Coexistence of Parathyroid Cancer and Papillary Thyroid Cancer: A Case Report with a Review of the Literature

KS Aljabri1*, SA Bokhari1, MA Alshareef1, PM Khan1, DA Abdulhafez2 and BK Aljabri3
1Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia
2Department of Pathology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia
3Medical Student, College of Medicine, Um Alqura university, Makkah, Kingdom of Saudi Arabia
*Corresponding Author: Khalid S Aljabri, Department of Endocrinology, King Fahad Armed Forces Hospital, Jeddah, Kingdom of Saudi Arabia.

Received: September 08, 2017; Published: October 11, 2017

Abstract

Parathyroid cancer (PTC) is a rare disease. It is most often diagnosed incidentally based on multi-organ non-specific symptoms of hypercalcemia as a consequence of primary hyperparathyroidism. We report a case of PTC and coexistence papillary thyroid cancer.

Keywords: Parathyroid Cancer; Papillary Thyroid Cancer; Saudi Arabia

Introduction

Parathyroid cancer (PTC) is an uncommon endocrine malignancy. It accounts for 0.4% to 5.2% of all reported cases of hyperparathyroidism. It is estimated to comprise 0.2 - 1% of malignant endocrine tumors which is approximately 0.005% of all cancers overall [1-15]. Two cases were reported from Saudi Arabia [16,17]. The majority of PTC are functional, with fewer than 10% of cases being nonfunctional [1]. Concomitant thyroid disease is not unusual among patients with primary hyperparathyroidism [18]. The coexistence of non-medullary thyroid cancer is found in 2.4 - 3.7% of patients operated on for primary hyperparathyroidism [19]. PubMed and MEDLINE searches yielded only 6 previous reports of synchronous PTC and non-medullary thyroid carcinoma [20-25]. This report is the second in the Saudi medical literature of a case of hyperfunctioning parathyroid carcinoma and concomitant papillary thyroid carcinoma.

Case Report

A 72-year-old Saudi female was referred to the endocrinology department clinic for primary hyperparathyroidism after routine blood work drawn by her primary care physician revealed a calcium level as high as 3.7 mmol/L as well as an intact parathyroid hormone level that was significantly increased at 199 pmol/L. The patient complained of generalized body aches and had history of chronic renal impairment and osteoporosis. She denied any radiation exposure or any personal or family history of cancer. On examination, diffuse goiter with thyroid mass was detected in the right neck without evidence of cervical lymphadenopathy. Subsequent work-up included blood work (Table) and an ultrasound thyroid and MRI neck showed a large inhomogeneous mass of the right lower thyroid lobe that measured 3.7 cm (Figure 1A and 1B). Fine needle aspiration of the right thyroid nodule showed Benign colloid nodules, Bethesda Category II. Tc99m-sestamibi scintigraphy demonstrated thyroid adenoma. At this time, the patient was scheduled for a neck exploration in the operating room with a differential diagnosis of a large thyroid adenoma. Total thyroidectomy was performed June 2017. The pathology report described a right thyroid lobe with a 4.5 cm PTC, The tumor was extending beyond the capsule and is reaching to the inked resection margins. Foci of vascular invasion and surrounding soft tissue invasion identified. The tumor cells are positive for Cyclin-D1 and glactin-3,

Coexistence of Parathyroid Cancer and Papillary Thyroid Cancer: A Case Report with a Review of the Literature

negative for thyroid transcription factor-1 (TTF-1) and cytokeratin 7 (CK7). Papillary thyroid cancer 0.2 cm was found (Figure 2A,B,C and D). At follow-up one month after surgery, the patient appeared disease free, her serum calcium was 1.6 mmol/L, albumin 34 gm/L, parathyroid hormone 1.9 pmol/L and TSH 0.9 mIU/L.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal reference (mmol/L)</th>
<th>Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>2.15 - 2.55</td>
<td>2.7</td>
</tr>
<tr>
<td>Albumin</td>
<td>34 - 52</td>
<td>45</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.7 - 1.2</td>
<td>0.97</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>40 - 129</td>
<td>224</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.66 - 1.06</td>
<td>0.6</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
<td>1.6 - 6.9 (pmol/L)</td>
<td>61.5</td>
</tr>
<tr>
<td>25-hydroxyvitamin D</td>
<td>75 - 250</td>
<td>7.7</td>
</tr>
<tr>
<td>Creatinine</td>
<td>62 - 106 (umol/l)</td>
<td>132</td>
</tr>
<tr>
<td>TSH</td>
<td>0.27 - 4.2 (mIU/L)</td>
<td>3.5</td>
</tr>
<tr>
<td>FT4</td>
<td>12.1 - 22 (pmol/L)</td>
<td>12.04</td>
</tr>
</tbody>
</table>

**Table:** Laboratory parameters.

**Figure 1:** Ultrasound thyroid (A) and MRI neck (B) showed a large inhomogeneous mass of the right lower thyroid lobe that measured 3.7 cm (Arrow).

**Figure 2:** A. White arrows shows dense fibrous bands surrounding islands of parathyroid tissue (black arrows). B. Islands of parathyroid tissue infiltrating the surrounding fat and sizable blood vessels which make the resection of the tumor difficult. Red arrows indicating the fat component and one large blood vessel. C. Follicles lined by crowded cells with vesicular large nuclei, nuclear grooving and intra-nuclear pseudoinclusions (White arrows) and focus of the tumor seen within dense fibrosis and scattered lamellated calcification (psammoma bodies)(black arrows). D. Thyroid parenchyma with variable sized follicles intermingled with aggregates of lymphocytes containing reactive follicles with germinal centers (white arrows).

**Discussion**

There has not been established any etiology for PTC and no predisposing factors were identified, it seems to be a result of a complex interaction of environmental factors and inherited genetic predispositions. There have not been established a definite progression.
Coexistence of Parathyroid Cancer and Papillary Thyroid Cancer: A Case Report with a Review of the Literature

sequence of benign to malignant lesions. The absence of conclusive data is attributed to the rarity of this tumor [26]. Neck radiation, adenoma, secondary and tertiary hyperparathyroidism have been reported in patients with parathyroid carcinoma [27]. A single glandular adenoma or hyperplasia are the most frequent cause of primary hyperparathyroidism. It is rarely caused by hyperfunctioning carcinoma, that accounts for 0.5% up to 5% of the patients with primary hyperparathyroidism. In one review of 4,239 patients with hyperparathyroidism, 2.1% had functioning parathyroid carcinomas [11].

Diagnosis of PTC is not easy; in fact 86% of the patients with primary hyperparathyroidism receive no pre-operative or intra-operative diagnosis of malignancy [28,29]. The first case was described over 100 years ago, but because of its rarity is difficult to establish clinical, histopathological and radiologic criteria of malignancy. The clinical presentation with symptoms of hypercalcemia, including anorexia, weight loss, fatigue, weakness, nausea, vomiting, bone pain, polyuria and polydipsia, complications such as pathologic fracture, renal colic, acute pancreatitis, peptic ulcer, occur more frequently than in benign disease. Hypercalcemia in parathyroid carcinoma tends to be more severe (> 3.5 mmol/L in 65 - 75% of patients) and recalcitrant to treatment. The positive predictive value and sensitivity of hypercalcemia were found to be 14% and 56% respectively. On the other hand, parathyroid hormone levels and tumor weight emerged as the more reliable surrogate indicators of parathyroid carcinoma. A tumor weight in excess of 2.5g, strongly favors a diagnosis of parathyroid carcinoma over that of adenoma. Serum parathyroid hormone levels tend to hover at about 10.3 times the upper limits of normal in parathyroid carcinomas as was the case in our patient. In contrast, mean parathyroid hormone levels in benign primary hyperparathyroidism will usually reach 2.6 times the normal values [30]. A palpable neck mass is present in up to 50% of PTC; hoarseness of voice due to recurrent laryngeal nerve palsy increase the possibility of malignancy; cervical lymph node metastases are present in 15 - 20% of cases. However, up to 30% of cancers haven't these characteristic features and benign disease can be similar to malignancy; then, a definitive diagnosis based on clinical or biochemical criteria is virtually impossible. Most of PTC are hyperfunctioning, with marked serum parathyroid hormone levels, and symptoms occurs more frequently than in benign disease [30].

There have been only 6 previous case reports of synchronous parathyroid carcinoma and papillary thyroid carcinoma. In 1979, a Japanese article described a patient with hyperfunctioning parathyroid carcinoma combined with papillary thyroid carcinoma [20]. In another case, occult parathyroid carcinoma was discovered incidentally after a patient had undergone thyroidectomy for papillary thyroid carcinoma and Hashimoto's thyroiditis [12]. The third case of hyperfunctioning parathyroid carcinoma and concomitant papillary thyroid carcinoma, without a previous history of neck irradiation, was reported in the English literature [18]. The fourth case illustrate the fact that concomitant hyperfunctioning parathyroid carcinoma and non-medullary thyroid carcinoma should not be overlooked, despite the rarity of such occurrence [24]. The fifth case showed multinodular goiter and parathyroid adenoma pre-diagnosis for which operation was planned that was postoperatively diagnosed with multifocal papillary thyroid carcinoma accompanying parathyroid carcinoma [23]. The sixth case revealed parathyroid carcinoma (3.5 cm mass) with extensive invasion, positive surgical margins, and positive angiolymphatic invasion with three foci of papillary thyroid carcinoma, the largest of which was 0.5 cm [25]. Our case will the seventh reported case reported in the literature.

Although the histopathological characteristics of PTC described in 1973 by Schantz and Castleman [9] are still used for diagnosis; none of them is pathognomonic of PTC and occur frequently in typical and atypical parathyroid adenoma as well as in parathyromatosis and it is often difficult to make diagnosis of PTC only on the basis of histology; but the presence of several findings in the same histological picture increase the possibility of malignancy [26].

The treatment of parathyroid carcinoma aims not only to cure the disease but to obtain its biochemical remission: normalization of blood calcium and parathyroid hormone levels, arrest of bone calcium depletion and regression of vascular, renal and neurological disorders. Surgical approach of PTC is the gold standard treatment, with en bloc resection of pathologic parathyroid gland, ipsilateral thyroid lobe and muscles. The majority of parathyroid neoplasms are found in the inferior gland position, which is likely related to the different embryologic descent paths taken by the superior and inferior glands [27].

Follow up involves periodic monitoring of calcium and PTH levels, markers for the disease's recurrence. Continued high postoperative calcium and parathyroid hormone levels are a sign of the disease’s persistence (metastasis or residual disease). Hypercalcaemia is the principal cause of morbidity and mortality from parathyroid carcinoma. The carcinomas grow slowly in most patients, but can occasionally be aggressive. The disease typically follows one of three courses: one third of patients are cured at initial or follow-up surgery, one third experience a recurrence after a prolonged disease-free survival but may be cured with re-operation, and one third experience a short and aggressive course [28]. The combined 5- and 10-year survival rates for patients with parathyroid carcinomas varied from 50 to 70 and 13 to 35 percent respectively, with a mean survival time of 6 to 7 years.

Competing Interests

The authors declare that they have no competing interests.

Bibliography


Coexistence of Parathyroid Cancer and Papillary Thyroid Cancer: A Case Report with a Review of the Literature


