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Case Report

Synchronous parathyroid carcinoma and papillary thyroid carcinoma: a case study and review of literature

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Abstract: Incidence of primary hyperparathyroidism due to parathyroid carcinoma along with non-medullary thyroid carcinoma is extremely rare. The authors present the unique case of a patient with a 4.3 × 3.1 × 2.5 cm parathyroid carcinoma on the left side, and a 5 mm papillary thyroid microcarcinoma on the right side. The patient was operated thrice because of persistent hyperparathyroidism. The literature relevant to this clinical condition, the diagnostic workup, surgical management, and pathological findings of these rare lesions is reviewed and discussed. When severe hypercalcemia is observed, hyperparathyroidism related to parathyroid carcinoma should be considered as a possible underlying cause. In such cases, an en-bloc resection of the parathyroid tumor and the adjacent thyroid lobe should be performed. In patients with hyperparathyroidism, thyroid imaging prior to neck exploration may be useful to identify any concomitant thyroid disease, including carcinoma.

Keywords: Hyperparathyroidism, parathyroid carcinoma, thyroid carcinoma

Introduction

Parathyroid carcinoma (PC) is a rare pathological condition, with fewer than 400 reported cases [1]. In 1904, the first case of PC was reported, in which the patient presented with a nonfunctioning lesion [2]. In 1933, the first functioning PC was described [3]. Diagnosis of PC is very difficult because the clinical manifestations of PC are similar to those of benign primary hyperparathyroidism (PHPT). Patients who eventually die of PC typically do so because of the devastating effects of excess parathyroid hormone (PTH) and hypercalcemia.

In 1974, the first case of concomitant thyroid and parathyroid disease was reported [4]. Thyroid pathology has been reported in 15-70% of patients with PHPT [5]. Non-medullary thyroid carcinoma has been reported in 1.7-6% of patients with PHPT [5, 6]. However, incidence of PHPT due to PC concomitantly with non-medullary thyroid carcinoma is extremely rare. Approximately, 11 such cases have been reported worldwide [1, 6-15].

Case report

The study was approved by the ethical committee of Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, Zhejiang Province, China. Written informed consent was obtained from the patient.

A 45-year-old woman was referred to the general surgery clinic with symptoms of nausea, vomiting, and polyuria for 2 weeks. The bone densitometry examinations were normal. Ultrasonography of the neck revealed a 4.3 × 3.1 × 2.5 cm sized cystic and solid mass at the left lower thyroid pole. The mass had well-defined border with hypervascularity in the solid part (**Figure 1A** and **1B**). On the other side, a 5 mm hypoechoic solid inferior lobe nodule was noted. The node had well-defined border with no calcifications (**Figure 1C**). No suspicious cervical lymph nodes were identified. Technetium-99 m-methoxyisobutylisonitrile (MIBI) cervical and whole body substraction scintigraphy scans revealed increased uptake of the left

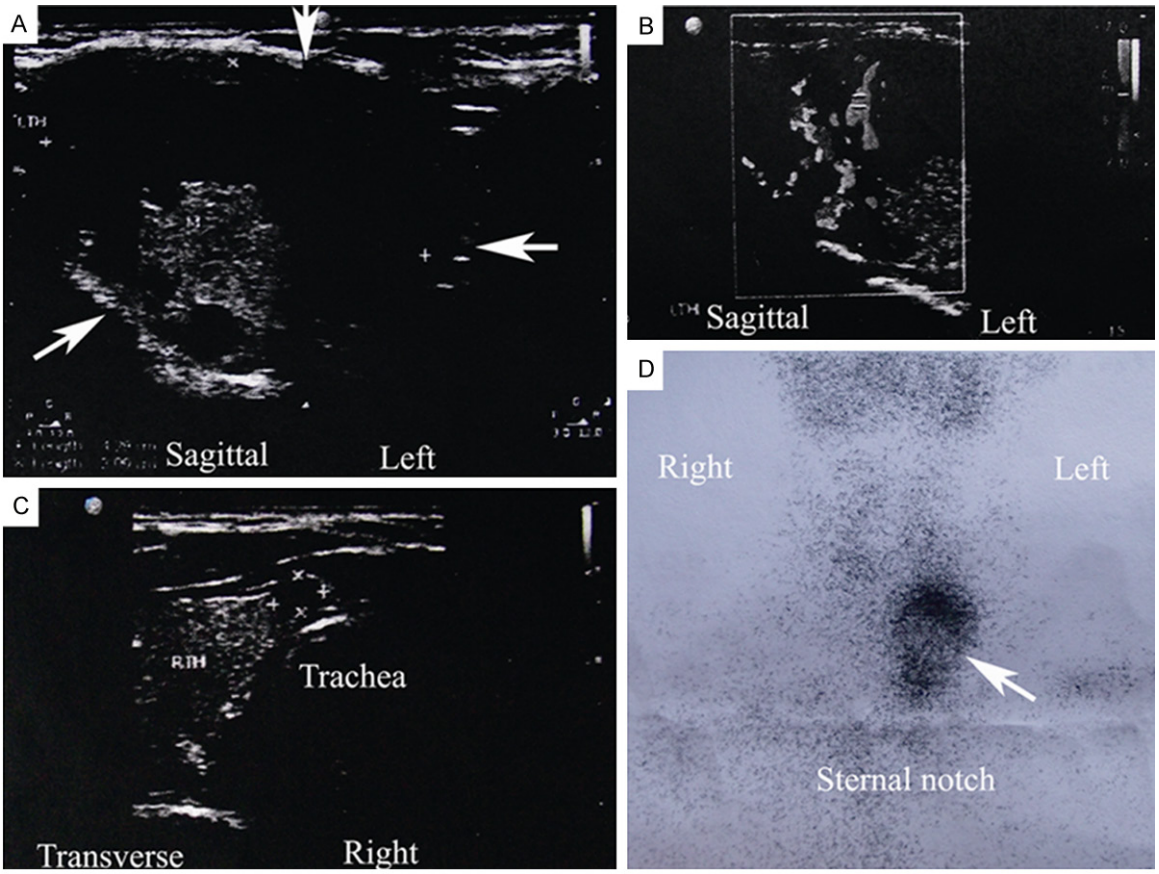

Figure 1. A and B. Ultrasonography of the neck showing a 4.3 × 3.1 × 2.5 cm cystic and solid mass at the left lower thyroid pole (white arrows; sagittal view) (B. Color Doppler US on square box). The mass had well-defined border with hypervascularity in the solid part. C. Ultrasonography demonstrating a 5 mm hypoechoic solid inferior lobe nodule (transverse view). The node had well-defined border with no calcifications. D. Technetium-99 m-methoxyisobutyl-isonitrile (MIBI) scintigraphy shows uptake (white arrow) of the left inferior lobe, consistent with a large functioning tumor originating from the left inferior parathyroid gland.

inferior lobe (**Figure 1D**). The MRI examination of the neck revealed a mass in the lower pole of the left thyroid lobe with hyperintensity in T2-weighted imaging (WI), and the same signal intensity with thyroid tissue in T1-WI (**Figure 2**). Blood, urine tests, and calcitonin levels were normal, making multiple endocrine neoplasia type 2 very unlikely. The patient had no recurrent nerve palsy. She had no familial history of thyroid cancer or multiple endocrine neoplasia of type 1 or type 2. She was immediately administered with intravenous infusion of fluids, primarily physiological saline, furosemide, and calcitonin, which resulted in the decrease of calcemia and improved general condition.

During the left parathyroidectomy, and right partial thyroidectomy, an approximately 4-cm wide cystic and solid tumor was identified behind the left thyroid lobe. The left thyroid lobe was markedly atrophied owing to the depression of the tumor. After surgery, the patient's condition significantly improved, and she became normocalcemic. Histopathological examination revealed a left inferior PC with extracapsular spread (**Figure 3**), and associated with papillary thyroid microcarcinoma (mPTC) in the right thyroid lobe (**Figure 4**). Complete thyroidectomy with left neck dissection was offered, but the patient opted for observation in conjunction with serial ultrasonography and PTH level monitoring.

One year ago, the patient was referred to our hospital with PTH levels of 523.7 pg/mL and calcium levels of 13.92 mg/dL. Ultrasonography of the neck revealed multiple vascularized hypoechoic nodules (**Figure 5**). The patient was

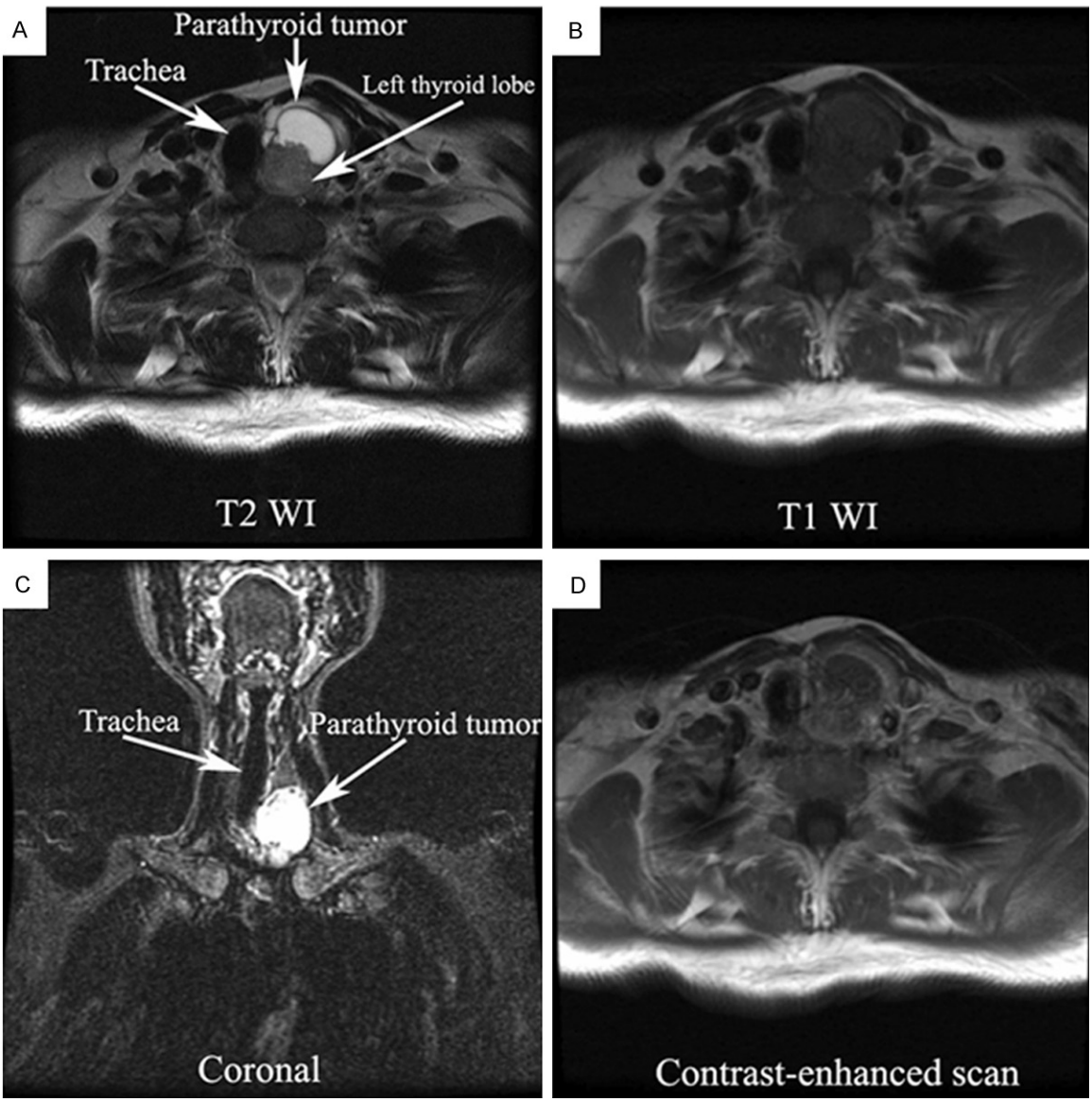

Figure 2. MRI examination of the neck showing a 4.2 × 3.0 × 2.2 cm-sized mass in the lower pole of the left thyroid lobe with hyperintense in T2 WI (A, C) and the same signal intensity with thyroid tissue in T1 WI (B). The mass had well-defined border and had enhancement in the contrast-enhanced scan (D).

cheduled to undergo total thyroidectomy in addition to left central and lateral neck dissection. During surgery, tumors in the lower pole of the left thyroid, in the suprasternal fossa, and in the supraclavicular fossa were identified. All these tumors were tightly adhering to the surrounding structures. The recurrent laryngeal nerve was identified, but was ultimately sacrificed because it was completely encased by the tumor. In order to avoid bilateral recurrent laryngeal nerve injury, total right lobectomy was not performed. Histopathological examination confirmed the neck multilocular metastatic parathyroid carcinoma (the nodules described in the ultrasound were all related to PC). Following surgery, the patient became normocalcemic with PTH levels ranging from 28.58 to 60.62 pg/mL. The patient remained normocalcemic with the most recent calcium level being 9.08 mg/dL 6 months after her third surgery.

Figure 6 presents the levels of PTH and calcium in time. Before the first surgery, PTH levels were in the 1455-1535 range, and serum calcium levels were in the 15-8-17.0 mg/dL range. Both PTH and calcium levels decreased after each

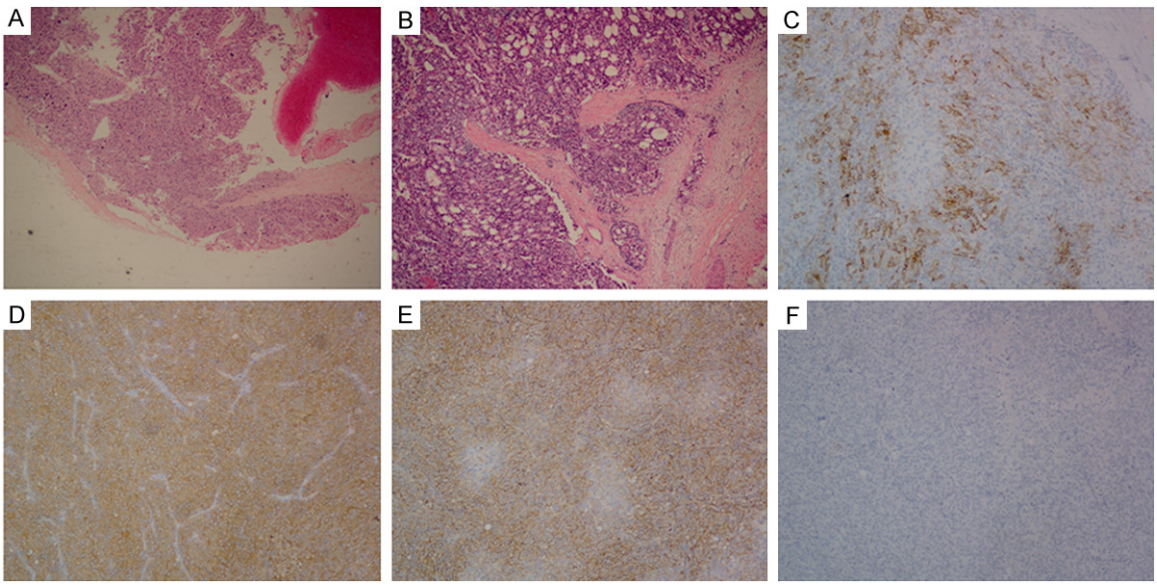

Figure 3. A and B. Histology of parathyroid carcinoma on the left side. Histopathological section demonstrating capsular invasion of the tumor. Original magnification × 40. Hematoxylin & eosin staining. C. PC shows strong parathyroid hormone immunoreactivity (Bovine serum albumin [BSA] technique; original magnification × 100). D. PC shows strong chromogranin A. immunoreactivity (BSA technique; original magnification × 100). E. PC shows strong synaptophysin immunoreactivity (BSA technique; original magnification × 100). F. PC lacks thyreoglobulin immunoreactivity (BSA technique; original magnification × 100).

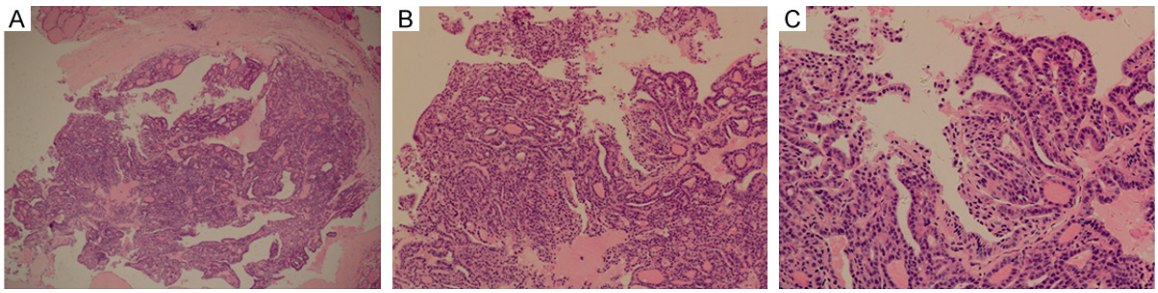

Figure 4. Histology of the 5-mm papillary carcinoma in the right thyroid lobe. Histopathological section demonstrating typical features of a papillary carcinoma. Original magnification × 40 (A), × 100 (B), and × 200 (C). Hematoxylin & eosin.

surgery, to rise again in the same ranges at each new presentation.

Discussion

PC is a rare malignant neoplasm derived from the parenchymal cells of the parathyroid gland. It accounts for 0.4% to 5% of patients with PHPT [16] but <1% in most series [17-19].

The clinical characteristics of patients with synchronous parathyroid and thyroid carcinomas and the case reported here are summarized in **Table 1**. Ten patients (83%) were females, and the patients were relatively young (mean age: 53 years). However, in previous reports (in PC patients without thyroid carcinoma), the distribution between men and women was relatively equal [20].

PC was active in 11 of the 12 patients described in **Table 1** (including the patients reported here), and 10 of the 11 patients with active parathyroid tumor had severe hypercalcemia and substantially elevated PTH levels ranging from 3- to almost 100-fold above normal levels. However, for the patient with slightly increased PTH levels, the PTH levels were reported in the literature 6 years before the patient was diag-

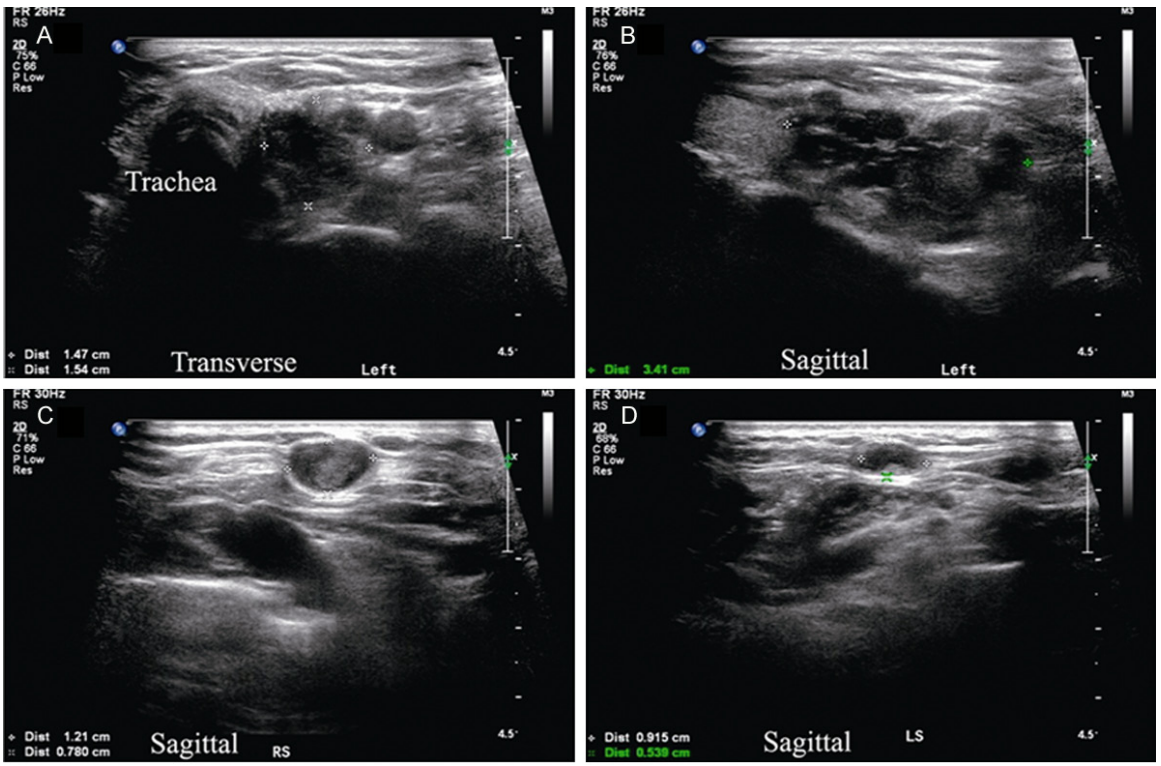

Figure 5. A and B. Ultrasonography of the neck showing one vascularized hypoechoic mass (transverse and sagittal views) in the lower pole of the left thyroid lobe extension to the suprasternal fossa (3.41 × 1.47 × 1.54 cm), with vague corticomedullary structure. C. Ultrasonography of the second vascularized hypoechoic nodule (sagittal view) in the right side of the suprasternal fossa (1.2 × 0.8 cm), without corticomedullary differentiation. D. Ultrasonography of the third vascularized hypoechoic nodule (sagittal view) in the left supraclavicular fossa (0.9 × 0.5 cm), without corticomedullary differentiation.

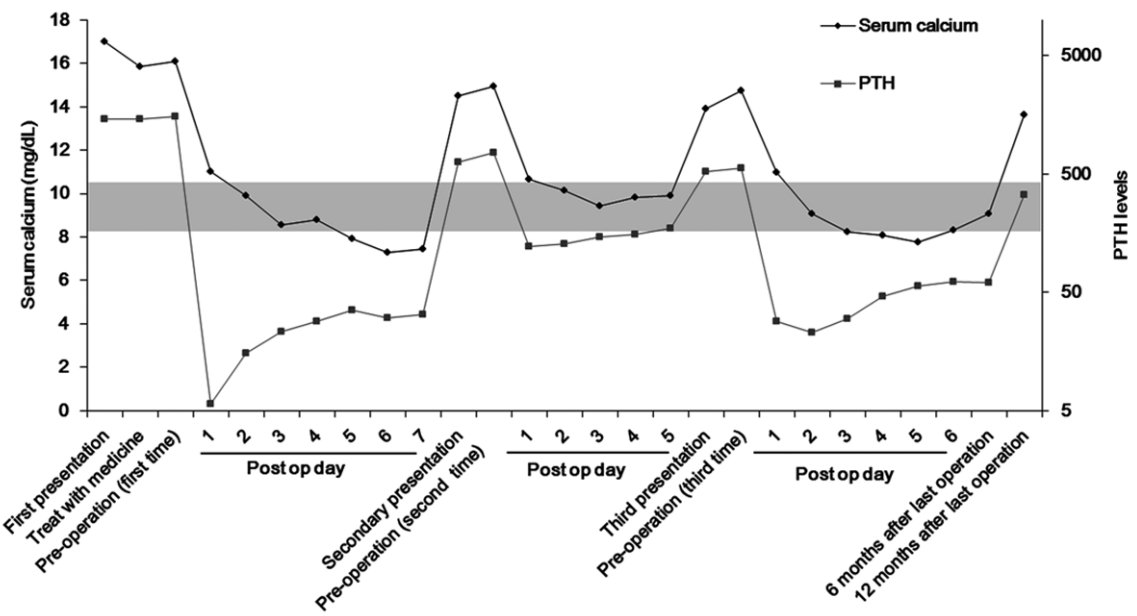

Figure 6. Changes in serum calcium and PTH levels in time.

Table 1. Clinical features of 12 patients with coexistence of parathyroid carcinoma and non-medullary carcinoma of the thyroid

Reference	Gender	Age	Calcium (mg/dL)	PTH (pg/mL)	Parathyroid Size (cm)	Carcinoma Location	Thyroid Carcinoma	Associated Parathyroid Disease	Surgical treatment	Outcome
Kurita, 1979	F	68	12.2	6,300	4.2 × 3.2 × 2.4	Left lower	Papillary	None	En-bloc Resection	Post-operative Normocalcemia
Christmas, 1988	F	62	Hyper-calcemia	Unknown	Unknown	Unknown	Follicular	None	Unknown	Died from metastatic parathyroid carcinoma
Savli, 2001	F	47	Normal	Normal	Unknown	Unknown	Papillary	Hyperplasia	Total thyroidectomy Parathyroidectomy (Excision of 2 Hyperplastic glands)	Normocalcemia (1 year)
Bednarek-Tupikowska, 2001	F	42	15.4	1,655	5 cm in diameter	Left lower	Follicular	None	En-bloc Resection	Persistent hypercalcemia
Schoretsanitis, 2002	F	55	14.2	>1,000	3 × 3	Left lower	Papillary	None	En-bloc Resection	Normocalcemia (6 years)
Kern, 2004	F	54	Unknown	465	2.5 × 1.8 × 1.6	Right Lower	Papillary and follicular	None	Right parathyroidectomy, Total thyroidectomy with local lymph node resection, Corticectomy in the right superior frontal gyrus	Died from intracranial metastatic parathyroid carcinoma
Lin, 2005	M	38	16.5	351	4 × 3 × 3	Left lower	Papillary	Two enlarged parathyroid glands on contralateral side	Total thyroidectomy, left parathyroidec tomy	Normocalcemia (6 years)
Goldfarb, 2009	M	58	14.4	2,023	3.4 × 3.3 × 2.2	Left lower	Papillary	Contralateral parathyroid adenoma	En-bloc Resection	Persistent hypercalcemia after resection of para- thyroid carcinoma. Normocalcemia after excision of contralateral parathyroid adenoma (1 year)
Marcy, 2009	F	42	14.1	383	1.3	Right lower	Papillary	None	Total thyroidectomy Right parathyroidectomy Central and lateral neck dissection	Normocalcemia (14 months)
Chaychi, 2010	F	79	10.4	89	1.1 × 1.2 × 4.8	Left superior	Papillary	None	Total thyroidectomy Left parathyroidectomy	Normocalcemia (6 months)
Amoodi, 2010	F	48	Unknown	186	>5	Left lower	Papillary	None	En-bloc Resection	Persistent hypercalcemia after resection of para- thyroid carcinoma. Hypoparathyroidism after completion parathyroidectomy
Present Case	F	45	17.0	1,455	4.28 × 3.09 × 2.54	Left lower	Papillary	None	Left parathyroidectomy Left thyroid lobectomy plus Left neck dissection	Persistent hyper-calcemia after Left parathyroidectomy Normocalcemia after left thyroid lobectomy plus left neck dissection (6 months)

PTH: parathyroid hormone.

nosed with PC, which cannot really reflect the PTH secretion character of the carcinoma. Therefore, these observations are in line with previous reports of PC unrelated to thyroid carcinoma. In the case reported here, both calcium and PTH levels increased with each recurrence.

Our patient did not have a previous history of neck irradiation or any other known risk factor for parathyroid or thyroid carcinoma. She was not tested for mutations of the HRPT2 gene.

The present report illustrates two important points that deserve to be emphasized. One, in patients with severe hypercalcemia, parathyroid carcinoma should be considered a possible underlying cause, and if the surgical finding supports the suspicion of parathyroid carcinoma, an en-bloc resection of the parathyroid tumor and adjacent thyroid lobe should be performed. In our patient, an en-block resection was not performed during the first surgical intervention. Therefore, she lost the opportunity of radical cure of PC. In addition, patients with HPT can have concomitant thyroid disease, including carcinoma, emphasizing the importance of thyroid imaging before neck exploration for HPT.

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Disclosure of conflict of interest

None.

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