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Case report

A patient with multiple brown tumors due to secondary hyperparathyroidism: A case report☆,☆☆,★

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ABSTRACT

Brown tumor is an uncommon non-neoplastic radiolucent bone lesion due to a rapid bone loss replaced by haemorrhage and reparative granulation tissue. It is a manifestation of hyperparathyroidism related to the high level of parathyroid hormone and represents a problem linked to the adherence to therapy. We present a case of a 44 years-old Caucasian female with hemodialysis-dependent chronic kidney disease in poor sanitary condition with CT evidence of innumerable and widespread bone tumors. At first, we considered these bone lesions strongly suspicious for metastasis, so we recommended an oncological consultation and laboratory studies, that showed a secondary hyperparathyroidism with elevated serum parathormone level of 923 pg/mL (normal range: 10-70 pg/mL). According to our experience, in case of radiological evidence of multiple bone lesions, a correct medical history is mandatory. When the patient has a history of chronic kidney disease and dialysis and high blood levels of parathyroid hormone are present, secondary hyperparathyroidism should always be considered in the differential diagnosis.

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Introduction

According to the literature, metastases and multiple myeloma are by far the most common cause of multiple bone tumors in patients older than 40 years, but not the only ones. In fact, we can find the same bone features in many other diseases both benign and malignant, such as brown tumors.[1] Also known as osteitis fibrosa cystica, brown tumor is an uncommon non-neoplastic radiolucent bone lesion due to a rapid bone loss replaced by haemorrhage and reparative granulation tissue. The presence of hemosiderin causes the brownish color that gives the name to the lesion. It is a manifestation of hyperparathyroidism (HPT), resulting by the increased level of parathyroid hormone (PTH).[2] There are three HPT forms: primary, secondary and tertiary. The first one is usually caused by an adenoma or, rarely, by a carcinoma of parathyroid glands. While chronic kidney disease (CKD) and end-stage kidney disease (ESKD) are the most common causes of secondary HPT. In addition, every disease characterized by hypocalcaemia (gastrointestinal malabsorption, severe vitamin D deficiency, inadequate dietary calcium intake etc.) represents a cause of secondary HPT. Tertiary HPT results from long-standing secondary HPT.[3]

Here we describe a case of a patient affected by secondary HPT related to CKD with multiple brown tumors.

Case presentation

A 44 years-old Caucasian female presented with a suspicion of pneumonia because of the presence of dry cough for about a month. She suffered from hypertension, hyperuricemia and CKD in dialysis. Her social and sanitary situation was poor, so adherence with treatments and dialysis was suboptimal. The patient had a chest-computed tomography (CT) without contrast and no evidence of pneumonia was found. However, we reported multiple bone lesions involving spine, several ribs and right scapula. (Fig. 1) An oncological consultation was required because we, at first, considered these bone lesions strongly suspicious for metastasis.

The patient underwent a total body CT scan with intravenous contrast agent in suspicion of cancer or multiple myeloma. Imaging confirmed innumerable and widespread bone lesions in almost all skeletal segments showing variable features. Some of them had well-defined or sclerotic margins while others were expansive with cortical destruction and associated soft tissue mass. One of them completely replaced the right part of L1 body, owing to a protrusion in the spinal canal. (Fig. 2) Despite this finding, the patient had no symptoms. We recommended a magnetic resonance imaging (MRI), but the woman refused consent. We also reported a generalized modified bone mineral density related to the abnormal bone metabolism. (Fig. 3) In addition, CT imaging showed a severe renal atrophy, according to the known condition of CKD. (Fig. 4)

Considering the CT findings and the patient's clinical history, laboratory studies were mandatory. They revealed an elevated serum parathormone level of 923 pg/mL (normal range: 10-70 pg/mL) with a calcium and phosphate level of 8.1 mg/dL (normal range: 8.5-10.5 mg/dL) and 7.5 mg/dL (normal range: 4-7 mg/dL), respectively. These values were associated to a very low glomerular filtration rate (GFR), that was about 4 mL/min/1.7m^2 (normal range: 90-120 mL/min/1.7m^2) with a high blood creatinine level of about 10.4 mg/dL (normal range for adult women: 0.59-1.04 mg/dL).

The absence of a known primary tumor, the presence of high blood level of parathormone and the patient's clinical history led to the diagnosis of bone brown tumors due to a secondary HPT.

Discussion

Secondary HPT is a frequent complication of CKD. The pathogenesis is complex and related to the high PTH levels that cause many disarrangements of mineral metabolism, including fibroblast growth factor-23 (FGF23) increase, active vitamin D reduction and calcium and phosphorus modifications.[4] Despite all the options of treatment, today secondary HPT represents a problem linked to the adherence to therapy.[5] Brown tumors usually occur in patients with very high PTH levels (more than 10 times the upper limit of normal) and for an extended time.[6] They are rare in developed countries and only seen in 3% of primary HPT cases.[7] The incidence is higher in people older than 50 with a female:male ratio of 3:1.[8] Brown tumors represent a reparative cellular process and consist in a locally destructive mass composed by osteoclast-like and multinucleated giant cells in a vascular and fibrous stroma that can replace bone and produce osseous expansion. They frequently involve facial bones, jaws, ribs, pelvis, femurs and the other long bones.

Clinical manifestations can be different depending on the affected district. Most are asymptomatic, while others can cause swelling, protuberance or even disfiguration. Pain is usually due to the consequence of the disease, in particular when pathologic fractures occur. Radicular pain and paraesthesia can be present. More severe manifestations are "cauda equina syndrome", paraparesis and paraplegia.[9,10,11]

Bone involvement can be monostotic or polyostotic and the radiological findings are extremely variable. Lesions usually are well-defined and radiolucent with cortical thinning[12] while others are poorly defined with an expansive growth associated to soft tissue mass and cortical destruction[13], suggesting an aggressive behavior. The difference in the time of appearance of the lesions during HPT can explain the multiple

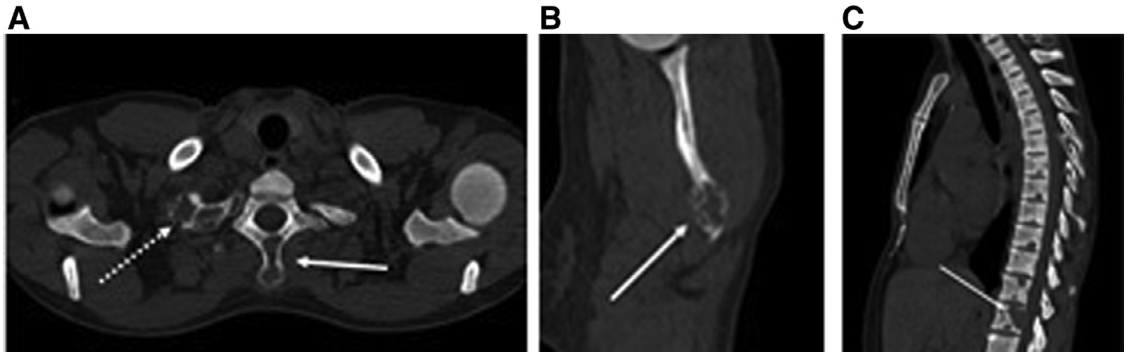

Fig. 1 – Chest CT illustrating multiple bone lesions that involve the spinous process of D1 (solid arrow in 1A) and the posterior arch of the first right rib (dashed arrow in 1A), the right scapula (arrow in 1B) and the spine (arrow in 1C).

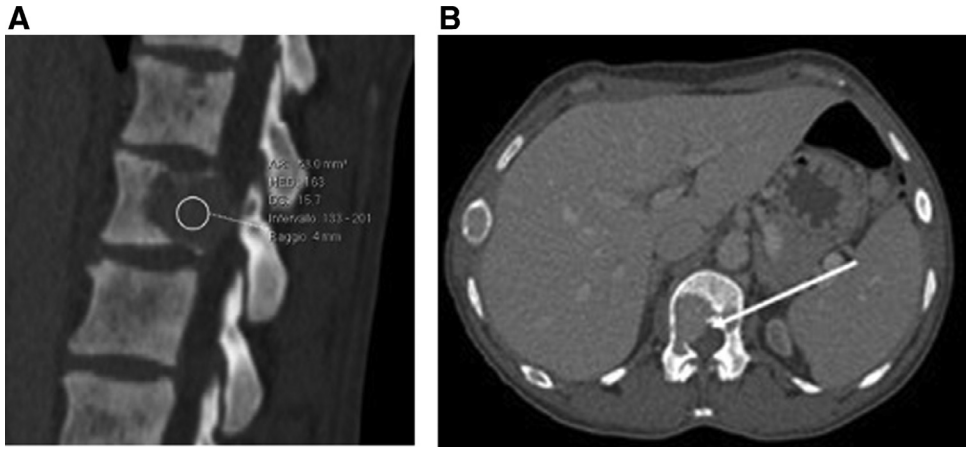

Fig. 2 – Sagittal and axial CT scan demonstrating the presence of soft tissue mass involving the body of L1 characterized by attenuation values in the range of fibrous tissue (2A). The arrow shows the mass extension in the spinal canal (2B).

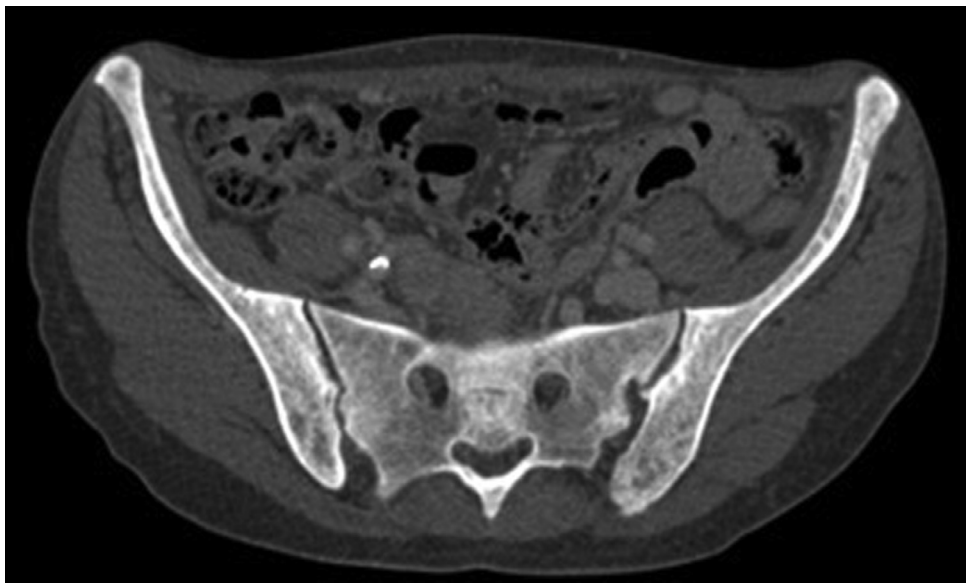

Fig. 3 – Axial CT scan showing an altered bone mineral density of the pelvic girdle.

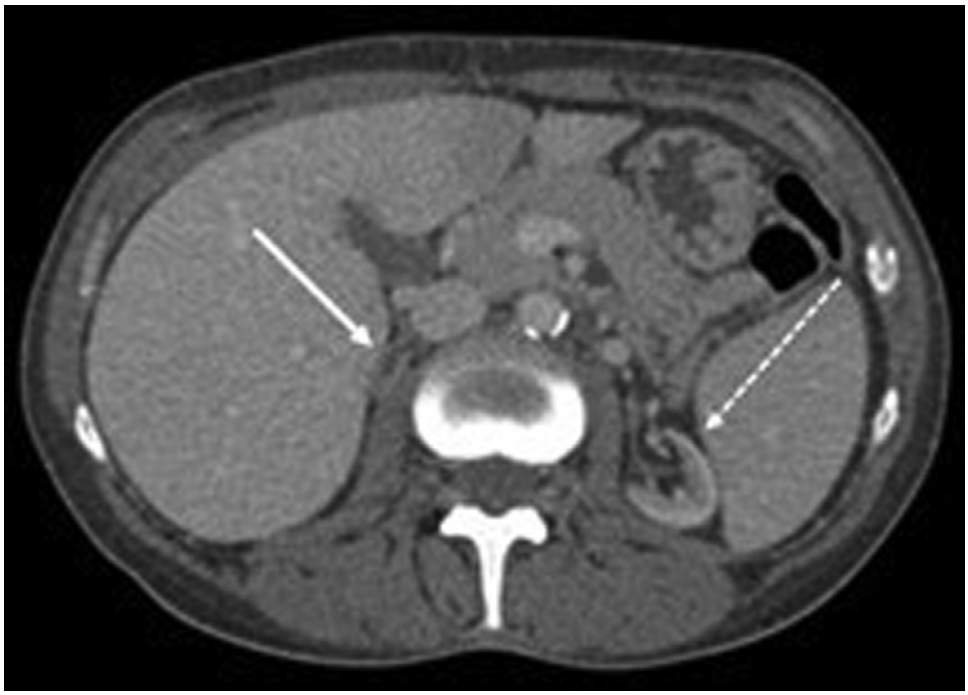

Fig. 4 – Axial CT scan at the portal vein phase. The left kidney (dashed arrow) is smaller than normal with reduced cortical thickness. The right one (solid arrow) is almost not recognizable due to its small size.

radiological aspects of brown tumors.

Our case report is of special interest because of the different features of brown tumors that can mimic metastasis, in particular from breast or prostate cancer. Differential diagnosis includes also multiple no ossifying fibroma, multiple myeloma, multiple bone cysts, Langerhans' cell histiocytosis, metabolic osteopathy and fibrous dysplasia.[14]

The history of the patient, the localization of the bone lesions and their CT features, associated with the absence of a known primary cancer, helped us to exclude the diagnosis of metastasis or of any other cause of multiple bone lesions and oriented towards the diagnosis of brown tumors.

2-deoxy-2-(fluorine-18) Fluor-D-glucose positron emission tomography (^{18}F-FDG PET) /CT was not considered appropriate, in fact, according to literature, it is not useful in differentiating metastasis from brown tumors because both have an increased signal uptake.[15]

We did not perform bone biopsy because the patient refused consent. Anyway, some studies showed that histology cannot guarantee a certain diagnosis, because other bone lesions, such as aneurysmal bone cyst, giant cell tumor or giant cell granuloma have similar microscopical and macroscopical features.[16,17]

Our case report confirms the important role of PTH blood level to distinguish brown tumors from other forms of bone lesions, in particular metastasis.[18]

In conclusion, in case of radiological evidence of multiple bone lesions, a correct medical history is mandatory. When the patient has a history of CDK and dialysis and high blood levels of PTH are present, secondary HPT should always be considered in the differential diagnosis.

Authors' contributions

Not applicable

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