominent fluid/inflammatory component. After contrast injection, only a mild contrast enhancement of fibrous septa can be observed (21).

Some authors have documented an ultrasonographic (US) approach to TC (22, 23). In acute cases, in which a mass is initially forming or beginning to enlarge and vascular signals are more detectable, TC may present as a well-circumscribed homogenous mass with an irregular border of calcifications. In chronic cases, which tend to be defined by more cystic changes and fibrous septa, US may reveal a lobulated cystic echogenic mass with septa and a calcified rim. The sedimentation sign may also be observed (22-26). However, the cystic appearance on US is aspecific since it may easily mimic as an abscess formation (27, 28).

Also the value of angiography in evaluating soft tissue calcific masses has been reported (29-33). Benign soft tissue masses do not typically change the normal vessel diameter, nor do they demonstrate neovascularity, blush, pooling, encasement, arteriovenous shunts or feeding vessels (34, 35). Angiography of benign soft tissue masses typically shows displaced or stretched vessels (36). TC is atypical for benign soft tissue masses in that it is a relatively vascular process. In a radio-pathologic correlation study (37), TC has been proven to be hypervascular during the active phase, similarly to myositis ossificans. Specifically, the active stage of tumoral calcinosis has fluid with sedimentation or calcific foci at the edges, cellular pleomorphism and a prominent vascular component (36, 37).

This active and hypervascular stage could take advantage of an early surgery (29). In this setting, some authors have proposed a vascular study of TC lesions by contrast-enhanced ultrasound (CEUS), which is a "new" simple, immediate, and effective US tool: microbubbles circulate freely inside the body and constitute an intravascular contrast agent (38, 39); therefore, they permit analysis of both macro- and microvascular lesional blood flow (40, 41). The technique yields information about contrast enhancement almost as CT (42, 43) and MRI (44, 45) do but in real time and without the use of ionizing radiation. To date, CEUS has obtained valid results in different areas (38-41), although the method has not yet entered in standardized vascular imaging protocols for clinical practice.

Differential diagnosis includes many conditions with similar periarticular soft tissues calcifications. Grossly periarticular soft-tissues calcifications can be observed in connective tissue diseases (polymyositis,

dermatomyositis, lupus erythematosus) or traumatic/degenerative diseases (synovial osteochondromatosis, calcific tendonitis, myositis ossificans, calcific myonecrosis). Clinical history, joint involvement and morphology and distribution of calcifications usually allow a correct differential diagnosis (46, 47). Differential diagnosis with malignant neoplasms is critical, particularly with synovial sarcoma, parosteal osteosarcoma and chondrosarcoma. Synovial sarcoma usually develops in periarticular regions as an inhomogeneous infiltrative mass only partially occupied by grossly calcified areas inside (48). Parosteal osteosarcoma and chondrosarcoma arise from bone surface extending in surrounding soft tissues as a densely calcified mass. Radiographic appeareance may suggest TC when bone don't show significant anomalies. Cross-sectional imaging accurately depicts sarcomatous malignant infiltrative growth toward underlying bone and surrounding structures and a high enhancing tissutal portion after CE inside the mass or around calcified components (1).

In the case presented the lesion had typical radiological features of TC. The mass was localized at the extensor surface of hip joint, with a benign expansive growth. It was largely occupied by calcifications and cystic areas with fluid-fluid levels inside ("sedimentation sign"); no nodular enhancing areas were evident. MRI also showed an inhomogeneous high signal intensity in T2-weighted sequences, although these features have been more frequently reported in younger patients with metabolically active lesions (1). Moreover, the disease showed an unusual course: after a typical onset in the first decade of life, disease had been silent until the sixth decade, when it recurred with a left hip active growth lesion.

Surgical excision is a well documented treatment, but recurrences after surgery due to poor circumscription are common, particularly in metabolically active lesions (5). Recurrences can also occur several years after intervention (49). Until now, however, only few reports in literature have described MRI findings in TC recurrences (5).

To conclude, TC can occur with different clinical and biochemical patterns. We report an unusual relapse with a metabolically active lesion in an adult man after a long period of quiescence. Differential diagnosis can be difficult in unusual clinical settings, but a careful evaluation of imaging findings and biochemical data can suggest the correct diagnosis.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Received: 26 February 2019
Accepted: 10 June 2019
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