Scintigraphic evaluation of multifocal osteolytic lesions in a patient with primary hyperparathyroidism: A case report

Case Report

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ABSTRACT

Osteitis fibrosa cystica is the classic patognomonic form of skeletal disease in hyperparathyroidism that characterizes with decreased cortical bone thickness compared to increased cancellous bone. We present a case of 52-year old female patient with osteolysis of the left calf on radiographic images. The bone scan detected multiple focal pathological accumulations in the skull, left tibia, both femurs and in the left ischium. The scan was indicative of secondary multiple skeletal metastases. Because the patient had no previous history of primary malignant disease, metabolic bone disease was suspected and also confirmed after i.v application of 99mTc-MIBI. The scan was in favor of parathyroid adenoma with bone complication (osteitis fibrosa cystica). Neck ultrasonography revealed hypoechoic oval mass below the left lower thyroid lobe that suggested the possibility of parathyroid adenoma. An increased ionized calcium level and PTH confirmed the diagnosis of primary hyperparathyroidism. Parathyroidectomy with radioguided surgery was performed. Hyperparathyroidism is a curable disease and a clinician should always bear in mind a metabolic bone disease when performing a nuclear bone scan where multiple bone lesions are detected (a hallmark of metastatic disease).

Key words: Parathyroid adenoma; ^{99m}Tc-MIBI; Scintigraphy; PTH

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INTRODUCTION

Metabolic bone disease is a term referring to bone abnormalities, most commonly caused by changes in mineral metabolism (calcium, phosphorus, magnesium) or vitamin D, that can lead to dramatic clinical disorders. They can be reversible, if diagnosed and properly treated. Hyperparathyroidism is an abnormal endocrine disorder, characterized by hyperactivity of one or any of the four parathyroid glands, with excessive secretion of parathyroid hormone (PTH), which causes hypercalcemia (increased resorption of calcium from the skeletal system, renal calcium reabsorption in the cortical thick ascending limb of Henle's loop, as well as enhancing the gastrointestinal absorption of both calcium and phosphorus indirectly through its effects on the synthesis of $1,25(OH)_2D$ (calcitriol). The pathophysiology of primary hyperparathyroidism (PHPT) relates to loss of normal feedback control of PTH by extracellular calcium [1].

As a clinical entity, hyperparathyroidism was recognized long time ago, but the scientific knowledge of this disorder has undergone remarkable change in the last 30 years [2]. Women are more often affected than men, and it occurs more frequently in the 5th and 6th decade [3].Throughout Europe and the United States, PHPT is considered as the third most common endocrine disease after type 2 diabetes and thyroid diseases [4].Osteitis fibrosa cystica (OFC) is the classic patognomonic form of skeletal disease in hyperparathyroidism, that characterizes with decreased cortical bone thickness, compared to increased cancellous bone [5].

CASE REPORT

We present a case of 52-year old female patient, admitted at the Clinic of Orthopedics, because of intensive and prolonged pain in the lower back and in the left calf. Radiographic images showed osteolysis of the left tibia and therefore the patient was scheduled for a bone scan procedure at our Department, with incoming diagnosis of multifocal bone osteolysis.

Three phase bone scintigraphy was performed with Mediso DHV Nucline Spirit dual-headed gamma camera, 1minute, 5minutes and 3 hours post i.v application of 740 MBq of ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP). The vascular and pool phase of the lower back showed zones of intensive vascularity. Late bone scintigrams presented multiple focal pathological accumulations in the fronto-parietal region of the skull, middle third of the left tibia, collar region of the both femurs and in the left ischium, as well as in the iliac bones, right scapula, left clavicle, sternum, multiple ribs bilaterally and thoracolumbar vertebrae. The scan was indicative of multiple secondary skeletal metastases (Figure 1).

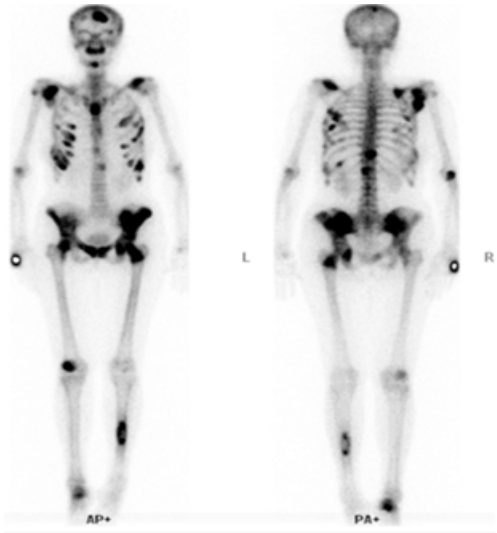

Fig 1. WBS with ^{99m}Tc-MDP presenting multiple skeletal pathological accumulations.

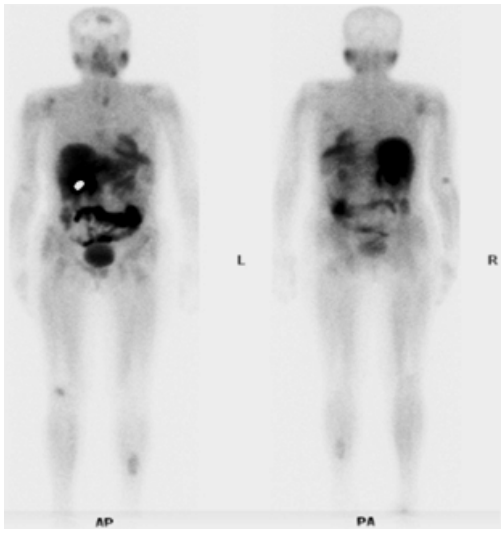

Fig 2. WBS with ^{99m}Tc-MIBI presenting a parathyroid adenoma with multiple skeletal pathological accumulations, in favor of osteitis fibrosa cystica.

The patient had no previous history of primary malignant disease, therefore blood test were indicated.They showed normal values of tumor markers (Ca 15-5, CEA, Ca 19-9), but an increased ionized calcium level 1.71 (1.16-1.36mmol/l), serum calcium 3.64 (2.2-2.7mmol/l) and PTH of 2190 (10-69 pg/ml), that were all in favor of primary hyperparathyroidism.

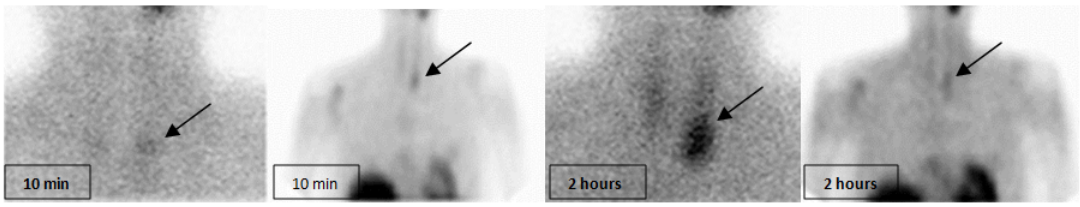

Fig 3. Double phase ^{99m}Tc-MIBI scan detecting a focal accumulation in the lower pole of the left thyroid lobe (parathyroid adenoma).

Ultrasonography revealed an increased hypoechoic oval mass, below the left lower thyroid lobe with a diameter of 30x18mm, that suggested the possibility of parathyroid adenoma. It was confirmed with computer tomography (CT) of the neck region, without any other pathologically increased size of parathyroid glands.

To exclude metabolic bone disease two days later a whole body scan was performed, 1 and 3 hours after i.v injection of 740 Mbq^{99m}Tc-MIBI (methoxy - isobutyl-isonitrile). Multiple focal accumulations were detected,with the same localization as those seen on the bone scan, but also a focal accumulation in the lower pole of the left thyroid lobe. Scintigraphy was in favor of parathyroid adenoma with bone complication (osteitis fibrosa cystica) (Figure 2 and 3).

Parathyroidectomy with radioguided surgery was performed. Firstly we marked the suspected location of the parathyroid adenoma with gamma probe, by i.v administration of 110MBq^{99m}Tc-MIBI, 2 hours prior the minimally invasive parathyroidectomy.

With the gamma probe in the operating room we detected the adenoma and confirmed the diagnosis by later histopathological evaluation of the extirpated specimen (Figure 4). A drop in PTH levels was detected afterwards (70 pg/ml).

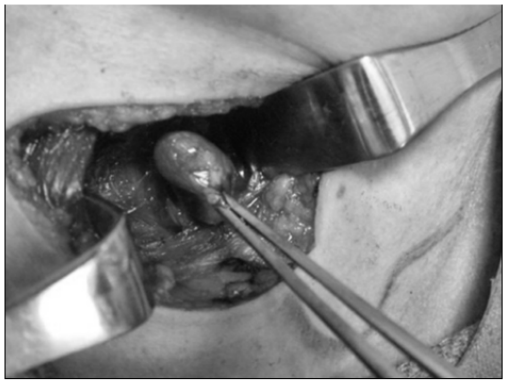

Fig 4. Localization of parathyroid adenoma in an operation room.

DISCUSSION

Primary hyperparathyroidism is a condition with increased secretion of PTH due to parathyroid adenoma (80%), hyperplasia of parathyroid glands (20%) and very rare cases of parathyroid carcinoma. The prevalence of PHPT in Europe, based on epidemiological studies was indicated as 21/1000 in women, between 55 and 75 years of age, which is an estimated equivalent of 3/1000 of the general population [6]. In the United States, about 100,000 people develop primary hyperparathyroidism each year [7]. If it occurs in the younger age (especially first decade), hereditary causes - multiple endocrine neoplasia type I/IIa/IIb should be excluded [8].

With the introduction of a chemical auto-analyzer in 1970s and the routine screening of serum calcium level, a new era in discovering unrecognized hypercalcemic patients begun [2]. Many cases of PHPT are diagnosed in the early stages of the disease process, before the development of classical clinical findings of prolonged disease (nephrolithiasis, brown tumors or osteitis fibrosa cystica, bone cysts, pathologic fracture), that resulted with a significant decline of what were once the common morbidities of the disease [9]. In 1891 von Recklingausen described the bone changes in osteitis fibrosa cystica and Askanazy described the relation between these changes and a tumor of parathyroid origin [10].

Pathology of PHPT involves excessive osteoclast resorption with cortical bone destruction, proliferation of fibrocytic tissue and formation of fibrous cysts [11]. Osteoclasts in Howship's lacunae are seen on bone surfaces beginning in the cancellous bone and tunneling through Haversian canals in the cortex [12]. Brown tumor is a benign localized bone cyst, that represents foci of a hemorrhage, within an enlarged fibrotic marrow space. Organization of these lesions results in the release of haemosiderin deposits,hence the brown color and the accumulation of macrophages, fibroblasts and giant cells [13, 14].

PHPT may develop swelling, bone pain and when brown tumor replaces 2/3 of the long bone cortex, especially in the weight bearing bones, it is of concern for developing pathologic fracture [15].

Destructive skeletal lesions heal within 6 months after the excision of a parathyroid adenoma [16].

Metastatic bone scan should always be differentiated carefully form a metabolic bone scan. The diagnosis of metabolic bone diseases may reflect disturbances in the organic matrix, the mineral phase and the cellular processes of remodeling.

There are two main features of metabolic bone disease due to PHPT in 99mTc-MDP bone imaging. The first is increased uptake in calvaria and jaw bone (the black skull) and the second is increased uptake in long bones and axial skeleton (metabolic "super scan"):

-generalized increased uptake with increased contrast between bone and soft tissue

-tie sternum and cage beds

-foci of increased uptake due to fracture or brown tumor in rib cage

-decreased uptake brown tumor in the right ileum as a doughnut [17].

^{99m}Tc-MDP is a proven agent in diagnosing metabolic bone disease. Increased bone remodeling and bone turnover in this conditions leads to increased uptake of radiolabeled bisphosphonates. Positive findings of benign skeletal lesions are seen in metabolic bone disease associated with hyperparathyroidism (rarely in primary hyperparathyroidism, but frequently in the carcinomas or in serious secondary hyperparathyroidism) [18].

^{99m}Tc-MIBI is one of the most broadly evaluated radiopharmaceutical, introduced in 1990s, for parathyroid imaging. It is a lipophilic cationic component, that injected in animals distributes proportionally to the blood flow, metabolic demand and mitochondrial activity. ^{99m}Tc-MIBI is initially concentrated in the thyroid gland and abnormal parathyroid tissue and then differentially clears from theseorgans in a time-dependent manner - wash out of the thyroid gland is more rapid than from the abnormal parathyroid tissue, that allows dual-phase ^{99m}Tc-MIBI scintigraphy to detect the hyperfunctioning parathyroid tissue.The sensitivity of sestamibi scanning is reported to be 87% of detection of parathyroid adenomas, but only 55% for detection of multiple parathyroid disease [19].

Radiological findings in the skeletal system cannot differentiate parathyroid adenoma and parathyroid carcinoma.MRI isimportant for determination of hemorrhage, cystic component and indirect estimation of fracture risk in brown tumor [20].

FDG PET/CT as a non-invasive method is useful in the diagnosis of brown tumor, that mimic metastatic bone disease, showing a significant uptake of FDG. The pattern of uptake is focal 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) [21].^{11}C-methioninePET-CT, a highly sensitive technique for localizing parathyroid adenomas, provides additional information that conventional imaging may not show [22]. Simultaneous PET–magnetic resonance imaging (MRI) is a new hybrid method of imaging that permits exact fusion of molecular and high-resolution anatomical imaging that provides excellent soft-tissue contrast [23].

After parathyroidectomy and drop of PTH, osteoclastic bone resorption stops and osteoblastic activity increases resulting in uptake of calcium and phosphate (hungry bone syndrome). Verlaan et al. presented a case of 40-year old male patient with multiple lesions (brown tumors) that healed 6 months after the excision of the parathyroid adenoma [14]. Airaghi et al in their case report confirmed increased lumbar and femoral mineralization on bone densitometry and disappearance of the osteolytic areas after two years of parathyroidectomy [21].

Our case is a rare presentation of the PHPT in the late phase, with long lasting symptoms of bone pain and multiple osteolytic bone lesions detected. Bone pain can be a symptom from various etiopathogenesis in all ages. Long lasting bone pain needs a thorough evaluation before conservative treatment with analgetics is applied. If there is no improvement of the pain with the medications, it suggests bone etiology rather than neurologic involvement. Biological markers of bone metabolism, as calcium and PTH, should be assessed for evaluation of bone pain syndrome. Our patient was diagnosed with typical changes of osteitis fibrosa cystica, but still no bone fracture. Radiographic images and bone scan can help in differentiating metabolic and metastatic bone disease and in diagnosing PHPT. Appropriate surgical removal of the causative parathyroid tumor has early and positive benefits on bone health, but the most severe form of PHPT osteodystrophy, brown tumors or OFC, may not structurally return to normal and continue to be at an increased risk for fracture [24].

CONCLUSION

Diagnostic imaging is an important tool in estimating the extent of the disease, but still a good clinical approach to the patient is essential for differential diagnosis. Hyperparathyroidism is a curable disease and a clinician should always bear in mind a metabolic bone disease when performing a nuclear bone scan where multiple bone lesions are detected, that are a hallmark of metastatic disease [20]. It will affect the treatment or further protocols for the patient. FDG PET/CT can help to correctly characterize the lesions.

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