Received: 20.7.2011 **Accepted: 12.8.2011**

Case Report

Unusual presentation in a case of primary hyperparathyroidism

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Abstract

This report describes a case of classic severe primary hyperparathyroidism (PH) with clinical presentation that is very infrequent nowadays, which was osteitis fibrosa cystica. As bone scintigraphy demonstrated multiple areas of increasing uptake associated with hypercalcemia, a thorough investigation was conducted to exclude the neoplasms which most frequently are responsible for bone secondarisms. A fludeoxyglucose (FDG) positron emission tomography/CT demonstrated diffuse and multiple foci of increased FDG uptake and a focal uptake at the left thyroid region. Parathyroid function was studied, revealing unexpectedly high parathyroid hormone (PTH) levels. Further tests confirmed the diagnosis of PH and localized a parathyroid adenoma in the lower left side.

KEYWORDS: Primary Hyperparathyroidism, Osteolysis, Neoplastic Hypercalcemia, Bone Scintigraphy, Bone Secondarisms, Parathyroid Adenoma.

J Res Med Sci 2011; 16(8): 1078-1081

Hyperparathyroidism has undergone a dramatic change in the latest 30 years. The development of classical findings such as nephrolithiasis, brown tumors, bone cysts, and pathologic fractures is exceptional nowadays.[1] We report a clinical case whose presentation initially elicited the suspect of disseminated malignancy.

Case Report

A 27-year old male patient with a history of progressive fatigue and pain at the left hip since three months presented at the Emergency Department, Ospedale Maggiore Policlinico, Milano, in 2008. On plain X-ray wide osteolytic shadows of the ileopubic and ischeopubic left branches were detected. Computed tomography (CT) scan confirmed several osteolytic areas bilaterally in the ilium and femoral necks. Bone scintigraphy with ^{99m}Tc-methylene diphosphonate (MDP) demonstrated diffuse tracer activity in the skeleton. Laboratory values were remarkable for serum calcium of 16.2 mg/dL (normal: 8.4-10.2), which prompted the immediate treatment with fluids and frusemide. Moreover, serum phosphorus and alkaline phosphatase concentrations were 2.0 mg/dL (normal: 2.4-4.5) and 1098 IU/L (normal: 42-98), respectively. Strongly suspecting neoplastic hypercalcemia, a thorough investigation was then conducted, with the following results. A bone biopsy did not confirm the cancer hypothesis, showing only the presence of osteoclasts in large number. Biochemical and imaging studies excluded the neoplasms most frequently responsible for bone secondarisms. A fludeoxyglucose positron emission tomography/CT (FDG PET/CT) with a dedicated PET/TC tomography (Biograph plus, Siemens, Erlangen, GER) was then planned: the maximum intensity projection image demonstrated multiple foci of increased FDG uptake, mimicking bone metastasis or myeloproliferative disease (Figure). A diffuse pattern of FDG

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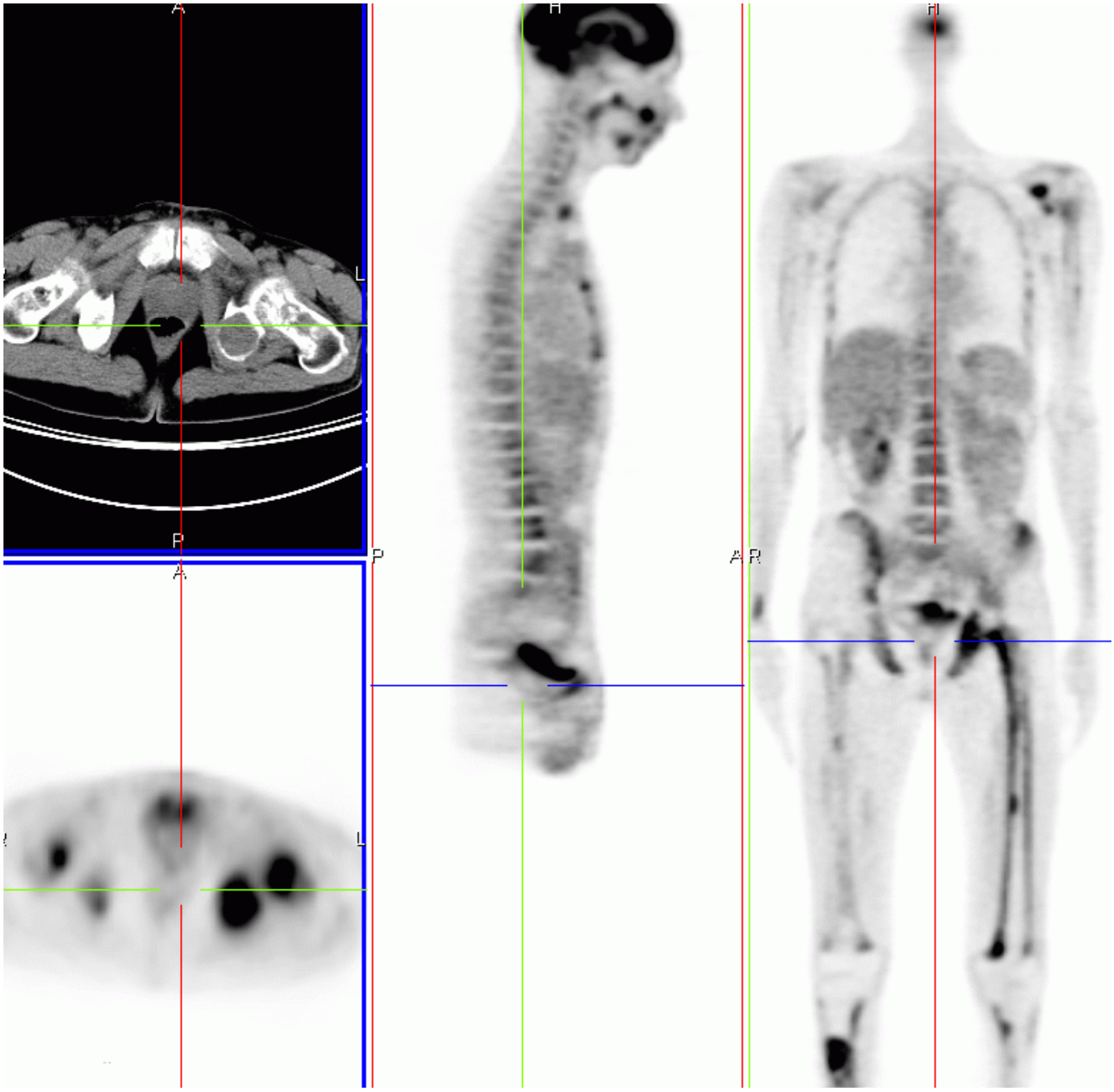

Figure 1. FDG PET/CT images show diffuse and multiple foci of increased FDG uptake throughout the skeleton

uptake was also assessed in some long bones of the limbs.

On the basis of the negative bone biopsy findings and of FDG focal uptake at the left thyroid region, parathyroid function was studied, revealing unexpectedly high parathyroid hormone (PTH) levels (906 pg/mL; normal: 15-65). Urinary calcium excretion and serum 25-hydroxyvitamin D levels were checked at that time, showing abnormal results (urinary calcium, 24-hour 520 mg, normal: < 300; vitamin D 20 ng/mL, normal: 8-40). Neck ultrasonography (US) revealed a hypoechoic oval structure, 3.4 cm in diameter, near the left lower thyroid pole that suggested the possibility of an enlarged parathyroid gland. Color Doppler US demonstrated plentiful pulsating blood flow. According to these results, a bilateral

neck exploration was performed in which the left parathyroid tumor was removed and the remaining three glands identified as normal. The pathological diagnosis was parathyroid adenoma.

Intraoperative PTH value dropped by 68% prior to completion of parathyroidectomy and serum calcium levels restored to the normal range a few hours after surgery. Oral calcium supplements (2.0 g daily) were provided as soon as oral intake was re-established and moderate doses of 1,25 $(OH)_2$ vitamin D_3 (1.0 mcg daily) were added. Two months after the operation, the patient's bone pain completely disappeared and he became able to walk without crutches after another three months. Persisting normalization of serum PTH value was detected after one year. Bone densitometry demonstrated a significant increase of lumbar and femoral mineralization, and plain X-rays confirmed the disappearance of the osteolytic areas after two years.

Comment

The present report describes severe PH in a young patient with clinical presentation very infrequent nowadays, and therefore misleading, i.e. diffuse bone disease. With the routine measure of serum calcium values in the early 1970s, a large cohort of previously unrecognized hypercalcemic patients was discovered,[1] changing the presentation of primary hyperparathyroidism. Many cases are diagnosed in the early stages of the disease process, when they have asymptomatic hypercalcemia, before the development of classical findings.[2]

In our patient the clinical picture suggested a malignancy rather than a benign endocrine disease as osteitis fibrosa cystica. In fact, the development of brown tumors or osteoclastomas is an exceptionally rare complication of longstanding PH today. Brown tumors present as single or multiple lesions that must be distinguished from metastatic bone disease.[3] Common sites of involvement are the facial bones, pelvis, ribs and femurs. Clinically, osteitis fibrosa cystica causes pain and sometimes pathologic fractures. Histologically, there are collections of osteoclasts intermixed with fibrous tissue and poorly mineralized bone. [3]

The FDG PET/CT is a non invasive method potentially useful in the diagnosis of brown tumors,[3-5] that may mimic metastatic bone disease showing a significant FDG uptake. Nuclear imaging of skeletal involvement in classical PH in the literature is limited to anecdotal reports,[6-9] especially for FDG PET/CT.[10, 11] The main FDG-PET/TC pattern in PH-related osteopathy seems a mix of focal FDG uptake in the substituted bone marrow (dense osteoclastic activation) and diffuse pattern of increased FDG uptake in the pars compacta of long bones of the limbs (disperse osteoclastic activation). The latter pattern is infrequently seen in bone marrow metastases as assessed by FDG imaging, which is primarily a tumor specific tracer, whereas in PH-related skeletal lesions FDG is not a specific tracer of bone and bone marrow metabolism.[12]

In conclusion, PH must be considered in the differential diagnosis of multiple bone uptake images at the FDG PET/CT. These lesions must be recognized and not misinterpreted as bone metastases.

Conflict of Interests

Authors have no conflict of interests.

Authors' Contributions

LA and MB followed the patient, collected clinical data, and prepared the manuscript. GP and EP provided clinical assistance and participated in manuscript preparation. RB provided nuclear imaging and assistance for the comment. All authors have read and approved the content of the manuscript.

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