

# Parathyromatosis or Recurrent Multiple Parathyroid Adenomas? A Case Report

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## ABSTRACT

*We present a case of recurrent parathyromatosis and hyperparathyroidism installed 14 years after parathyroidectomy that we attribute to spillage of tumor cells during previous parathyroidectomy. Due to lack of knowledge about the imaging characteristic of this entity, we aim to describe the imaging appearance of parathyromatosis and emphasize on the diagnostic utility of ultrasonography in preoperative localization and successful surgical resection of parathyromatosis.*

## INTRODUCTION

**P**arathyromatosis is a multiple hyperfunctioning parathyroid tissue in the neck (1). In rare conditions it can cause hyperparathyroidism (1). It becomes hyperfunctioning after subtotal or total parathyroidectomy due to primary or secondary hyperparathyroidism (pHPT and sHPT). Palmer et al reported the first case of parathyromatosis (2), and were followed by the report of other 32 cases (1, 3-5). The treatment of parathyromatosis remains a challenging issue due to the difficulty in differentiating this entity from other neck pathologies and the fact that re-exploration of the neck after primary surgery is challenging for most experienced surgeons (5).

## CASE REPORT

**A**-64 -years-old woman was referred by her primary physician to our hospital due to recurrent hypercalcemia with duration of one year. She had history of subtotal parathyroidectomy due to two parathyroid adenomas (right and left inferior PTCs) fourteen years ago. Her serum calcium was 11.2 mg/dl prior to surgery and dropped to 8.8 mg/dl after operation. Serum iPTH was 732 pg/ml before surgery and decreased to 51 pg/ml after surgery. At admission for surgery the only medical investigation performed was the Tc- 99m MIBI scan which revealed two focus of increased uptake in the lower pole of both thyroid lobe and was compatible with bilateral parathyroid adenoma.

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Past medical history was consistent with recurrent nephrolithiasis. She had no family history of hyperparathyroidism or any other medical problems. The patient was complaining of "in and off" symptoms of loss of appetite, vomiting, dyspepsia and bone pain for past one year. Laboratory evaluation showed hypercalcemia and marked osteoporosis evident on Dual Energy X-ray Absorptiometry (DXA) (lumbar spine: T score =  $-4.5 \pm 1.01$ , Z score =  $-4.4 \pm 2.04$  and hip: T score =  $-5.1 \pm 1.97$  and Z scores =  $-5.1 \pm 2.03$ , 1/3 distal of radius T score =  $-4.3 \pm 2.40$ , Z score =  $-4.4 \pm 2.44$ ).

On physical examination, she had a classic surgical scar of previous bilateral neck dissection with no palpable mass. The laboratory results showed elevated serum calcium (10.8 mg/dl) (corrected calcium for albumin was 11.04 mg/dL), low serum phosphate (2.5 mg/dl) and elevated serum intact parathyroid hormone (iPTH) (680 pg/ml with reference range of 10-60 pg/ml). Serum alkaline phosphatase was 287 U/l (normal range 40-130 U/l) and serum creatinine was 1.15 mg/dl. Urinary calcium was 81 mmol/24 hours (normal range: 25 to 75) and total 25-hydroxy vitamin D was 26 ng/ml.

Ultrasonography of neck was performed using Sonoline G40 Ultrasound (US) device (Siemens, Germany). On US examination there were two oval shaped homogenous hypo-echoic nodule measuring 3\*2 cm and 1\*1 cm in the right lower part of the neck adjacent to the posterior part of right thyroid lobe (Figure 1).

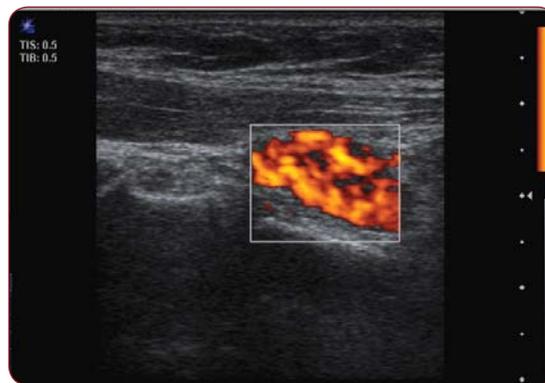
Color and Power Doppler study showed marked hypervascularization of both nodules (Figure 2). Tc- 99m MIBI scan was performed and revealed a focus of increased uptake in the same region (Figure 3).

In the operation room, two soft solid tumors measuring 3\*2.5 cm and 1\*1 cm with no adhesion to the surrounding structure were removed. One of the nodules was removed from the deep soft tissue of the neck above sternoclavicular joint and inferoposterior to the lower pole of the right thyroid lobe and the other was removed from the soft tissue of the neck posterior to right thyroid lobe. Postoperative (24 hours) serum calcium and iPTH were 9.1 mg/dl and 82 pg/ml respectively.

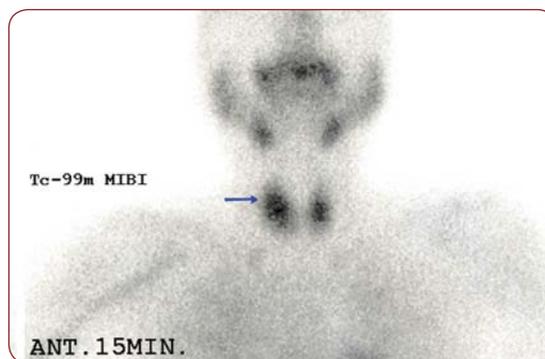
On anatomopathological examination there were two reddish brown encapsulated nodular lesions. Histopathology showed an adenomatous proliferation of type I parathyroid cells



**FIGURE 1.** Sagittal ultrasonogram of the lower neck region shows two hypoechoic nodules (arrows) adjacent to the right of thyroid lobe

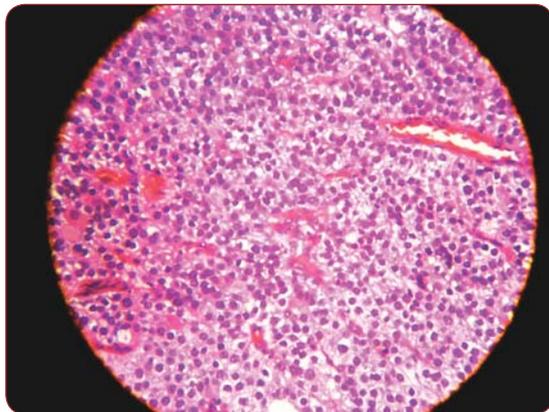


**FIGURE 2.** Power Doppler ultrasonogram shows a marked hypervascularization of parathyromatosis nodule as if Parathyroid is on fire



**FIGURE 3.** Tc-99m MIBI scan shows area of increase uptake in the region compatible with Ultrasonogram

with prominent vessel compatible with parathyroid adenoma (Figure 4). One month after surgery the labs were repeated, and they were within normal limit (serum calcium 8mg/dl, serum iPTH 45pg/ml). The patient refused to take any medication for improving osteoporosis (because of intolerance).



**FIGURE 4.** Histopathology (H&E Stain) shows; Hypercellular parathyroid tissue, which is mostly composed of chief cells and without atypical nuclear features

## DISCUSSION

Approximately 85% of patients with hyperparathyroidism have single benign adenoma and less than 1% patients have parathyroid carcinoma. Parathyroid adenomas can be ectopic or intrathyroidic (6). Parathyromatosis is an extremely rare cause of recurrent or persistent hyperparathyroidism after parathyroidectomy due to hyperparathyroidism (7). It usually presents as multiple small nodules in the neck region and infrequently as a palpable mass (8).

It's postulated to arise from three possible etiologies: A low-grade malignancy, seeding of parathyroid neoplasm during parathyroidectomy and overgrowth of embryologic foci of parathyroid tissue (main concept of sHPT) (7). It is yet to be proven that parathyromatosis is induced by Fine needle aspiration or sonography guided PTH sampling (9).

The spectrum of malignant parathyroid neoplasm according to the degree of invasiveness start with parathyromatosis followed by atypical parathyroid adenoma and parathyroid carcinoma. There are controversial reports saying that parathyromatosis could be or not a low-grade parathyroid carcinoma (5,7). Fernandez et al (7) reported that some markers (Rb-retinoblastoma expression, loss of parafibromin and overexpression of galectin-3) can be useful to distinguish parathyromatosis from parathyroid carcinoma.

Parathyroid carcinoma is more common in men unlike parathyromatosis, which is more common in women. Matsuoka et al. reported 10 cases of parathyromatosis (out of 1932 sHPT patients) during 30 years of experience. Preop-

erative diagnosis of parathyromatosis was obtained only in 4 patients (5).

Some believe that a supernumerary parathyroid gland that has been missed at the initial surgery could be mistaken with hyperplasia of a subtotally resected parathyroid gland or autograft transplanted parathyroid tissue (10).

Padberg et al. demonstrated that absence of RET proto-oncogene mutations in parathyromatosis is useful in excluding MEN syndrome (11).

Parathyromatosis most frequently occurs after parathyroidectomy and most surgeons are not in favor of performing second neck exploration. Accurate preoperative localization of parathyromatosis is critical for all surgeons prior to the second exploration.

We found parathyromatosis as an oval hypoechoic nodule with marked hyper-vascularization in color Doppler sonography similar to those in parathyroid adenoma. Gray scale sonography appearance of parathyromatosis can mimic other cervical malignancies. Color and Power Doppler sonography can aid in differentiation between parathyromatosis and other cervical malignancy. There was no vascular or muscle invasion in our case report similar to the case by Tublin et al (1).

In our case report, color Doppler sonography showed two nodules on the right side while MIBI scan only showed the larger nodule. According to our expertise, color Doppler sonography is superior to MIBI scan in preoperative localization of parathyroid adenoma since small nodules (<500 mg) may not be visible in scintigraphy.

Surgery is the treatment of choice in management of parathyromatosis. In all previously published series, it has been emphasized that complete eradication is very difficult (1) due to lack of knowledge about the distinct site of superficial and deep parathyromatosis nodules. Using preoperative color Doppler ultrasonography increases the chance of eradication of this entity and will decrease the risk of morbidity due to persistent hyperthyroidism.

Perez-Ruiz et al has demonstrated that by dissecting through the lateral wall (by electrocautery) and maintaining the blood supply (through small mediastinal and thymic vessels) of the neoplastic and placing the gland in the subcutaneous position (in the lowest part of the operative field just above the sternal border) it is possible to prevent parathyromatosis formation (12).

Hage et al. showed that in “most cases of parathyromatosis diagnosis was made intraoperative and the condition was often refractory to surgery”(13) thus revealing that calcimimetic with a bisphosphonate combining with medical management may be preferred alternative.

One of the limitations of our study is the lack of intraoperative measurement of iPTH by surgery. It is better to measure the intraoperative serum iPTH in order to confirm the presence of parathyroid adenoma and also to see the adequacy of surgical exploration.

Due to difficulties in removing parathyromatosis in second neck exploration, surgeons must be careful to prevent spillage of cells from resecting parathyroid adenomas.

In conclusion successful surgical eradication of challenging parathyromatosis depends on accurate preoperative diagnosis of parathyroid. The parathyromatosis foci have characteristic sonography appearance and by using color Doppler sonography and combining it with Tc 99m-MIBI scan, we will be able to successfully localize it.

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