Pre-operative Tc-99m Sestamibi Parathyroid Scan and Bone Scintigraphy in a Case of Synchronous Parathyroid Carcinoma and Papillary Microcarcinoma

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ABSTRACT

Background:

Parathyroid carcinoma is an uncommon, aggressive, endocrine malignant neoplasm and subsequent parathyroidectomy of such cases may lead to the life-threatening hypocalcemic condition called Hungry Bone Syndrome. We present a very rare case of parathyroid carcinoma with concomitant thyroid microcarcinoma with Hungry Bone Syndrome as its sequalae.

Case Presentation:

A 54/F initially presenting with hypogastric pain was showed to have nephrolithiasis. Subsequent Endocrinology referral revealed hypercalcemia and osteoporosis – and with a working impression of hypercalcemia secondary to a parathyroid adenoma. Sestamibi parathyroid scan showed persistently avid uptake in the left thyroid lobe highly suspicious for a parathyroid adenoma, but a concomitant thyroid nodule was not ruled out. Bone scan showed intense and diffuse tracer uptake in the skull and irregular tracer activity in the ribs, suggestive of metabolic bone disease, with no evidence of metastatic-looking bone lesions. She underwent left thyroid lobectomy with isthmusectomy and Sestamibi-guided left parathyroidectomy. Histopathology report showed a parathyroid gland carcinoma with papillary thyroid microcarcinoma. Two weeks post-surgery, hypocalcemic signs developed and ionized calcium was low. Hungry Bone Syndrome was considered and was treated with calcium gluconate and Zoledronic acid.

Conclusion:

Nuclear imaging techniques and radioguided surgery are helpful in the diagnosis and management of both parathyroid and thyroid lesions – especially in difficult cases.

Keywords*: parathyroid carcinoma, thyroid microcarcinoma, Hungry Bone Syndrome*

INTRODUCTION

Parathyroid carcinoma is an aggressive endocrine malignant neoplasm that was first described by De Cuervain in 1904. It has a prevalence of 0.005% of all cancers and accounts for 0.46% of primary hyperthyroidism cases. There is no gender dominance, and the mean age of onset is 45 to 59 years old [1]. There is no reported predominance in terms of race, income level, or geographic region [2].

Hungry Bone Syndrome is a sequela of parathyroidectomy described as severe, prolonged, and sometimes life-threatening hypocalcemia. It has an incidence of 12% among post parathyroidectomy patients [3].

While thyroid disorders are common in cases with primary hyperparathyroidism, a concomitant parathyroid carcinoma with thyroid carcinoma is extremely rare and only eight cases have been published thus far [4]. This study aims to describe a patient with parathyroid carcinoma with synchronous papillary thyroid microcarcinoma and subsequent Hungry Bone Syndrome post-parathyroidectomy, wherein multiple nuclear medicine procedures were essential in the diagnosis and management.

CASE STUDY

A 54-year-old woman initially presented with intermittent hypogastric pain in the past eight months prior to admission. It is important to note that no clinically palpable neck mass was noted. An executive check-up was done. Transvaginal ultrasound and abdominal CT scan revealed para-ovarian cysts. Hence, she was considered negative from a gynecology standpoint.

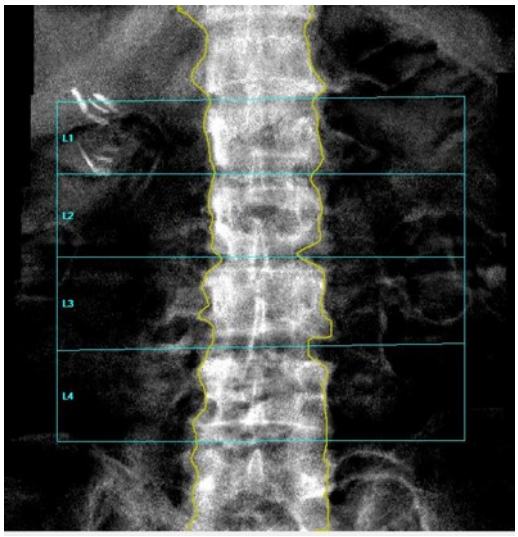
Kidney and urinary bladder ultrasound showed right nephrolithiasis. Referral to Endocrinology service revealed hypercalcemia (ionized calcium of 1.75 mmol/L, NV 1.09-1.30 mmol/L). PTH was elevated (3,124.00 pg/mL; NV 11.1—79.50 pg/mL) and bone densitometry revealed osteoporosis (T—score of spine is -4.0). The working impression was hypercalcemia secondary to a parathyroid adenoma.

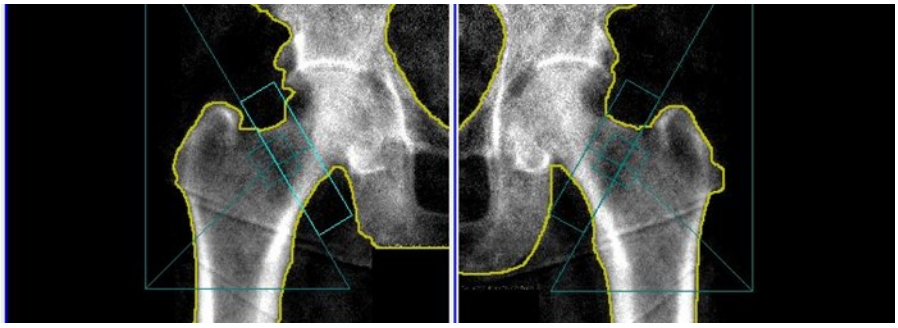
The patient was referred to otorhinolaryngology service for co-management. A Technetium-99m (Tc-99m) Sestamibi parathyroid scan as seen in Figure 2 showed persistent Sestamibi-avid uptake in the left thyroid lobe highly suspicious for a parathyroid adenoma. However, a concomitant thyroid nodule was not completely ruled out .

A subsequent neck computed tomography (CT) scan revealed a heterogeneous left parathyroid mass that indents to the left thyroid lobe and esophagus and partially extends to the mediastinum (C7-T1 level). A repeat ionized calcium at this point is still elevated (1.80 mmol/L).

A chest CT scan revealed an incidental finding of a nodular left breast. Digital mammography revealed nodular breasts with clustered microcalcifications with a BIRADS of 0. Bone scan in Figure 3, showed intense and diffuse tracer uptake in the skull and irregular tracer activity in the ribs, suggestive of metabolic bone disease. There was no evidence of metastatic-looking bone lesions .

The patient underwent Sestamibi-guided left thyroid lobectomy and isthmusectomy and left parathyroidectomy with frozen section, One (1) mCi of Tc-99m Sestamibi was intravenously injected one hour prior to the scheduled operation. Serum PTH before the surgery was 2,723.4 pg/mL, which dropped to 103.4 pg/mL immediately after the procedure. Ionized calcium two days after the procedure also dropped to 1.08 mmol/L .





Scan Site	Region	BMD	T-Score	Percentage
AP Spine	L1-L4	0.698 g/cm²	-4.0	59%
DualFemur	Neck Right	0.557 g/cm²	-3.5	54%
DualFemur	Neck Left	0.566 g/cm²	-3.4	55%

FIGURE 1. Bone densitometry of the spine and hips

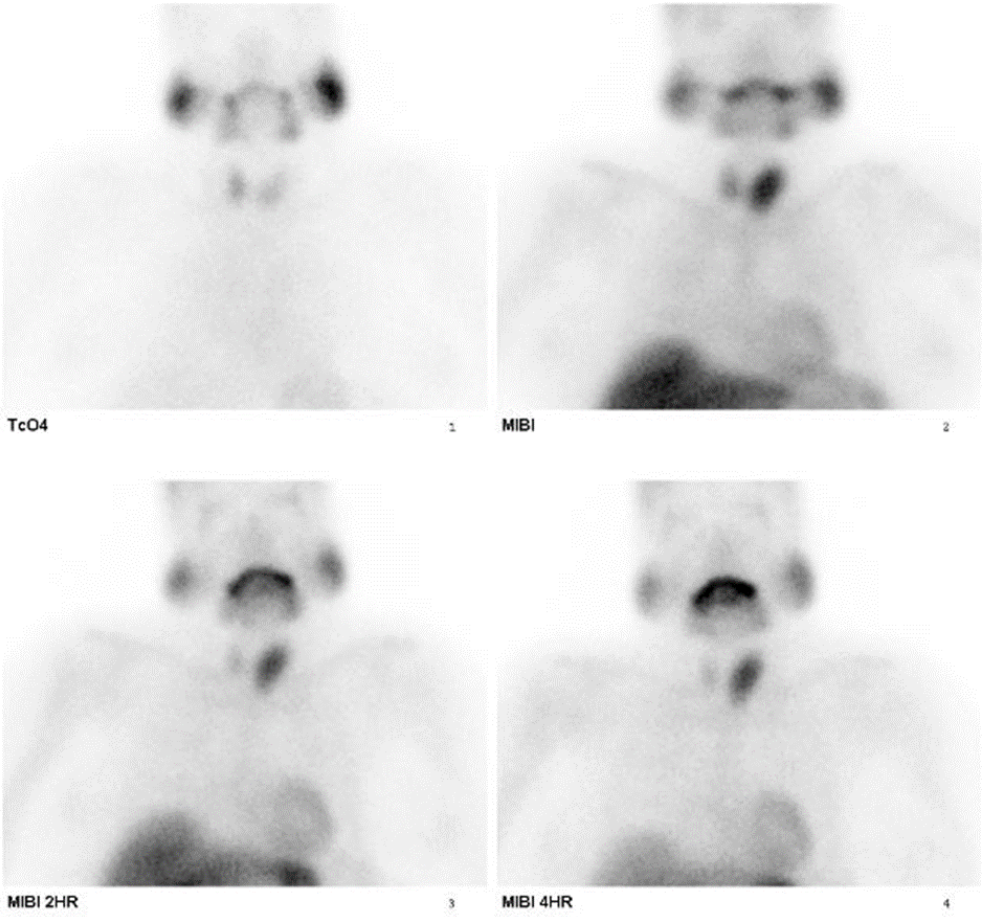


FIGURE 2. Tc-99m Sestamibi parathyroid scan. (A) Tc-99m pertechnetate image. (B) Tc-99m Sestamibi image. (C) and (D) Delayed 2-hour and 4-hour images, respectively

A surgical pathology report was released three days after the operation. It revealed a parathyroid carcinoma 15.2 cm) with penetration into the thyroid tissue. A papillary thyroid microcarcinoma (conventional type, single focus of 0.1 cm was also noted. The final diagnoses of the patient were parathyroid gland carcinoma (pT2N0M0) and papillary thyroid microcarcinoma (pT1aN0M0).

Two weeks post-surgery, the patient developed signs of hypocalcemia presenting with numbness of hands and feet. Ionized calcium currently was 0.87 mmol/L and the consideration was Hungry Bone Syndrome. Two cycles of calcium gluconate were infused and repeat ionized calcium after three days was 106 mmol/L. The patient was observed for two more days and subsequently discharged stable. She was advised to undergo Zoledronic acid infusion every three months.

DISCUSSION

The incidence of a double primary parathyroid carcinoma with papillary thyroid microcarcinoma is extremely rare [5]. Additionally, parathyroid carcinoma as a cause of primary hyperparathyroidism is also nfrequent as it only accounts for 1% of cases [6]. Ninety percent (90%) of parathyroid carcinomas are hormonally functional and exhibit profound hypercalcemia at presentation [4,6]. Nephrolithiasis is a common renal complication [6], while osteopenia/osteoporosis and bone fractures are the usual skeletal manifestations [5,7]. Common digestive symptoms include abdominal pains and nausea [6]. All of these were present in our patient.

Albeit no neck mass was palpated in our patient, parathyroid carcinomas usually present with a neck mass in 40-70% of cases. Lymph node metastasis occurs in 15—30% of patients and around one-third have distant metastases to the lungs, liver, and bone [6,8]. In our patient, a chest CT scan had almost unremarkable findings other than the incidental nodular left breast. Bone scintigraphy showed metabolic bone disease with no metastatic-looking disease.

Resection of distant metastases has been proven to

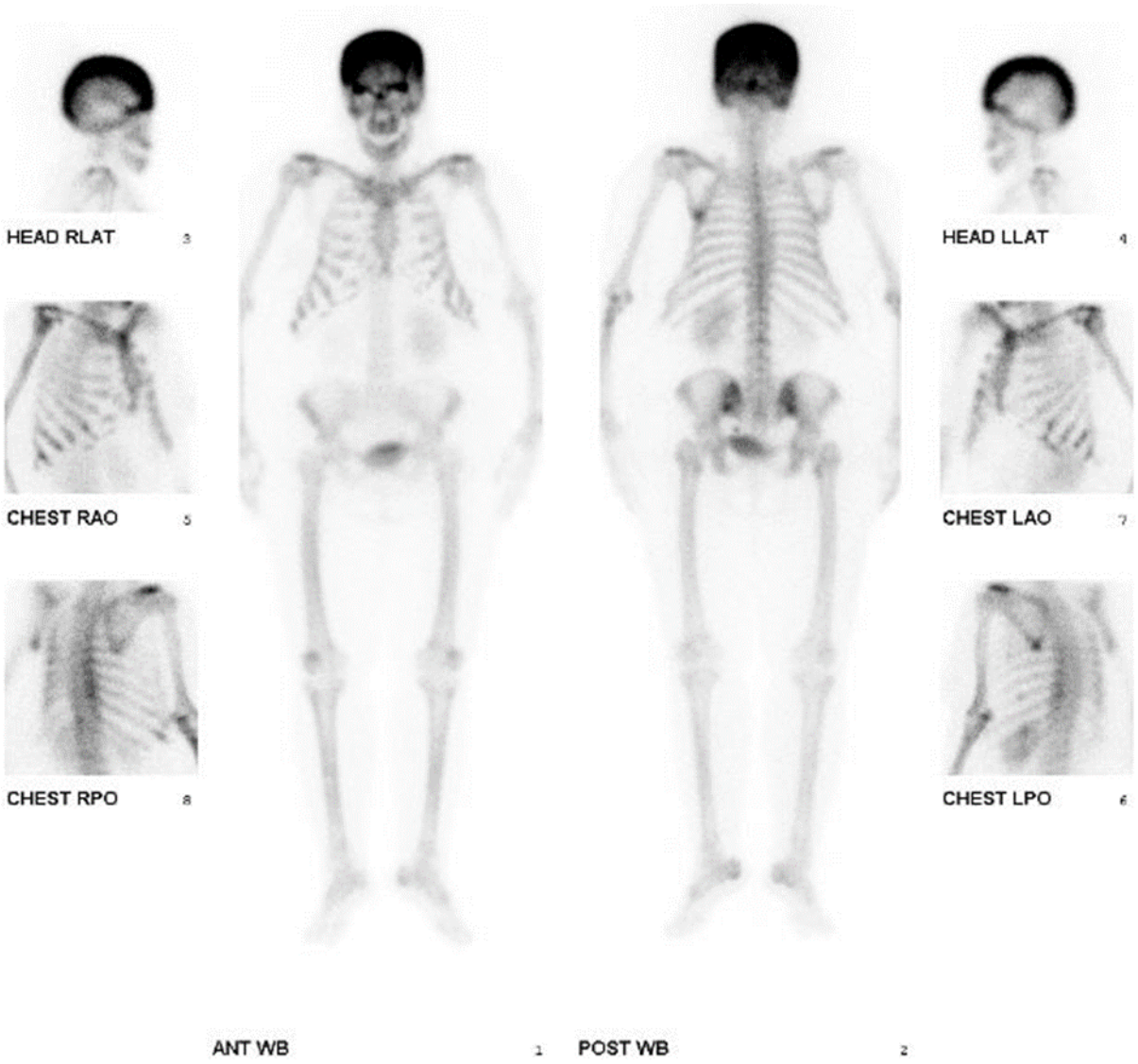


FIGURE 3. Tc-99m MDP bone scintigraphy of the patient

improve patient survival because mortality in these cases is linked mainly to severe hypercalcemia. As the common metastatic sites of parathyroid carcinoma involve the lung, liver, and bone, operations may include pulmonary resection, hepatectomy, or bone resections. Even incomplete resections can lead to periods of normocalcemia that can last years and allow easier control of hypercalcemia [8]. In our patient, there were no metastatic-looking osseous lesions. The irregular tracer activity seen in the skull and ribs are characteristic bone scintigraphy findings of any hypercalcemia syndromes [5,9].

Parathyroid carcinoma usually presents as the main clinical problem rather than the thyroid disorder [2] and serum PTH is commonly 3 to 10 times elevated [6]. This was the case in our patient.

The diagnostic sensitivity and disease localization accuracy are increased when a combination of neck CT scan/ultrasound and Tc-99m Sestamibi scan is used as an initial approach prior to surgery [6, 10] - although they are not generally useful to assess malignancy potential. While the sensitivity is almost the same for all modalities, the combined specificity of neck ultrasound and Tc-99m Sestamibi is higher (77.78%) compared to neck ultrasound (38.9%) or Tc-99m Sestamibi with pinhole (72.2%) or SPECT-CT (66.7%) alone [11]. Parathyroid carcinomas in neck CT scan/ultrasound are more likely to be heterogeneous and lobulated compared to parathyroid adenoma [12]. This was true for our patient.

Tc-99m Sestamibi scan for parathyroid adenoma is essential as a preoperative localization tool. Its accuracy in identifying parathyroid lesions is 95.8% using planar images and 98.8% using SPECT-CT images [13]. It also has a relatively high sensitivity to locate ectopic parathyroid

glands compared to other imaging modalities. It has an overall sensitivity of 29% for ectopic glands with 89% sensitivity for mediastinal parathyroid lesion [14]. While no ectopic parathyroid gland was seen in the Sestamibi scan, it was able to localize the parathyroid lesion to the left thyroidal bed only.

A previous study has demonstrated synchronous parathyroid carcinoma and thyroid carcinoma using Tc-99m Sestamibi scan as two lesions were seen in their scan: in the region of the left thyroid lobe and in the left lower cervical region lateral to the thyroid [15]. This was not seen in our patient with only a persistent tracer uptake seen in the left thyroid lobe. This could be due to the small thyroid lesion (0.1 cm) which is too small for gamma camera resolution, or the tracer uptake in the parathyroid mass is too intense that the thyroid lesion could not be appreciated.

Parathyroidectomy with bilateral neck exploration has long been the standard cure for parathyroid adenomas. But this has been largely replaced by localization radio-guided parathyroidectomy [15]. Radio-guided surgery (RGS) using an intraoperative gamma probe has been influencing the management and surgical technique of different malignancies including breast cancer, melanoma, gastrointestinal cancers, and head and neck cancers among others. It was first described by Harris in 1956 and minimally invasive parathyroidectomy is synonymous with radio-guided parathyroidectomy. Multiple protocols have been described in radio-guided parathyroidectomy [16] and no standard has been established. A previous study, using Tc-99m Sestamibi, concluded that any excised tissue showing more than 20% more than the background can be assessed as a parathyroid adenoma [17]. It has been shown to be accurate in 98% of adults and 100% of children with proven parathyroid adenoma. Radio-guided parathyroidectomy is also associated with a reduction in operative time, length of hospital stays, and total hospital and operative costs [18]. The prognosis is similar for both bilateral neck exploration and radio-guided parathyroidectomy [5]. In our patient, Sestamibi-labelled parathyroid was essential in reducing operative morbidity since it was shown in the CT scan that the parathyroid mass extends to the mediastinum. It is important to note that no mediastinoscopy nor mediastinostomy was done during the operation.

Since a papillary thyroid microcarcinoma was incidentally noted in the surgical pathology of the left thyroid, a question as to recommend completion thyroidectomy arises. Locoregional recurrence and risk of death were not statistically significant between patients who only had a thyroid lobectomy as compared to total thyroidectomy in patients with papillary thyroid microcarcinoma [19]. Doing thyroid lobectomy compared to a total thyroidectomy also preserves thyroid function. hence thyroid hormone replacement is not needed. Our patient did not undergo completion thyroidectomy.

Hungry bone syndrome is related to a sudden decrease in PTH release and attenuation of its effect on bone's contribution to serum calcium concentrations. Features predictive of the development of such disease include high serum calcium, elevated serum alkaline phosphatase, size of parathyroid adenoma/carcinoma, mean PTH of 95.8 +/- 16.8 pg/mL and patient mean age of 61.0 +/- 2.9 or older [20]. Our patient had three of the five features. No alkaline phosphatase was done. Bisphosphonates inhibit osteoclast-mediated bone resorption and prevent hungry bone syndrome [20], hence zoledronic acid infusion was advised to our patient.

Parathyroid carcinoma pathogenesis is unknown, and it may occur sporadically or as part of a genetic syndrome. These syndromes include hyperparathyroidism — jaw tumor syndrome (HPT—JT), MEN1, MEN2A, and isolated familial hyperparathyroidism. It usually arises in patients with secondary/tertiary hyperparathyroidism from chronic renal failure [5]. Meanwhile, papillary thyroid carcinoma has been associated with BRAF gene mutation, among others [21]. Other than neck radiation exposure, no common pathogenesis has been implicated in having synchronous parathyroid carcinoma and thyroid carcinoma.

In conclusion, as demonstrated by our case, nuclear imaging techniques such as Tc 99m Sestamibi, Tc-99m MDP bone scintigraphy, and bone densitometry may help in the diagnosis of a parathyroid lesion, The thyroid lesion was not detected in the parathyroid scan most likely due to its small size or intense tracer uptake in the parathyroid mass. Radio-guided parathyroidectomy is beneficial in the localization of the parathyroid lesion, especially in difficult cases.

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