

# Multiple Brown Tumors in Primary Hyperparathyroidism Caused by an Adenoma Mimicking Metastatic Bone Disease with False Positive Results on Computed Tomography and Tc-99m Sestamibi Imaging: MR Findings

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**Abstract.** We encountered an unusual case of hyperparathyroidism with both hemosiderin deposits on the ribs and low intensity on T2-weighted magnetic resonance imaging (MRI) caused by a parathyroid adenoma with multiple brown tumors that mimicked metastatic bone tumor due to false positive results on computed tomography (CT) and Tc-99m sestamibi (MIBI) imaging. The patient, a middle-aged woman, had very high serum levels of calcium (14.1 mg/dl), alkaline phosphatase (9,369 IU/l) and intact-PTH (12,400 pg/ml), and a large tumor (2.5 cm in diameter) in the lower portion of the left lobe of the thyroid. Plain X-ray revealed a soft tumor in the left chest wall. On CT scan, there were multiple destructive masses in the ribs, including large intramedullary masses on both 3rd ribs. On MIBI scintigraphy, there was strong late uptake in the lower portion of the left cervical region, both 3rd ribs, and the left 7th, 8th, and 10th ribs. T2-weighted image MRI scans showed that both 3rd ribs had a low intensity with hemosiderin deposits. These findings suggested that the patient had hyperparathyroidism with multiple bone metastases due to carcinoma of the parathyroid gland. However, on pathology, the resected tumor of lower portion of the left lobe of thyroid was diagnosed as a parathyroid adenoma, and the tumors of the left 3rd and 7th ribs, as well as the right 2nd rib, were shown to be brown tumors. After resection, the patient's serum levels of calcium, alkaline phosphatase, and intact-PTH normalized. At 1.5-years follow-up, CT, MIBI, and MRI scans showed no abnormal findings. It is necessary to determine whether MRI can be used to distinguish between brown tumors and metastases caused by carcinoma of the parathyroid gland.

**Key words:** Brown tumor, Hyperparathyroidism, Carcinoma, CT, MIBI, MRI

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**THE** most common cause of primary hyperparathyroidism is a solitary adenoma, followed by hyperplasia

and carcinoma [1]. Conventional techniques for detecting the location of abnormal parathyroid glands are associated with many difficulties and often yield false negative and false positive results.

Recently, Tc-99m hexakis methoxyisobutylisonitrile (MIBI) imaging was established as the best and most convenient localization method for detecting adenoma [1], after having been first reported by Coakley *et al.*

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[2]. Currently, it has also been demonstrated that MIBI scanning is able to localize metastatic parathyroid carcinoma [3], as well as the primary lesion [4].

We describe an unusual case of hyperparathyroidism and brown tumor due to parathyroid adenoma that mimicked metastatic bone tumor due to false positive results on CT and MIBI scans, but in which the T2-weighted image (WI) from MRI showed the rib with low intensity and with hemosiderin deposits, which result in the characteristic brown seen in these tumors [5].

### Case Report and Methods

A 55-year-old woman was found to have high concentration (9,369 IU/l) of hyperalkaline-phosphatase (ALP) while being investigated for lumbago and joint pains after hysterectomy for a uterine myoma. She was found to have hypercalcemia, hypophosphorusemia, and a markedly high level of serum intact PTH (12,400 pg/ml). She had no history of parathyroid disease or other diseases.

The patient was 152 cm tall and weighed 51.5 kg. Her blood pressure and pulse rate were normal. There was no sign of edema, dehydration, or pigmentation. She was fully conscious. She had not previously received any therapy for the hypercalcemia or the hypophosphorusemia.

Laboratory findings showed hypercalcemia, hypophosphorusemia, and hyperalkaline-phosphatasemia with polyuria (Table 2). Serum corrected Ca concentration, serum intact PTH concentration, and urinary excretion of Ca were high, while serum concentrations of PTH-rP and calcitonin were within the normal range (Table 2). There was no other laboratory evidence to suggest multiple endocrine neoplasms. On plain chest X-ray, a soft tumor was seen in the left chest wall. Whole body skeletal X-rays showed osteolytic shadows in the cranium, ribs, diaphyses, and lumbar vertebrae, and cystic shadows in the ilia and femoral necks.

Neck ultrasound showed a highly echogenic tumor (2.5 cm in diameter) with a cystic mass in the lower portion of the left lobe of the thyroid. Abdominal ultrasound showed multiple radiolucent stones in both kidneys. On computed tomography (CT) scan, a 3 cm diameter mass with a cyst was located in the lower portion of left lobe of the thyroid; its margin was regular and its border was clear. In addition, multiple destruc-

**Table 1.** Admission laboratory data\*

Blood chemistry	
GOT	18 IU/l
GPT	12 IU/l
LDH	139 IU/l
$\gamma$ GTP	30 IU/l
Total bilirubin	0.9 IU/l
Na	138 mEq/l
Cl	108 mEq/l
K	4.1 mEq/l
BUN	11.1 mg/dl
Cr	0.5 mg/dl
Uric acid	5.8 mg/dl
Total protein	7.7 g/dl
Albumin	4.7 g/dl
T-Cholesterol	266 mg/dl
TG	440 mg/dl
HDL	52 mg/dl
Glucose	130 mg/dl
CRP	0.2 mg/dl
Hematological data	
RBC	$468 \times 10^4/\text{mm}^3$
Hb	13.7 g/dl
Hct	42.3%
WBC	$5000/\text{mm}^3$
Baso	1%
Seg	41%
Lympho	50%
Mono	8%
PT	$14.7 \times 10^4/\text{mm}$
APTT	32.5 second
Urinary data	
Glucose	negative
Protein	negative
Urobilinogen	$\pm$
Ketones	negative
Sediment	
Red cells	30–40/HPF
White cells	10–19/HPF

\* All data were obtained 1 hour after breakfast.

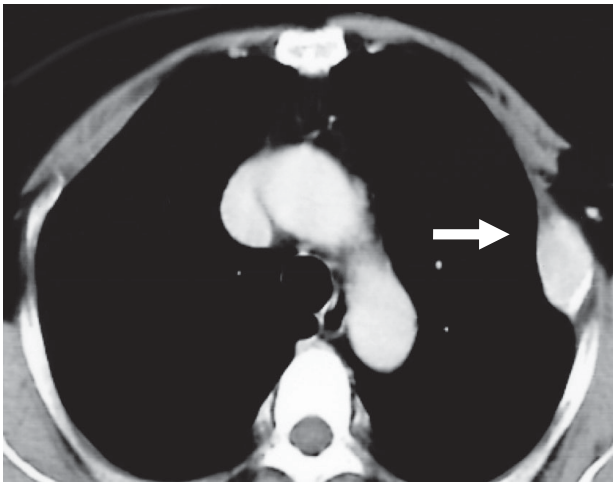
tive masses were seen in many ribs, including a large intramedullary mass in both 3rd ribs, particularly in the left 3rd rib (Fig. 1) and in both femoral necks; multiple stones were noted in the right kidney. Whole body MIBI scans taken after 2 hours revealed strong late uptake in the left lower portions of the cervical region, both 3rd ribs, and the left 7th, 8th, and 10th ribs (Fig. 2A). On MRI, coronal T1WI scanning showed that the left parathyroid lesion had a slightly high intensity. Coronal T2WI and post-contrast T1WI showed that the lesion had a homogenous high intensity portion and a slightly enhanced portion with a low intensity

**Table 2.** Laboratory data related to hypercalcemia and hypophosphorusemia before and after resection of the tumor in the lower portion of the left parathyroid gland\*

		Before resection	After resection	Normal range
Blood				
Ca	mg/dl	13.9	9.3	
Corrected Ca <sup>#</sup>	mg/dl	13.2	9.4	8.5~10.3
P	mg/dl	2.3	2.3	2.5~4.5
ALP	IU/l	8869	3523	105~340
ALP3	%	100		31~71
Intact PTH (10~65)	pg/ml	12400	<2.0	10~65
PTH-rP	pmol/l	<1.1		<1.1
Calcitonin (21.6~54.0)	pg/ml	44.1		21.6~54.0
Urine				
Volume	ml/day	3200	1600	<3000
Ca	mg/dl (mg/day)	12.2 (390)	17.4 (278)	(100~200)
P	mg/dl (mg/day)	19.9 (637)	0.1 (1.6)	(359~1650)
24 hour creatinine clearance	ml/min	108		75~110

\* All data were obtained on admission and 3 months after resection of the parathyroid tumor.

<sup>#</sup> The value was obtained by Payne's method.

**Fig. 1.** CT shows destructive masses in both 3rd ribs, particularly in the left 3rd rib (indicated by arrow).

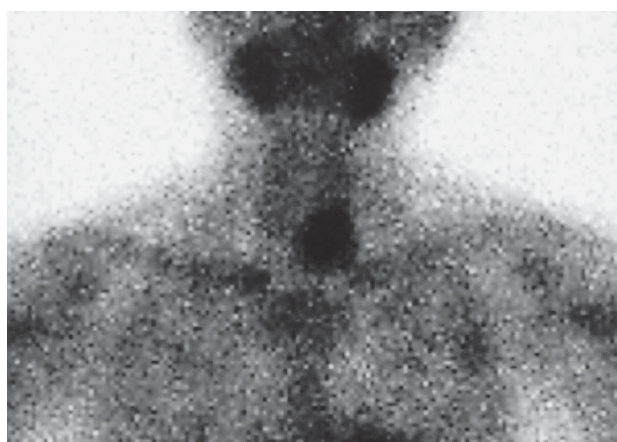
part in the center of the parathyroid gland. In addition, T2 WI showed that both 3rd ribs had low intensity with hemosiderin deposits, particularly in the left 3rd rib (Fig. 3).

These findings suggested that the patient had primary hyperparathyroidism with multiple metastases secondary to carcinoma of the parathyroid gland. The lower portion of the left lobe of the thyroid including the parathyroid glands was subsequently resected. We decided to examine the swollen lesions to determine whether the bone lesions were indeed suspected me-

tastases. Therefore, the left 3rd and 7th ribs and right 2nd rib were also resected because they were swollen macroscopically. The right 3rd rib, though suspicious on MIBI scan, was not resected because it was not swollen macroscopically. On frozen section, the tumor mass of the left lower lobe of the thyroid was diagnosed as being an adenocarcinoma that showed a relatively high proportion of cells in cycle and nuclear features including prominent nucleoli with suspicious invasion, and the tumors in left 3rd and 7th ribs and the right 2nd rib were diagnosed as brown tumors (Fig. 4).

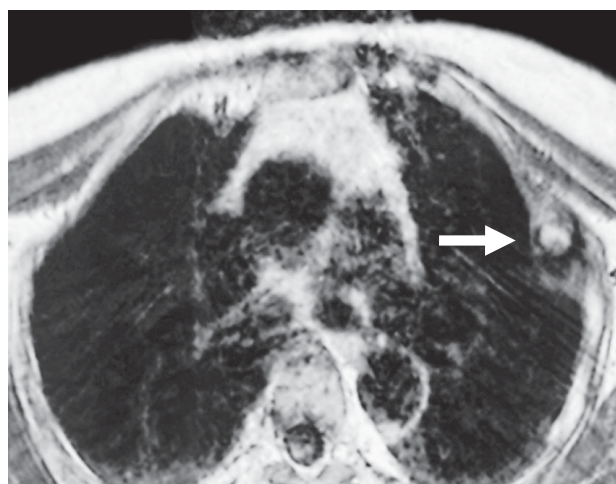
Later, the parathyroid tumor was reviewed by our colleague Dr. Dillwyn Williams. As shown in Fig. 5, the histological findings suggested that the tumor, although it was composed of giant cells, was a parathyroid adenoma rather than an adenocarcinoma.

Immediately after the resections, catecholamine was transiently infused as blood pressure decreased. On the first day after the operation, calcium and alfacalcidol were administered because of developing hypocalcemia and continued for 5 months. Two months after resection, the patient's hypercalcemia, hypophosphorusemia, and polyuria normalized, and the high level of ALP decreased (Table 2). The intact PTH level also decreased (Table 2). Whole body CT and MRI scans showed no tumor mass in the lower portion of the left lobe of the thyroid and no masses in the ribs, including the left 3rd and 7th ribs and right 2nd rib which were

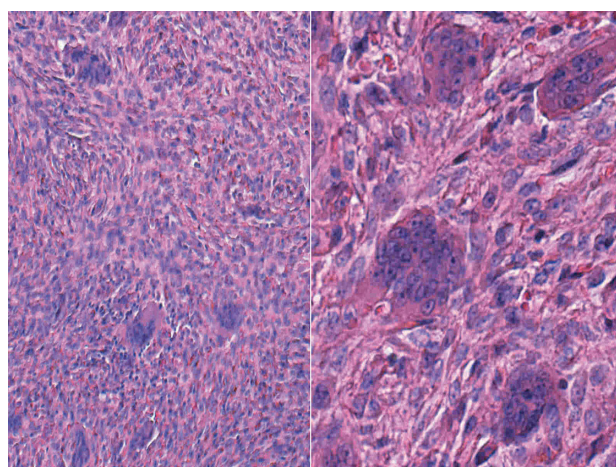
**A****B**

**Fig. 2.** On MIBI scan before resection of the parathyroid tumor, there was strong uptake in the left lower portion of the cervical region, both 3rd ribs and the left 7th, 8th, and 10th ribs (2A). These shadows disappeared two months after resection, although the MIBI was uptaken into the thyroid gland (2B).

resected, and the femoral necks, in contrast to the pre-operative findings. Repeat MIBI scanning showed no uptake in the left lower portion of the cervical region and in the ribs where there had been increased uptake prior to resection (Fig. 2B). Five months later, the renal staghorn stones were destroyed by electrohydraulic shock wave lithotripsy. On follow-up 1.5 years after resection, serum levels of corrected calcium (9.0 mg/dl), phosphate (3.6 mg/dl), ALP (393 IU/l) and intact PTH (61 pg/ml) were all within the normal range. CT, MIBI, and MRI scans showed no abnormal findings.



**Fig. 3.** T2-weighted image of MRI scanning before resection of the parathyroid tumor showed that both 3rd ribs, especially the left 3rd rib (indicated by arrow) shadows had a low intensity with hemosiderin deposits.

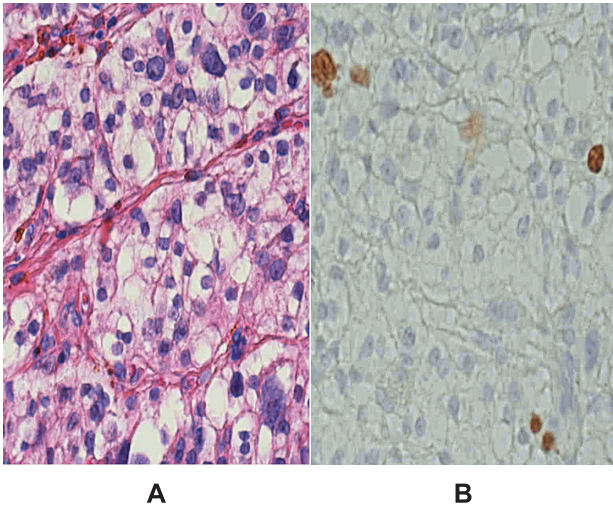
**A****B**

**Fig. 4.** Histological findings of the tumor in left 3rd rib. The tumor is numerous multinucleated giant cells and spindle- or oval-shaped stromal cells with tiny hemorrhagic foci (4A;  $\times 100$  and 4B;  $\times 200$ , hematoxylin eosin stain), which are characteristic findings of the brown tumor of hyperparathyroidism.

## Discussion

It is clear that this patient's hypercalcemia was caused by primary hyperparathyroidism. Initially, CT and MIBI of multiple destructive masses in the ribs suggested that the bone lesions were brown tumors or metastases from a malignant parathyroid. However,





**Fig. 5.** Histological findings of the tumor in the left inferior parathyroid gland. The tumor is composed mostly of sheets of cells with foamy cytoplasm and regularly shaped nuclei. Cords of chief cells also are seen (5A;  $\times 200$ , hematoxylin eosin stain); there is little fibrous stroma (5B;  $\times 200$ , double staining using the avidin-biotin-peroxidase complex method using anti-Ki-67 antibody and hematoxylin). There was no convincing evidence of invasion.

the very high levels of Ca and intact PTH in the serum, and the palpable and large neck tumor indicated that the patient might have primary hyperparathyroidism and multiple bone metastases caused by carcinoma of the parathyroid gland rather than a benign tumor, although there were no findings of enlarged lymph nodes or invasion [3, 6]. In fact, on frozen section the tumor mass of the left lower lobe of the thyroid was diagnosed as adenocarcinoma.

However, after review, the parathyroid tumor was diagnosed as a parathyroid adenoma rather than carcinoma. The tumors in the left 3rd and 7th ribs, and the right 2nd rib were diagnosed as brown tumors. At one and a half years after tumor resection, there has been no recurrence of either the hyperparathyroidism or the metastases. These findings indicate that this patient did not have carcinoma of the parathyroid gland.

The findings suggest that the laboratory data and the

CT and MIBI scans were not able to distinguish between benign and malignant parathyroid gland tumors. In fact, since 1994, when Joyce *et al.* first reported that multiple brown tumors in primary hyperparathyroidism due to adenoma can mimic metastatic disease on MIBI scan [7], there have been many similar reports [8–10]. Thus, even in the presence of very high levels of Ca and intact PTH in the serum, urolithiasis and bone abnormalities with multiple destructive masses in the ribs on CT and MIBI and a palpable neck tumor, the presence of brown tumors should be considered as the differential diagnosis of metastasis of malignant parathyroid.

Interestingly, in this case, T2 WI image showed that both third ribs had a low intensity with hemosiderin deposits. There is limited discussion of this MRI finding with brown tumors in the literature. Erem *et al.* [11] and Takeshita *et al.* [12] reported a brown bone tumor that on MRI was seen as an expansive mass lesion with heterogeneous hyperintensity on T2-WI in the sphenoid sinus, but without hemosiderin deposits. Accordingly, the present report is most likely the first to document MRI findings in the ribs. Brown tumors contain osteoclasts and mononuclear cells and fibroblasts with focal hemorrhage, and the hemosiderin from the hemorrhage produces the grossly brown color [5]. Therefore, further study is required to determine whether MRI can be used to distinguish between brown tumors and metastases caused by carcinoma of the parathyroid gland in ribs, particularly MRI that shows low intensity with hemosiderin deposits on the ribs.

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