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Case report- Primary hyperparathyroidism with Brown tumors masquerading skeletal metastases – Role of functional imaging in diagnosis and management

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ABSTRACT

Brown tumors of bone are highly vascular, lytic bone lesions representing a reparative cellular process rather than a neoplastic process seen in patients with hyperparathyroidism. These tumors may behave aggressively and can be destructive. We present a case of 33 year old male who presented with progressively increasing swelling in right leg region. A lytic lesion involving right tibia was seen in regional CT which was suspicious for malignancy. Whole body F18-FDG PET-CT was done for further evaluation. PET-CT showed multiple sites of skeletal lesions with a large mass in right lobe of thyroid gland. Biopsy from tibial lesion revealed it to be osteoclast rich tumor raising a possibility of parathyroid mass with multiple brown tumors. Biochemical parameters revealed high Serum Calcium, Serum Total Alkaline Phosphatase and Serum parathyroid hormone (S. PTH). 99mTehnitium Sestamibi (99 m Tc MIBI) imaging was done which localized a right superior parathyroid adenoma with a suspicious right inferior parathyroid adenoma. The patient underwent right superior and inferior parathyroidectomy along with right hemithyroidectomy. Intra-operative fresh S.PTH sample was sent which dropped down to 73.4 ng/ml from 1500 ng/ml. Brown tumor is a potential cause of false-positive result in evaluation of a patient for unknown primary tumor or skeletal metastases with F18-FDG PET-CT imaging.

Introduction: Brown tumors are a misnomer and are actually not tumors. They arise in the setting of long standing high levels of parathyroid hormone, like in primary or secondary hyperparathyroidism. It usually affects people in their 5th or 6th decades of life. They can be monostotic or polyostotic with preferentially affecting sites such as skull, jaw, phalanges, pelvis, clavicles, femur and ribs. Chronic primary hyperparathyroidism may lead to excessive osteoclast activity and increased resorption which leads to destruction of cortical bone, formation of fibrous cysts with deposits of hemosiderin-so called brown tumors. These benign, osteolytic lesions may demonstrate abnormal FDG avidity on F18-FDG PET-CT imaging and may be misinterpreted as skeletal metastases. These lesions are benign and may regress after successful parathyroidectomy.

1. Case

We present case of a 33 year old male who presented with progressively increasing pain and swelling in the right leg. A regional CT was advised which revealed a lytic expansile lesion involving right tibia with associated soft tissue component. He underwent routine blood investigations which revealed high S. Calcium levels of 10.9 ng/dl and S. Total Alkaline Phosphatase of 298 IU/ml.

In view of the destructive nature of skeletal lesion a possibility of primary bony neoplastic etiology was raised as a differential diagnosis. He was advised to undergo F18-FDG PET-CT imaging as part of further management. Whole body F18-FDG PET-CT revealed multiple FDG avid lytic expansile skeletal lesions involving bilateral ribs, pelvic bones, left scapula, left humerus and right tibia (Fig. 1, Fig. 3) along with large lobulated mildly FDG avid soft tissue mass involving right lobe of thyroid which measured approximately 7.4 × 4.8cm in size (Fig. 2). In view of thyroid mass another differential of thyroid malignancy with extensive skeletal metastases was also raised. The patient underwent biopsy from the right tibial lesion which showed large number of osteoclastic giant cells in background of round to spindled mononuclear cells. Tumor stroma was very vascular with bands of cellular fibrous stroma, areas of hemorrhage, cystic changes and hemosiderophages. No necrosis or increased mitosis was seen. The final histopathological impression was Giant cell rich lesion (Fig. 4). Serologic correlation with S.PTH was advised which was 1500 ng/ml. A provisional diagnosis of primary hyperparathyroidism with colloid goiter in right lobe of

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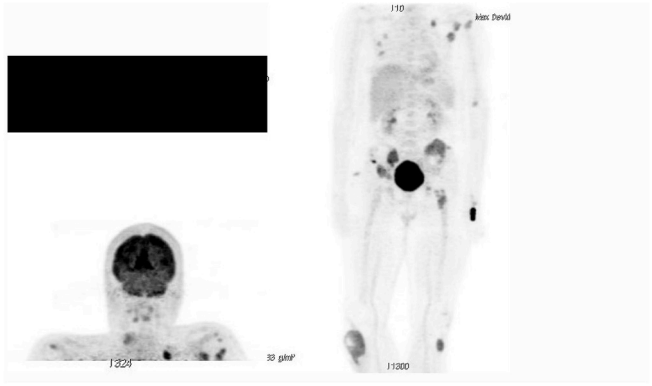

Fig. 1. Maximum Intensity Projection (MIP) images of F18-FDG PET-CT showing multiple FDG avid lesions in ribs, left scapula, pelvic bones, left femur and tibiae.

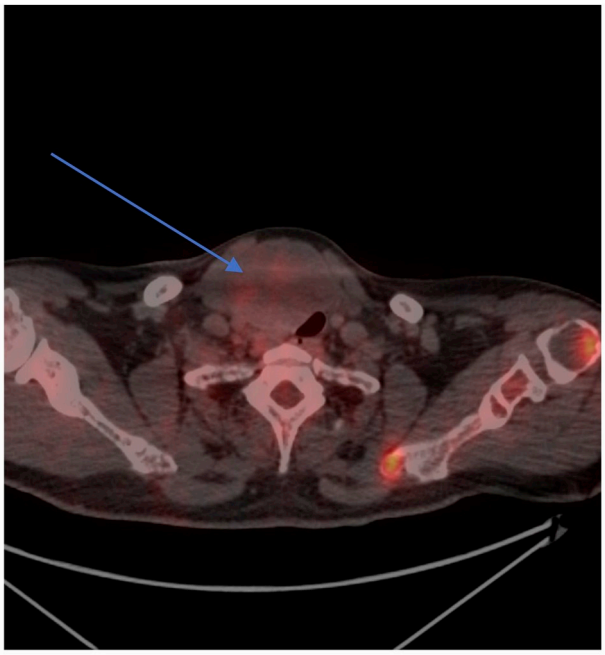

Fig. 2. Fused images of F18-FDG PET-CT showing a large mildly FDG avid mass in the right lobe of thyroid gland.

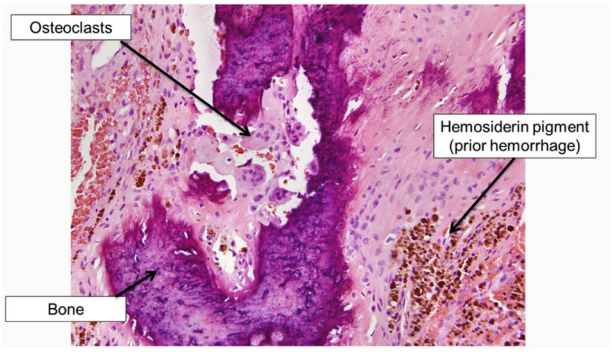

Fig. 4. Slide images of biopsy from tibial lesion showing osteolast rich lesion with hemosiderin pigment in the bone.

thyroid, associated with multiple brown tumors was made.

For preoperative evaluation, the patient underwent 99mTc MIBI scan in our department to localize parathyroid adenomas within the neck mass. 25 mCi 99mTc labelled MIBI was injected intravenously and images were obtained in GE Infinia Hawkeye SPECT CT. Flow images of the neck were taken followed by 20 mins static image and delayed images were obtained at 1hr, 2hrs and 3hrs. A large parathyroid adenoma was localized in superior pole of enlarged right lobe of thyroid gland with another suspicious small adenoma seen in the inferior pole (Fig. 5, Fig. 6).

The patient underwent right hemithyroidectomy + right superior and inferior parathyroidectomy. There was a curative fall in the Intraoperative S.PTH level from 1500 to 73.4ng/ml. Final histopathological examination of the specimen of parathyroid glands showed the presence of hypercellular nodules with chief cell hyperplasia, surrounded by thin capsule. The pattern of growth of chief cells was diffuse, acinar, pseudoacinar and pseudopapillary. The pathological diagnosis revealed it to be parathyroid adenomas in right superior and inferior parathyroid glands. There was no capsular invasion, perineural or vascular invasion with absence of mitosis or necrosis ruling out the possibility of parathyroid carcinoma. The thyroid gland showed features of colloid goiter with the enlarged follicles filled with abundant colloid and hyperplasia of the lining epithelum.

2. Discussion

Skeletal manifestations in the form of Brown tumors are rare and occur in less than 2% of patients suffering from any form of

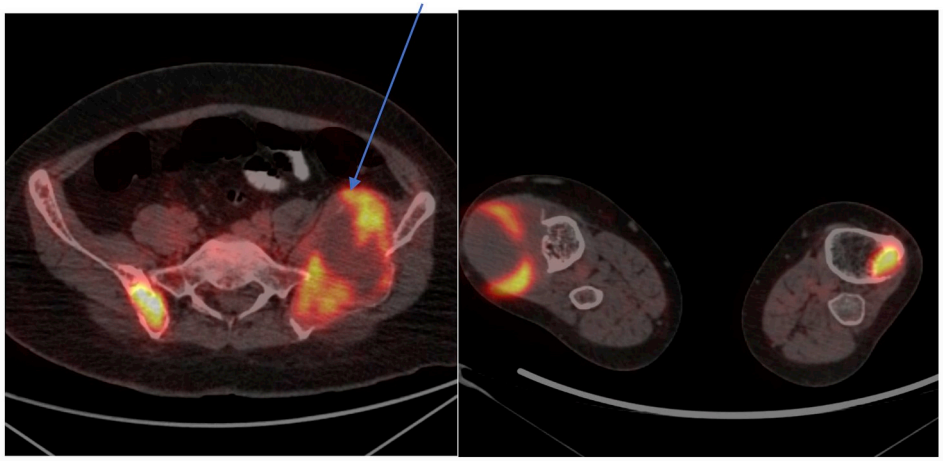

Fig. 3. Fused images of F18-FDG PET-CT showing FDG avid lesions in bilateral iliac bones and bilateral tibiae with associated soft tissue component in left iliac region and left leg.

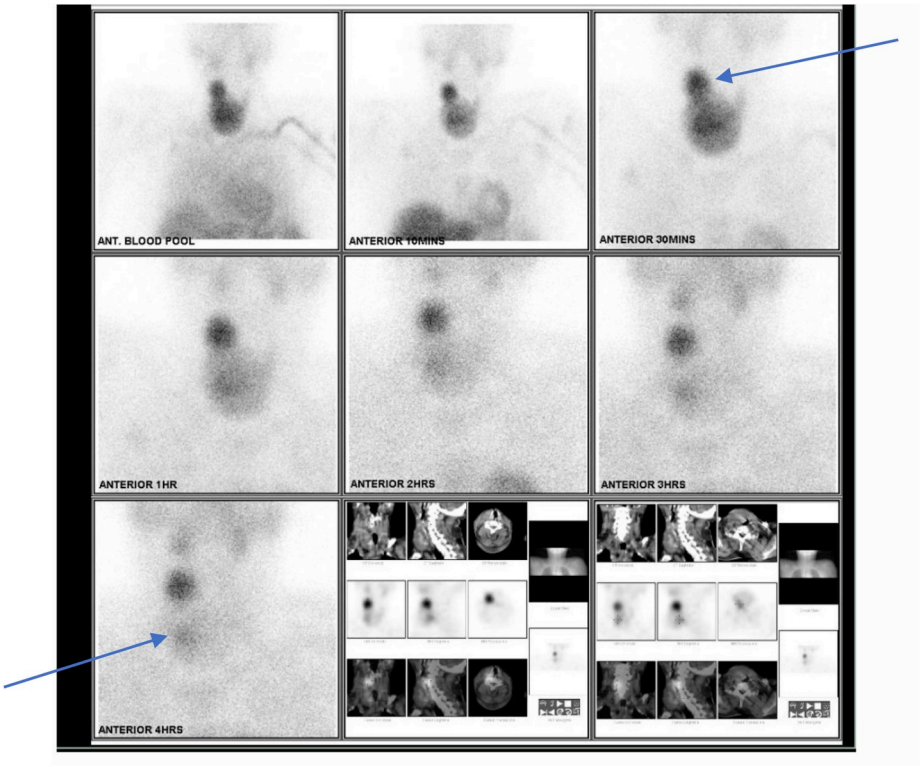

Fig. 5. 99mTechnitium Sestamibi scan images demonstrating blood pool, 30 mins, 1 hour, 2 hour, 3 hours and 4 hours images showing persistent increased Technitium sestamibi uptake in the upper pole of right lobe (arrow marked – top right corner) with a small focal area in lower pole of right lobe of thyroid gland (arrow marked-bottom left corner).

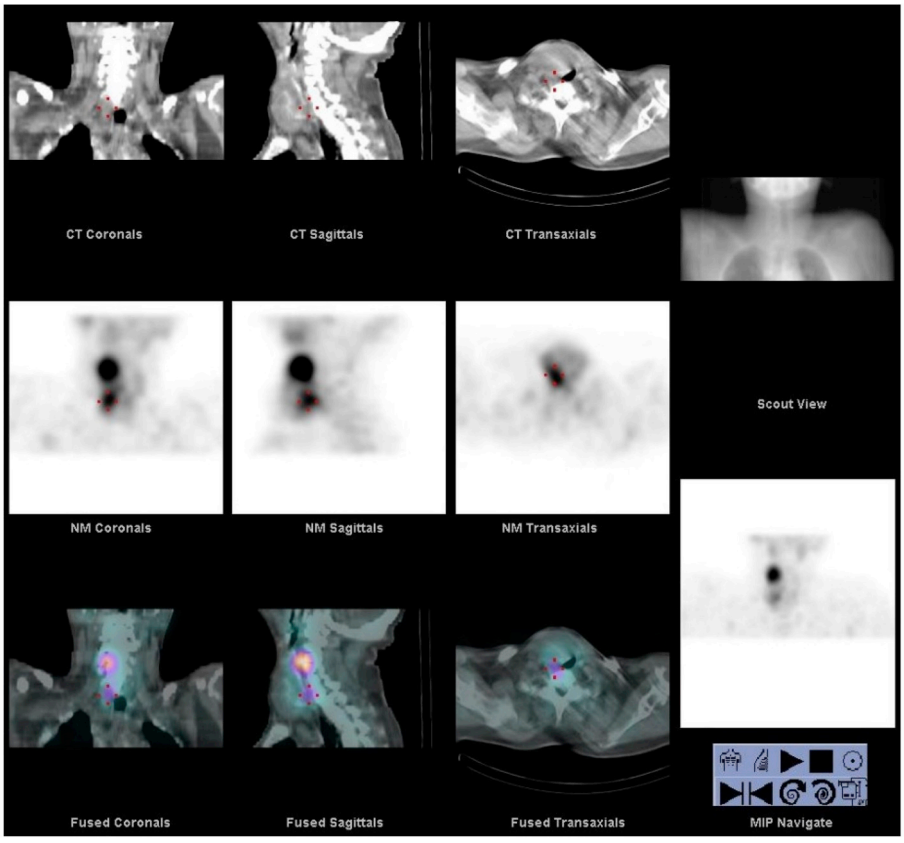

Fig. 6. 99mTechnitium sestamibi Single Photon Emission Tomography-Computed Tomography images showing a large nodular lesion with persistent tracer uptake in the upper pole of right lobe and similar smaller lesion in the lower pole of thyroid gland.

hyperparathyroidism. Multiple Brown tumors in the setting of primary hyperparathyroidism is very rare with female:male ratio being 5:2. Multiple brown tumor cases associated with primary hyperparathyroidism were initially reported by Joyce et al. in 1994. Also five more cases have been observed since then [6]. This clinical picture is more commonly seen in cases of severe secondary hyperparathyroidism or parathyroid carcinoma, being only 2% incidence in patients with primary hyperparathyroidism [5,6]. Since the long bones of extremities are rarely involved in hyperparathyroidism, such rare and multiple benign lesions may simulate a cancer and pose a real challenge for the clinician during its differential diagnosis [4].

Brown tumors may be observed more commonly in the facial bones, pelvis, ribs and femur. A diagnostic confusion arises mainly when the clinician encounters multiple lytic lesions involving different areas of the skeleton as was the case in our patient [3]. Classically, the clinical symptoms of 'brown tumor' have been described as "bone, stone, abdominal groan, and psychic moan". These symptoms have been attributed to hypercalcemia, excessive resorption of bone, and mental agony that comes along. It affects women mostly in the fourth and fifth decades of life and, rarely, younger individuals have been seen to be affected [1,2]. The initial step in the management of primary hyperparathyroidism involves control of hyperparathyroidism and parathyroidectomy is considered effective in spontaneous regression of small skeletal lesions [4].

About 70% of the patients with skeletal metastases present with multiple lesions. In the case of hypercalcemia and radiographic evidence of multiple lytic lesion, primary hyperparathyroidism should always be kept in differential diagnosis and should be looked into once more common causes such as malignancy has been excluded [5]. A high index of suspicion will lead to an early diagnosis. The increased FDG uptake, which can be seen in these lesions (possibly due to the presence of osteoclast-like giant cells and macrophage glucose metabolism), may mimic skeletal metastasis on F18-FDG PET-CT [1,2].

A young male with multiple brown tumors is a rare presentation of the disease since there is female preponderance and incidence of disease being higher in 5th-6th decades of life. Also, the long bones of extremities are an uncommon site of presentation [3,7]. In the case of hypercalcemia and radiographic evidence of multiple lytic lesion, primary hyperparathyroidism should always be kept in differential diagnosis and should be looked into more common causes especially when malignancy has been excluded. A high index of suspicion will lead to an early diagnosis [7].

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jecr.2019.100054.

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