CLINICS

CLINICAL SCIENCE

Is local resection sufficient for parathyroid carcinoma?

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OBJECTIVES: Parathyroid carcinoma is a rare malignant disease of the parathyroid glands that appears in less than 1% of patients with primary hyperparathyroidism. In the literature, the generally recommended treatment is en bloc tumor excision with ipsilateral thyroid lobectomy. Based on our 12 years of experience, we discuss the necessity of performing thyroid lobectomy on parathyroid carcinoma patients.

RESULTS: Eleven parathyroid carcinoma cases were included in the study. All operations were performed at the Department of Endocrine Surgery at Ankara University Medical School. Seven of the patients were male (63.6%), and the mean patient age was 48.9 ± 14.0 years. Hyperparathyroidism was the most common indication for surgery (n = 10, 90.9%). Local disease was detected in 5 patients (45.5%), invasive disease was detected in 5 patients (45.5%) and metastatic disease was detected in 1 patient (9.1%). The mean follow-up period was 99.6 ± 42.1 months, and the patients' average disease-free survival was 96.0 ± 49.0 months. During the follow-up period, only 1 patient died of metastatic parathyroid carcinoma.

CONCLUSION: Parathyroid carcinoma has a slow-growing natural progression, and regional lymph node metastases are uncommon. Although our study comprised few patients, it nevertheless showed that in selected cases, parathyroid carcinoma could be solely treated with parathyroidectomy.

KEYWORDS: Parathyroid; Carcinoma; Surgery; Thyroid Lobectomy.

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INTRODUCTION

Parathyroid carcinoma is a rare parathyroid gland malignancy, accounting for less than 1% (1) of primary hyperparathyroidism cases. Although extremely high blood calcium levels may indicate parathyroid carcinoma (2), it is usually diagnosed through detailed pathological analysis after surgery. Currently, surgery is the only effective and curative treatment for parathyroid carcinoma. The goal of the surgery (3) is to remove the tumor en bloc with any adherent tissue and enlarged lymph nodes as well as the ipsilateral thyroid lobe. In this study, based on our 12 years of experience, we discuss the necessity for performing a thyroid lobectomy in cases of parathyroid carcinoma.

MATERIALS AND METHODS

Eleven patients diagnosed with parathyroid carcinoma between 2000 and 2012 were included in our study. Demographics, previous neck surgery history, parathyroidectomy indications, surgery type, disease duration, follow-up periods, disease-free survival, pathological findings, and metastatic disease presence were retrospectively evaluated.

RESULTS

Of the 522 patients who underwent parathyroid surgery at the Department of Endocrine Surgery at Ankara University Medical School, 11 had parathyroid carcinoma (a 2.1% ratio). The patient demographic data are provided in Table 1.

The mean patient age was 48.9 ± 14.0 years. Seven of the patients were male (63.6%), and the mean age of the male patients was 53.3 ± 12.0 years. The mean age of the female patients was 41.3 ± 15.7 years. Two of the patients had undergone a previous thyroidectomy (18.2%). Although hyperparathyroidism was the most common indication for surgery (n = 10, 90.9%), suspected parathyroid carcinoma (n = 3), papillary thyroid carcinoma (PTC) (n = 2), and nodular goiter (n = 1) were also indications for the surgery (Table 1).

Parathyroidectomy was performed on each patient. The surgical procedures and pathological analysis results are shown in Table 2. Frozen sections were obtained from 5 patient samples, revealing suspected malignancy in 4 patients and parathyroid cancer in 1 patient. Parathyroidectomy was used as a stand-alone procedure in 5 patients;

No potential conflict of interest was reported.

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Table 1 - Demographic features and indications for surgery of parathyroid carcinoma patients.

Mean age (y)	48.9 ± 14
Male (n = 7)	53.3 ± 12
Female (n = 4)	41.3 ± 15.7
Gender	
Male	63.6%
Female	36.4%
Indications for parathyroidectomy (n, %)	
Hyperparathyroidism	10 (90.9%)
Suspected parathyroid carcinoma	3 (27.3%)
Papillary thyroid carcinoma	2 (18.2%)
Nodular goiter	1 (9.1%)

based on pathological analyses, 3 of these patients had local disease, and 2 had invasive disease. Due to a suspicion of parathyroid cancer, ipsilateral thyroid lobectomy with frozen section analysis was performed on 3 patients, one of whom had nodular goiter. Total thyroidectomies were also performed on 3 patients, 2 with PTC and 1 with metastatic parathyroid cancer. Central neck dissection was performed in 4 of 11 patients, and lymph node metastasis was histopathologically detected in only 1 case.

According to pathological analyses, 5 patients (45.5%) had local disease, 5 patients (45.5%) had invasive disease, and only 1 patient (9.1%) had metastatic disease. The mean follow-up period was 99.6 ± 42.1 months. Only 1 patient died of metastatic parathyroid carcinoma, and death occurred 37 months after diagnosis. Locoregional or systemic recurrence did not occur in any of the patients during follow-up.

DISCUSSION

Parathyroid carcinoma is an infrequent malignant disease of the parathyroid glands. Parathyroid carcinoma occurs with an annual incidence of approximately 1.25 cases per 10,000,000 persons (4) and accounts for less than 1% of primary hyperparathyroidism cases (1,5). Parathyroid carcinoma can be difficult to preoperatively diagnose (6,7) due to the similarity of its clinical features to benign diseases. However, a patient with hyperparathyroidism might have parathyroid carcinoma because these malignant tumors produce massive quantities of parathyroid hormone, greater than those produced by benign parathyroid tumors (adenomas or hyperplasia). All patients with hyperparathyroidism have elevated parathyroid hormone levels in their blood; those with benign disease tend to have levels in the "hundreds," whereas those with parathyroid cancer tend to have values in the "thousands," with a parathyroid hormone level that is commonly 3 to 10 times the upper limit of the normal range (7–9). Patients with normal serum calcium and parathyroid hormone levels (10) should not be excluded from a suspected prediagnosis of parathyroid carcinoma because nonfunctional parathyroid carcinomas are also observed, with an incidence of less than 10% of parathyroid carcinomas (11). In our study, nonfunctional parathyroid carcinoma was found in 1 patient (9.2%), and this patient underwent surgery due to papillary thyroid carcinoma and suspected parathyroid carcinoma. The majority of parathyroid carcinomas are hormonally active (7) and usually exhibit symptoms and complications of hyperparathyroidism due to elevated parathyroid hormone levels. However, we only operated on 1 out of 10 patients who were admitted to our clinic with hyperparathyroidism symptoms during the course of our study.

Table 2 - Surgical procedures and pathological diagnoses.

Surgical procedures	Number of patients (%)
Parathyroidectomy (stand-alone procedure)	5 (45.5%)
Parathyroidectomy + Thyroid lobectomy	1 (9.1%)
Parathyroidectomy +Thyroid lobectomy + Unilateral central lymph node dissection	2 (18.2%)
Parathyroidectomy + Total thyroidectomy	1 (9.1%)
Parathyroidectomy + Total thyroidectomy + Central lymph node dissection	2 (18.2%)
Pathological diagnoses	
Parathyroid carcinoma	11 (100%)
Nodular goiter	1 (9.1%)

A survival analysis for parathyroid carcinoma extrapolated from cancer databases such as the Surveillance, Epidemiology and End Results (SEER) database, the National Cancer Data Base (NCDB), and the Swedish Cancer Registry and from longitudinal retrospective studies showed overall survival rates of 85% and 49–77% (6) at 5- and 10-year follow-up, respectively. In our study, 1 patient died in the 37th month of the follow-up, and all of the other 10 patients were followed for a period of at least 5 years (mean follow-up period 99.6 ± 42.1 months). The 5-year survival rate of our patients was 90.9%, which was greater than that indicated in the literature. This may be explained by the low number of patients included in our study or because our surgical procedures were performed earlier than those in the literature. Furthermore, 5 of our patients had over 10 years of disease-free survival.

Parathyroid carcinoma usually presents between 45 and 59 years of age (7) and occurs with equal distribution in males and females. We determined a mean age of 48.9 ± 14.0 years, with 4 of the patients being less than 45 years of age (19, 36, 37, and 42 years); these data differ from the literature (7). Therefore, a parathyroid cancer diagnosis must be considered for younger patients with hyperparathyroidism.

Surgical treatment is essential for parathyroid carcinoma (12, 13). Preoperative suspicion and intraoperative recognition of parathyroid carcinoma require en bloc tumor resection (3,14). Regional lymph node metastases are not common, but a compartmental dissection (14) must be performed if any lymph nodes are enlarged. Adjacent thyroid lobe removal has also been recommended (15,16). We performed ipsilateral thyroid lobectomy on 3 patients, total thyroidectomy on 3 patients, and central lymph node dissection on 4 patients. Parathyroidectomy alone was performed on 5 patients. These 5 patients were closely followed, and no residual or recurrent disease was detected. Local disease was histopathologically identified in 3 patients, and locally invasive disease was observed in 2 patients. Thus, parathyroidectomy may be appropriate as a stand-alone procedure for the treatment of parathyroid carcinoma in selected cases, but these patients should be followed closely. However, based on the available literature, courage is required to diverge from the standard procedure of performing en bloc resection for parathyroid carcinoma if its presence is suspected.

In conclusion, parathyroid carcinoma has a slow-growing natural progression, and regional lymph node metastases are uncommon. Although the data in the literature compel us to perform ipsilateral thyroid lobectomies, our results showed that parathyroid carcinoma could be treated with parathyroidectomy alone in select cases. This result must be further evaluated in larger studies.

Table 3 - Patient characteristics.

Patient	Age	Previous operation	Indications for parathyroidectomy	Frozen section	Surgical treatment	Extent of disease	Pathological findings	Follow-up period (months)
1	42	None	HPT, nodular goiter	Suspected malignancy	Thyroid lobectomy, parathyroidectomy, and central lymph node dissection	Invasive	Nodular goiter and locally invasive parathyroid carcinoma	139
2	36	None	HPT, parathyroid carcinoma	Malignant	TT, parathyroidectomy, and central lymph node dissection	Metastatic	Invasive parathyroid carcinoma	37
3	64	None	HPT	None	Parathyroidectomy	Local	Parathyroid carcinoma	149
4	37	None	PTC, suspected parathyroid carcinoma	Suspected malignancy	TT, parathyroidectomy, and central lymph node dissection	Invasive	PTC and invasive parathyroid carcinoma	138
5	19	None	HPT	None	Parathyroidectomy	Local	Parathyroid carcinoma	79
6	56	None	HPT	Suspected malignancy	Thyroid lobectomy and parathyroidectomy	Local	Parathyroid carcinoma	134
7	56	None	HPT	Suspected malignancy	Thyroid lobectomy, parathyroidectomy and central lymph node dissection	Invasive	Invasive parathyroid carcinoma	140
8	65	None	HPT, PTC	None	TT and parathyroidectomy	Local	Papillary thyroid carcinoma and parathyroid carcinoma	83
9	54	TT	HPT	None	Parathyroidectomy	Invasive	Parathyroid carcinoma	86
10	59	TT	HPT	None	Parathyroidectomy	Invasive	Parathyroid carcinoma	36
11	50	None	HPT	None	Parathyroidectomy	Local	Parathyroid carcinoma	75

HPT: hyperparathyroidism, TT: total thyroidectomy, PTC: papillary thyroid carcinoma.

AUTHOR CONTRIBUTIONS

Genc V and Bayram IK designed the study. Basceken SI and Celik SU acquired the data. Sevim Y, Genc V, Bayram IK, and Basceken SI analyzed and interpreted the data. Sevim Y, Ersoz S, and Basceken SI drafted the manuscript. Sevim Y and Genc V offered critical revisions.

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