

TURKISH JOURNAL OF INTERNAL MEDICINE

Original Article

Coexistence of Medullary and Papillary Thyroid Carcinomas Detected Incidentally

Ensar AYDEMİR¹, Özen ÖZ GÜL¹, Erdinç ERTÜRK¹, Canan ERSOY¹, Soner CANDER¹, Yasemin ÜNSAL¹, Coşkun ATEŞ¹

¹ Bursa Uludağ University Faculty of Medicine, Division of Endocrinology and Metabolic Diseases, Bursa, Turkey

Abstract

Papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC) are extremely rare and constitute less than 0.5% of all thyroid malignancies. In this study, the prevalence and characteristics of 8 patients with simultaneous PTC and MTC diagnoses were evaluated.

Turk J Int Med 2021;3(Supplement 1):S1-S3 DOI: <u>10.46310/tjim.882858</u>

Keywords: papillary thyroid carcinoma, medullary thyroid carcinoma, thyroid cancer, germline RET mutation

Introduction

The incidence of thyroid cancer, the most common cancer of the endocrine system, has increased over the years. Thyroid cancer is the 12th most common cancer with 2.9% of all new cancer cases in the U.S.¹ Papillary thyroid carcinoma (PTC), originating from thyroid follicular epithelial cells, is the most common form of thyroid cancer which accounts for about 70% of thyroid malignancies.² Medullary thyroid carcinoma (MTC) develops from parafollicular cells that express calcitonin, and accounts for 1-2% of all thyroid cancers.³ Coexistence of PTC and MTC is extremely rare, accounts for less than

0.5% of all thyroid malignancies.⁴ Here, we report 8 cases of co-existing papillary and medullary thyroid carcinomas with histopathological features, imaging and laboratory findings, outcomes and impact of treatment with the data in the literature.

Material and Methods

We retrospectively analyzed data of 31 patients with medullary thyroid carcinoma between 2012 and 2020 at our institution. The information collected included age, gender, type of surgery, histopathological findings (tumor



Received: February 18, 2021; Accepted: March 3, 2021; Published Online: March 6, 2021

Address for Correspondence:

Ensar AYDEMIR

Department of Endocrinology, Bursa Uludag University, Faculty of Medicine, Bursa, Turkey

E-mail: <u>ensaraydemir@uludag.edu.tr</u>



Copyright © 2021

localization, maximal diameter, capsule invasion, lymphovascular invasion, lymph node involvement and number, tumor stage), presence of RET protooncogene, time since diagnosis of thyroid cancer, previous and current sonographic findings, treatments received for thyroid malignancies, and related comorbidities. Calcitonin, thyroglobulin and anti-thyroglobulin levels were measured with local methods and commercial kits. The staging of thyroid cancers were re-evaluated based on Tumor–Node–Metastasis (TNM) cancer staging system by the new, 8th editions of the relevant Union for International Cancer Control (UICC) and American Joint Committee on Cancer.

Results

The mean age of all patients (MTC and MTC/ PTC) was 53.7±12.01 years at the time of diagnosis. The mean age of only MTC patients (23/31) was 50.6±10.6 years. Eight of 31 patients (25%) with MTC had PTC and MTC simultaneously. Overall, median age was 64.5 years (range, 41-83) in MTC/PTC group, and seven of eight participants were female, five patients among 8 were treated in Uludag University hospital. Median follow-up for these patients was 25 months, with a range of 16-104 months. In 7 of the 8 patients, the maximal diameter of PTC was 10 mm or less. In 7 patients the largest tumor diameter was 23.5±18.5 mm for MTC and 6.75±4.6 mm for PTC. 3 patients had lymph node involvement. Calcitonin, CEA and thyroglobulin were respectively 380 pg/ mL (range: 2-16072), 24.6 mcg/L (range: 1-551.6), and 9.2 mcg/L (range: 0.19-25) preoperatively. Same blood tests were performed after surgery and measurements of serum calcitonin, CEA and thyroglobulin were 2 pg/mL (range: 2-10071), 2.5 mcg/L (range: 0.9-419.3), and 0.27 mcg/L (range: 0.13-1.4), respectively. Fifty percent of patients (50%, 4/8) had received adjuvant RAI treatment and one patient received tyrosine kinase inhibitor (TKI) therapy.

Discussion

Three previous studies have reported that mean age of only MTC and MTC/PTC patients were respectively 48.2±16.9, 44.5±12.6, median age 44.3 (range: 43-45.7) years for only MTC and 49.9±13.9, 53.5±6.5, median age 50.2 (range: 44.6-55.8) years for MTC/PTC patients.⁵⁻⁷ In these studies, MTC/PTC patients were older than only MTC patients at the time of diagnosis. The median age in our study was also higher. Despite low numbers, similar to previous studies reported, the median age of patients with MTC/PTC was higher than that of patients with only MTC in our study.

Several studies have shown different frequencies of coexistence of MTC and PTC between 3.6% and 19%. The higher frequency (25%) in our study can be explained by the fact that the patients have been diagnosed in recent years and the frequency of PTC has increased significantly in the last 2 decades.⁸

In this study, the mean follow-up period of the patients was 25 months. In the previous studies, follow-up time was 32 months (range: 0-261) and 49.1±33.4 months, respectively. The medical records were reviewed from 1996 to 2006 and from 1992 to 2014 by these studies.^{5,9} Follow-up period was shorter in this study because most of our patients diagnosed lately. For instance, six of 8 patients with MTC/PTC were diagnosed in 2018 and later.

PTC diameter of seven patients was equal or less than 1 cm. In Limh et al.'s study⁸, the largest tumor diameter was equal or less than 1 cm in 32.5% of patients with PTC. The fact that mPTC was detected in most of the patients in our study can be explained by the advanced age of the patients. In addition, the reason for this high rate may be related to the fact that fine needle aspiration biopsy is not performed for nodules smaller than 1 cm detected by thyroid ultrasound before surgery. In our study, only 2 patients were diagnosed with PTC preoperatively by FNAB. Similarly, in the Korean study, 9 of 10 patients had mPTC.⁶

In conclusion, although our results support the coincidental existence of MTC/PTC, physicians should be aware of the coexistence of these thyroid malignancies to avoid possible misdiagnosis.

Conflict of Interests

Authors declare that there are none.

Acknowledgment

This study has been presented in 17th Uludag Internal Medicine National Winter Congress, 6th Bursa Family Medicine Association National Congress, 11th Uludag Internal Medicine Nursing Congress, 5–7 March 2021, Bursa, Turkey.

References

- SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute. Available at: https://seer.cancer.gov/explorer/. Accessed September 14, 2020.
- 14, 2020.
 2. Lloyd RV, Buehler D, Khanafshar E. Papillary thyroid carcinoma variants. Head Neck Pathol. 2011 Mar;5(1):51-6. doi: 10.1007/s12105-010-0236-9.
- 3. Wells SA Jr, Asa SL, Dralle H, Elisei R, Evans DB, Gagel RF, Lee N, Machens A, Moley JF, Pacini F, Raue F, Frank-Raue K, Robinson B, Rosenthal MS, Santoro M, Schlumberger M, Shah M, Waguespack SG; American Thyroid Association Guidelines Task Force on Medullary Thyroid Carcinoma. Revised American Thyroid Association guidelines for the management of medullary thyroid carcinoma. Thyroid. 2015 Jun;25(6):567-610. doi: 10.1089/thy.2014.0335.

- 4. Bayrak E, Serter R. Coexistence of papillary and medullary thyroid carcinoma: A rare entity. The Turkish Journal of Endocrinology and Metabolism. 2020;24:168-72. doi: 10.25179/tjem.2019-72499.
- 5. Biscolla RP, Ugolini C, Sculli M, Bottici V, Castagna MG, Romei C, Cosci B, Molinaro E, Faviana P, Basolo F, Miccoli P, Pacini F, Pinchera A, Elisei R. Medullary and papillary tumors are frequently associated in the same thyroid gland without evidence of reciprocal influence in their biologic behavior. Thyroid. 2004 Nov;14(11):946-52. doi: 10.1089/thy.2004.14.946.
- 6. Kim WG, Gong G, Kim EY, Kim TY, Hong SJ, Kim WB, Shong YK. Concurrent occurrence of medullary thyroid carcinoma and papillary thyroid carcinoma in the same thyroid should be considered as coincidental. Clin Endocrinol (Oxf). 2010 Feb;72(2):256-63. doi: 10.1111/j.1365-2265.2009.03622.x.
- 7. Machens A, Dralle H. Simultaneous medullary and papillary thyroid cancer: a novel entity?. Ann Surg Oncol. 2012 Jan;19(1):37-44. doi: 10.1245/s10434-011-1795-z.
- 8. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974-2013. JAMA. 2017 Apr 4;317(13):1338-1348. doi: 10.1001/jama.2017.2719.
- 4,317(13):1338-1348. doi: 10.10017/affia.2017.2719.
 Appetecchia M, Lauretta R, Barnabei A, Pieruzzi L, Terrenato I, Cavedon E, Mian C, Castagna MG, Elisei R; SIE (Italian Society of Endocrinology) Working Group. Epidemiology of simultaneous medullary and papillary thyroid carcinomas (MTC/PTC): An Italian multicenter study. Cancers (Basel). 2019 Oct 9;11(10):1516. doi: 10.3390/cancers11101516.