

Thyroid pathologies accompanying primary hyperparathyroidism: a high rate of papillary thyroid microcarcinoma

Koray Kutlutürk, Emrah Otan, Mehmet Ali Yağcı, Sertaç Usta, Cemalettin Aydın, Bülent Ünal

ABSTRACT

Objective: Thyroid pathologies and non-medullary thyroid cancer often accompany primary hyperparathyroidism (PHPT). The purpose of this study was to examine the association between thyroid diseases, especially micropapillary thyroid cancer, with PHPT.

Material and Methods: Data regarding 46 patients who were operated on with a diagnosis of PHPT at Inonu University Faculty of Medicine, General Surgery Clinic between June 2009 and March 2013 were retrospectively analyzed. Age, gender, levels of preoperative calcium, parathyroid hormone and phosphorus, and the histopathological results of the removed parathyroid and thyroid tissues were evaluated. All of the patients had a preoperative diagnosis of PHPT and there was no history of radiation to the head and neck region in any of the patients.

Results: Out of the 46 patients who were operated on for PHPT, 39 were female and 7 were male. The mean age was 52.8 years (25-76). Simultaneous thyroidectomy was performed in 35 patients (76.1%) due to an accompanying thyroid disorder. Papillary microcarcinoma was detected in 5 of these 35 (10.9%) patients who underwent thyroidectomy, two of which (40%) were multifocal tumors. The benign thyroid pathologies detected in the remaining 30 (65.2%) cases included lymphocytic thyroiditis in 3, Hashimoto thyroiditis in 1, follicular adenoma in 3 (two of which was Hurtle cell), and nodular colloid goiter in 23 patients. The preoperative serum phosphate level was significantly higher in the group with papillary thyroid microcarcinoma ($p=0.013$).

Conclusion: In regions where goiter is endemic, thyroid diseases and thyroid papillary microcarcinoma occur in association with PHPT at a higher rate compared to the normal population. Therefore, we believe that patients who are planned for surgery due to PHPT should be thoroughly investigated for the presence of any concomitant malignant thyroid pathologies in the preoperative period. It should also be kept in mind that patients with high blood serum phosphate values may have an increased risk of papillary thyroid microcarcinoma.

Key Words: Primary hyperparathyroidism, thyroid papillary microcarcinoma, goiter

INTRODUCTION

Primary hyperparathyroidism (PHPT) is a disease characterized by an increase in serum parathyroid hormone levels due to parathyroid adenoma, hyperplasia or rarely cancer. Its treatment requires surgical resection of the related parathyroid gland or glands. Thyroid cancer and benign thyroid pathologies usually accompany PHPT. Therefore, in order to avoid re-operations and to provide appropriate surgical treatment, patients who will undergo surgery for PHPT should be thoroughly evaluated in the preoperative period for the presence of possible accompanying thyroid diseases.

In this study, accompanying thyroid disorders in patients operated for PHPT between June 2009 and March 2013 were analyzed.

MATERIAL AND METHODS

Medical records of 46 patients who underwent surgery at our center between June 2009 and March 2013 for PHPT were retrospectively analyzed. Data regarding age, gender, preoperative calcium, parathyroid hormone and phosphorus levels, and the histopathology results of removed parathyroid and thyroid tissues were evaluated. All of the patients had a preoperative diagnosis of PHPT, and none had a previous history of radiation to the head and neck radiation.

Concomitant thyroid pathologies were identified either on physical examination, neck ultrasonography, scintigraphy or during surgery.

Statistical Analysis

Predictive Analytics SoftWare (PASW) statistics 18.0 (Chicago, IL, USA) software was used for analyses. $P<0.05$ was considered significant. Pearson's chi-square test was used for comparison of categorical data between groups, in terms of numeric value, percentage, and homogeneity. Continuous variables were analyzed by Student's t-test. A frequency analysis was performed for quantitative variables. The mean, standard deviation (SD), minimum and maximum values were used for descriptive statistics.

Department of General Surgery,
İnönü University Faculty of
Medicine, Malatya, Turkey

Address for Correspondence
Koray Kutlutürk

Department of General Surgery,
İnönü University Faculty of
Medicine, Malatya, Turkey
Phone: +90 488 411 22 66
e-mail:
kkutluturk@gmail.com

Received: 09.02.2014

Accepted: 28.03.2014

©Copyright 2014
by Turkish Surgical Association

Available online at
www.ulusalcerahidergisi.org

Table 1. Demographic data of patients with thyroid papillary carcinoma

	Age	Gender	Focus count	Accompanying parathyroid pathology	Lymph node metastasis	Distant metastasis
1	45	K	Single focus	Adenoma	-	-
2	39	E	Single focus	Hyperplasia	-	-
3	47	K	2 foci	Hyperplasia	-	-
4	62	K	Single focus	Adenoma	-	-
5*	60	K	3 foci	Normal	-	-

*the patient was operated 1 month later and parathyroid adenoma was excised

RESULTS

Forty-six patients underwent surgery due to primary hyperparathyroidism, 39 of them were females and seven were males. The mean age was 52.8 (25-76) years. Simultaneous thyroidectomy was performed in 35 patients (76.1%) due to an accompanying thyroid disorder. Papillary microcarcinoma was detected in 5 of 35 thyroidectomy patients (10.9%). The mean diameter of papillary microcarcinoma was 0.42±0.2 cm. In two of these patients (40%) more than one tumor foci were identified (Table 1). The following benign thyroid diseases were detected in the remaining 30 (65.2%) cases: lymphocytic thyroiditis in three patients, Hashimoto's thyroiditis in one patient, follicular adenoma (two with Hurtle cell) in three patients, and nodular colloid goiter in the remaining 23 patients (Table 2). A statistically significant relationship was not detected between preoperative serum calcium or parathyroid hormone levels and thyroid papillary micro-carcinoma, whereas preoperative serum phosphate levels were significantly higher (p=0.013) in the group with thyroid papillary micro-carcinoma (Table 3).

DISCUSSION

Thyroid gland pathologies are frequent, and 11% of the world population has thyroid gland pathology (1). In our country, there are approximately 5 million patients with goiter (2). Thyroid malignancy can be detected in 5% of surgically treated thyroid nodules (3). In a study from Turkey, thyroid malignancies were identified in 8.9% of patients who had thyroid diseases. In the same study, the rate of papillary thyroid cancer was reported as 6.6% (4).

In our study, the rate of thyroid pathologies accompanying PHPT was identified as high as 65.2%. In the literature, the rate of benign thyroid diseases concomitant with PHPT ranges from 17 to 66% (5).

Although the incidence of papillary thyroid micro-carcinoma varies according to geographic regions, there are no studies on the prevalence of thyroid papillary micro-carcinoma within the normal population in our country. In our study, the rate of thyroid papillary micro-carcinoma concomitant with PHPT was identified to be high, 10.9%.

Ogburn et al. (6) have reported the presence of papillary thyroid cancer concomitant with primary hyperparathyroidism for the first time in 1956. In several studies, the frequency of this association has been reported as 1.3-17.6% (5, 7-12). To the best of our knowledge, the highest rate of papillary thyroid cancer accompanying PHPT was reported from Van Yüzüncü Yıl University (Table 4). To the best of our knowledge

Table 2. Thyroid pathologies concomitant with PHPT

Pathology	Number	Percent
Benign pathologies	30	65.2
Nodular colloid goiter	23	50.0
Lymphocytic thyroiditis	3	6.5
Hashimoto's thyroiditis	1	2.2
Follicular adenoma	3	6.5
Hurtle cell	2	
Malignant pathologies	5	10.9
Thyroid papillary microcarcinoma	5	10.9
Multicentric	2	
Single focus	3	
Total	35	76.1

PHPT: primary hyperparathyroidism

Table 3. Demographic and biochemical findings of benign and malignant thyroid pathologies accompanying PHPT

	Patients with no accompanying thyroid pathology or those with an accompanying benign thyroid disease	Thyroid papillary microcarcinoma	p value
Number of patients	41	5	
Age (mean)	52.8±12.3	50.6±9.9	0.703
Gender (F/M)	35/6	4/1	0.759
Laboratory data			
Serum calcium level	12.1±1.1	11.9±2.1	0.725
Serum phosphate level	2.9±0.5	4.1±1.2	0.013
Serum parathormone level	559.2±521.8	806.4±737.9	0.349

PHPT: primary hyperparathyroidism

the rate detected in our study, 10.9%, is the third highest rate reported in the literature. We believe that more frequent diagnosis of thyroid diseases in some endemic regions may contribute to this high rate. The city of Malatya is among endemic goiter regions in our country. In a study conducted in 2003 by the Ministry of Health, Division of Family and Child Health, and UNICEF Turkey, the ultrasonographic prevalence of goiter was found to be 45% (13).

Table 4. Published thyroid papillary cancer rates accompanying PHPT (in patients with no previous radiation exposure to the neck)

First author	Year	Number of patients	Thyroid papillary microcancer rate, %
Presented study	2013	46	10.9
Morita et al.*(11)	2008	199	5.5
Ogawa et al. (8)	2007	85	10.6
Masatsugu et al.* (7)	2005	109	17.4
Kösem et al. (5)	2004	51	17.6
Sidhu et al.* (9)	2000	64	4.6
Fedorak et al. (10)	1994	100	7
Nishiyama et al.* (12)	1979	407	1
Ogburn et al. (6)	1956	230	1.7

*In these studies patients with a history of radiation to the head-neck were excluded and thyroid papillary microcarcinoma rate was re-calculated.
PHPT: primary hyperparathyroidism

In our study, none of the patients with papillary thyroid microcarcinoma had distant metastasis. However, metastatic cases have been reported in the literature (11). There are also studies that reported mortality due to metastasis (14, 15). Additionally, 2 (40%) patients were found to have multicentric disease in our study (Table 1). The rate of multicentricity in papillary thyroid microcarcinoma ranges from 9.5 to 24.9% (16).

There is no agreement on the treatment of incidental thyroid papillary micro-carcinoma. Some studies suggest only follow-up of these lesions due to their indolent course in general, while some studies advocate a more aggressive treatment (bilateral total thyroidectomy) due to the possibility of their being multifocal and leading to mortality by metastasis (15, 17).

In our study, there were no statistically significant differences in terms of preoperative serum calcium and parathyroid hormone levels between patients with thyroid papillary microcarcinoma and those either without an accompanying thyroid pathology or with benign thyroid pathology. However, serum phosphate levels were detected to be significantly higher ($p=0.013$). In a study conducted with PHPT patients with or without concomitant thyroid pathologies, it was reported that preoperative serum calcium levels were significantly higher in patients with thyroid diseases; however, a statistically significant difference in serum parathyroid hormone levels was not detected. In the same study, serum phosphate levels were significantly higher in patients with concomitant thyroid pathologies (7). Therefore, we believe that high phosphate levels increase the probability of detection of thyroid papillary micro-carcinoma in patients with concomitant thyroid pathologies. Nevertheless, we believe that larger series are required to make a definitive statement.

CONCLUSION

Thyroid diseases and thyroid papillary micro-carcinoma accompany PHPT at a higher rate than the normal population, especially in regions with endemic goiter. Therefore, we believe that patients who are scheduled for an operation due

to PHPT in these regions should be thoroughly evaluated in the preoperative period for the presence of concomitant malignant thyroid pathologies. In addition, in patients who are prepared to undergo parathyroidectomy for PHPT, it should be kept in mind that the risk of thyroid papillary microcarcinoma may have increased if their preoperative serum phosphate values are high.

Ethics Committee Approval: This study is retrospective so that the ethical approval has not been received.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - K.K., B.Ü.; Design - B.Ü., C.A.; Supervision - C.A., B.Ü.; Funding - K.K., E.O.; Materials - S.U., M.A.Y.; Data Collection and/or Processing - K.K., E.O.; Analysis and/or Interpretation - E.O., S.U., M.A.Y.; Literature Review - K.K.; Writer - K.K., S.U., M.A.Y.; Critical Review - B.Ü., C.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

- Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Int Med* 2000; 160: 526-534. [CrossRef]
- Bender Ö, Yüney E, Çapar H, Höbek A, Ağca B, Akat O, et al. Total tiroidektomi deneyimlerimiz. *Endokrinolojide Diyalog* 2004; 1: 15-18.
- Hegedüs L. The thyroid nodule. *N Engl J Med* 2004; 351: 1764-1771. [CrossRef]
- Ünal B, Işık B, Bozkurt B, Dirican A, Karabeyoğlu M, Kahraman L. Tiroid hastalıklarında sık kullanılan preoperatif testlerin patolojik inceleme ile korelasyonu. *Endokrinolojide Diyalog* 2009; 6: 25-28.
- Kösem M, Algün E, Kotan Ç, Harman M, Öztürk M. Coexistent thyroid pathologies and high rate of papillary cancer in patients with primary hyperparathyroidism: controversies about minimal invasive parathyroid surgery. *Acta Chir Belg* 2004; 104: 568-571.
- Ogburn P, Black B. Primary hyperparathyroidism and papillary adenocarcinoma of the thyroid: Report of four cases. *Proc Staff Meet Mayo Clin* 1956; 31: 295-298.
- Masatsugu T, Yamashita H, Noguchi S, Nishii R, Watanabe S, Uchino S, et al. Significant clinical differences in primary hyperparathyroidism between patients with and those without concomitant thyroid disease. *Surg Today* 2005; 35: 351-356. [CrossRef]
- Ogawa T, Kammori M, Tsuji E, Kanauchi H, Kurabayashi R, Terada K, et al. Preoperative evaluation of thyroid pathology in patients with primary hyperparathyroidism. *Thyroid* 2007; 17: 59-62. [CrossRef]
- Sidhu S, Campbell B. Thyroid pathology associated with primary hyperparathyroidism. *Aust N Z J Surg* 2000; 70: 285-287. [CrossRef]
- Fedorak IJ, Salti G, Fulton N, Straus FH, Kaplan EL. Increased incidence of thyroid cancer in patients with primary hyperparathyroidism: a continuing dilemma. *Am Surg* 1994; 60: 427-431.
- Morita SY, Somervell H, Umbricht CB, Dackiw AP, Zeiger MA. Evaluation for concomitant thyroid nodules and primary hyperparathyroidism in patients undergoing parathyroidectomy or thyroidectomy. *Surgery* 2008; 144: 862-867. [CrossRef]
- Nishiyama RH, Farhi D, Thompson NW. Radiation exposure and the simultaneous occurrence of primary hyperparathyroidism and thyroid nodules. *Surg Clin North Am* 1979; 59: 65-75.

13. Tiroid Hastalıkları Tanı, Tedavi ve İzlem Kılavuzu. Ankara: Türkiye Endokronoloji ve Metabolizma Derneği; 2012.p.52.
14. Laskin W, James L. Occult papillary carcinoma of the thyroid with pulmonary metastases. Hum Pathol 1983; 13: 83-85. [\[CrossRef\]](#)
15. Hay ID, Grant CS, van Heerden JA, Goellner JR, Ebersold JR, Bergstralh EJ. Papillary thyroid microcarcinoma: a study of 535 cases observed in a 50-year period. Surgery 1992; 112: 1139-1146.
16. Erol V, Makay Ö, Ertan Y, İçöz G, Akyıldız M, Yılmaz M, Yetkin E. Multicentricity in thyroid papillary microcarcinomas. Ulusal Cer Derg 2010; 26: 199-202.
17. Carlini M, Giovannini C, Castaldi F, Mercadante E, Zazza S, Nania A, et al. High risk for microcarcinoma in thyroid benign disease. Incidence in a one year period of total thyroidectomies. J Exp Clin Cancer Res 2005; 24: 231-236.