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

Chunyi Song1, Jianbiao Wang1, Xiujun Cai2, Li Gao1

1Department of Head and Neck Surgery, Institute of Minimally Invasive Surgery of Zhejiang University, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China; 2Second Department of General Surgery, Institute of Minimally Invasive Surgery of Zhejiang University, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang Province, China

Received October 12, 2015; Accepted November 25, 2015; Epub January 1, 2016; Published January 15, 2016

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 subtraction scintigraphy scans revealed increased uptake of the left
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 ultrasound 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).
Scheduled 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 surgery.
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-
Synchronous parathyroid and thyroid carcinoma

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.
Synchronous parathyroid and thyroid carcinoma

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

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

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.

Acknowledgements

This research was supported by the Major Science and Technology Project of Zhejiang Province (grant no. 2012C13020-1) and the key project from the Health and Family Planning Commission of Zhejiang Province (grant no. 2015101112), China.

Disclosure of conflict of interest

None.

Address correspondence to: Jianbiao Wang, Department of Head and Neck Surgery, Institute of Minimally Invasive Surgery of Zhejiang University, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou 310016, Zhejiang Province, China. Tel: +86-13634176814; Fax: +86-64085875; E-mail: wangjianbiao0722@sina.com

References

Synchronous parathyroid and thyroid carcinoma


