CASE REPORT

DOI: 10.5336/caserep.2021-85940

# Primary Squamous Cell Carcinoma of the Thyroid Coexisting with Tall Cell Variant Papillary Thyroid Carcinoma: Report of Two Cases

Ezgi HACIHASANOĞLU[a], Zeynep ALKAN[b], Günter HAFIZ[b], Sina ERCAN[c], Ferda ÖZKAN[a]

[a]Department of Pathology, Yeditepe University Faculty of Medicine, İstanbul, Türkiye
[b]Department of Ear Nose Throat Diseases, Yeditepe University Faculty of Medicine, İstanbul, Türkiye
[c]Department of Thoracic Surgery, Yeditepe University Faculty of Medicine, İstanbul, Türkiye

**ABSTRACT** Primary squamous cell carcinoma of the thyroid (PSCCT) is a rare and aggressive neoplasm of the thyroid, usually presenting with a rapidly growing mass. In order to diagnose a tumor as PSCCT, tumor should entirely consist of cells with squamous differentiation without any evidence of other types of carcinomas. Tall cell variant papillary thyroid carcinoma (TCVPTC) is an aggressive variant of papillary thyroid carcinoma, composed of cells that are two-three times as tall as they are wide. We report two cases of PSCCT coexisting with TCVPTC. In the literature, there are less than 50 cases showing coexistence of PSCCT and TCVPTC. In all these cases, apart from the ones in which pure squamous cell carcinoma (SCC) is seen as a recurrence of TCVPTC, SCC and TCVPTC areas were intermingled. The 2 cases we report here are unique in the way that PSCCT and TCVPTC are seen concurrently in these patients but they are separate tumors, not admixed with each other.

**Keywords:** Squamous cell carcinoma; thyroid; papillary thyroid carcinoma; tall cell variant papillary thyroid carcinoma

Primary squamous cell carcinoma of the thyroid (PSCCT) is an extremely rare, aggressive neoplasm representing less than 1% of all primary thyroid malignancies.[1] It is more common in elderly and women.[1] PSCCT usually presents with a rapidly growing mass and pressure symptoms related to tracheal and/or esophageal compression.[2] For diagnosis, tumor should exclusively consist of cells with squamous differentiation without any evidence of other types of carcinomas.[1] Perithyroidal extension and lymphovascular invasion is frequent.[2,3] PSCCT shows poor radiotherapy and chemotherapy response and the choice of treatment remains surgical resection.[3] The prognosis is poor, with a median survival of 9 months.[3]

Tall cell variant papillary thyroid carcinoma (TCVPTC) is an aggressive variant of papillary thyroid carcinoma (PTC), usually seen in elderly and associated with frequent extrathyroidal extension and metastasis.[1,4] Histologically, TCVPTC is composed of at least 30% of tall cells, which are two-three times as tall as they are wide, with typical nuclear features of PTC.[1] TCVPTCs account for a substantial proportion of radioactive iodine-refractory thyroid carcinomas and prognosis is less favorable than conventional PTCs.[1] We report 2 cases of PSCCT coexisting with TCVPTC.

## CASE REPORTS

### CASE 1

A 64-year-old woman referred to ear-nose-throat policlinic with dyspnea and stridor. On physical examination, thyroid was firm and enlarged. Bilateral

**Correspondence:** Ezgi HACIHASANOĞLU
Department of Pathology, Yeditepe University Faculty of Medicine, İstanbul, Türkiye
**E-mail:** ezgi.hacihasanoglu@yeditepe.edu.tr

Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

***Received:*** 27 Aug 2021 ***Received in revised form:*** 26 Nov 2021 ***Accepted:*** 02 Dec 2021 ***Available online:*** 06 Dec 2021

nodules were detected in ultrasonography (USG). USG guided fine needle aspiration biopsy (FNAB) from right lobe was performed in another center and pathological examination revealed PTC. Computed tomography (CT) visualized 37x37x34 millimeter ill-defined mass in the right thyroid lobe, invading trachea. Bilateral thyroidectomy, bilateral cervical lymph node dissection was performed.

Macroscopically, a 5x3x3 centimeter ill-defined gray-white firm area and 1.5-centimeter well-demarcated yellowish-white nodule was present in the right lobe. In the left lobe, a 2-centimeter well-demarcated yellowish-white nodule was present. The specimen was totally sampled.

Microscopy of the ill-defined area showed moderately differentiated squamous cell carcinoma (SCC), invading perithyroidal tissues. Immunohistochemically, tumor cells were positive for p63, CK19, PAX8. The nodules in both lobes were unencapsulated TCVPTCs. SCC and TCVPTC in the right lobe were separate tumors (Figure 1). No metastasis was detected in bilateral cervical lymph nodes.

The patient received radiotherapy and radioactive iodine therapy. Six months after surgery, she presented with a 5-centimeter mass at the resection site, visualized by CT. The patient died of disease 9 months after surgery.

## CASE 2

A 83-year-old man referred to ear-nose-throat policlinic with dyspnea and neck mass. On physical examination, thyroidal mass and cervical lymphadenopathy was palpated. The patient had USG-guided FNAB from lymph node in another center and was diagnosed with PTC metastasis. CT revealed a 48x44x32 millimeter ill-defined mass in the right thy-

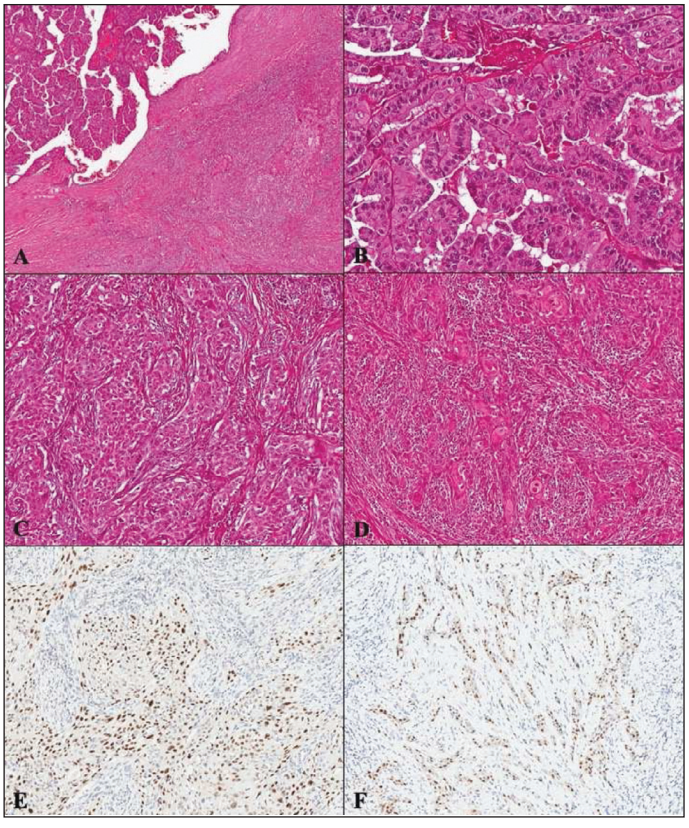


**FIGURE 1: A)** TCVPTC (left upper side) and PSCCT (right lower side) seen in very close proximity to each other but as separate tumors (H&E, x40); **B)** TCVPTC area in higher magnification. The tumor is entirely composed of cells that are two-three times as tall as they are wide with eosinophilic abundant cytoplasm (H&E, x200); **C)** PSCCT area in higher magnification. The tumor is composed of nests and cords of squamous cells (H&E, x100); **D)** Marked squamous differentiation and occasional keratin pearls are seen in some areas of PSCCT (H&E, x100); **E)** p63 positivity in PSCCT areas (p63x100); **F)** PAX8 positivity in PSCCT areas (PAX8x100).
TCVPTC: Tall cell variant papillary thyroid carcinoma; PSCCT: Primary squamous cell carcinoma of the thyroid.

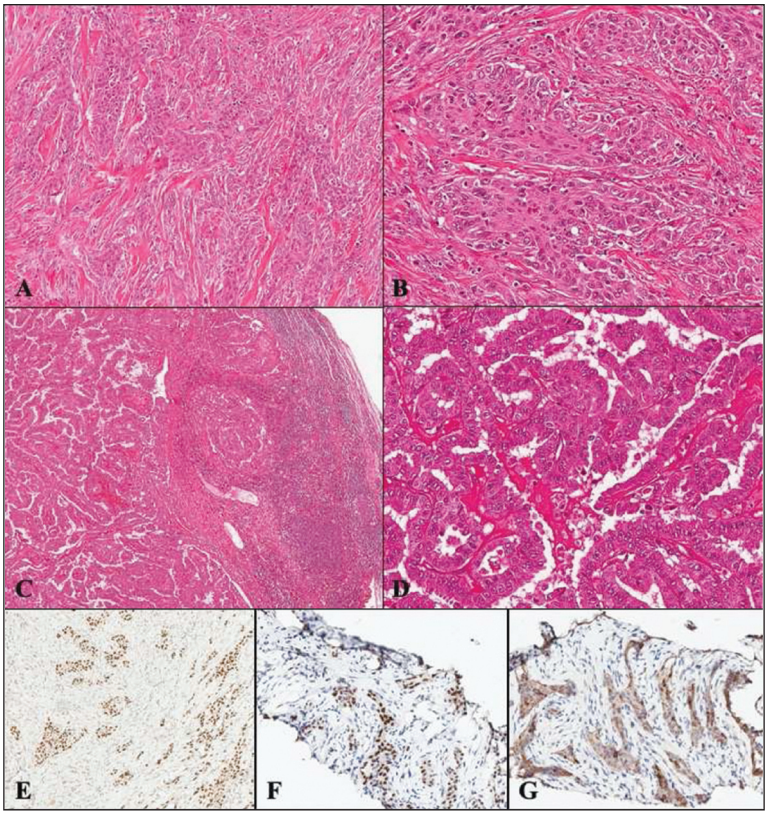


**FIGURE 2: A)** PSCCT composing of nests and cords of squamous cells (H&E, x100); **B)** PSCCT area in higher magnification (H&E, x200); **C)** TCVPTC metastasis in the lymph node (H&E, x40); **D)** TCVPTC metastasis in higher magnification. The tumor is entirely composed of cells that are two-three times as tall as they are wide with eosinophilic abundant cytoplasm (H&E, x200); **E)** p63 positivity in PSCCT areas (x100); **F)** PAX8 positivity in PSCCT areas (PAX8x200); **G)** CK19 positivity in PSCCT areas (CK19x200). PSCCT: Primary squamous cell carcinoma of the thyroid; TCVPTC: Tall cell variant papillary thyroid carcinoma.

roid lobe, invading larynx. He underwent bilateral thyroidectomy and right cervical lymph node dissection.

Macroscopically, a 5x4x3 centimeter ill-defined yellowish-white firm area was seen in right lobe. Left lobe parenchyma was heterogeneous with scant colloid. Both lobes were totally sampled.

Microscopic examination of the right lobe showed poorly differentiated SCC with extrathyroidal invasion. Immunohistochemically tumor cells were positive for p63, CK19, PAX8 (Figure 2). Left lobe showed adenomatous hyperplasia. Among 20 lymph nodes from the right cervical dissection, 7 showed TCVPTC metastasis.

The patient received radiotherapy and radioactive iodine therapy. Six months after surgery, a 3.5-centimeter paratracheal mass was detected by CT and biopsy revealed SCC. The patient is alive with disease 8 months after surgery. Informed consent was obtained from both patients for the case report.

## DISCUSSION

PSCCT is a rare and aggressive neoplasm of the thyroid, consisting predominantly or entirely of tumor cells with squamous differentiation.[1] The most important entities in the differential diagnosis are metastasis or direct invasion from other sites, squamous differentiation in other carcinomas, squamous metaplasia associated with nodular goiter and lymphocytic thyroiditis. Immunohistochemical staining is helpful for differentiating metastatic SCC from PSCCT. PAX8 is a sensitive marker for confirming thyroidal origin.[2] TTF-1 and thyroglobulin positivity can be seen.[2]

Over the years, an association between PSCCT and TCVPTC has been noticed.[5-15] Bronner and

LiVolsi reported 5 cases of spindle cell SCC admixed with TCVPTC and suggested that this association was not coincidental and may represent a histopathologic link in thyroid carcinogenesis.[5] Gopal et al. studied 31 cases of spindle cell SCC in association with TCVPTC; in 18 cases, both tumors were present at the same time; in 5 cases, SCC was seen as a recurrence of TCVPTC; 8 cases presented with laryngeal mass, sections of which revealed SCC admixed with TCVPTC.[7] In the cases reported by Evans and Basnet et al., SCC was seen as a recurrence of TCVPTC.[8,9] Kallel et al. reported the first case of PSCCT associated with TCVPTC and Hashimoto thyroiditis.[10] SCC and TCVPTC were separate tumors; authors stated that SCC probably originated from Hashimoto thyroiditis following a phase of metaplasia. Gadde et al. reported a recurrent TCVPTC case with metastatic lymph node showing areas of SCC and TCVPTC.[11]

Apart from the cases presenting as pure SCC with a history of TCVPTC, all cases in the literature showed mixed areas of SCC and TCVPTC. In our first case, SCC and TCVPTC were separate tumors. Immunohistochemical studies of SCC were consistent with thyroidal origin. No sign of squamous differentiation was seen in TCVPTC. The second case showed SCC in thyroid and TCVPTC metastasis in cervical lymph nodes. No sign or history of TCVPTC in thyroid was present. This case might represent TCVPTC undergoing complete transition to SCC after metastasizing to lymph nodes.

As seen in our cases, patients with SCC and TCVPTC have poor prognosis. By FNAB, these cases are mostly diagnosed as PTC, but not SCC; probably because the firm consistency of SCC makes sampling difficult. In patients diagnosed with PTC, presenting with rapidly growing neck mass; coexistence of SCC should be kept in mind, despite its rarity. Other diagnostic procedures, such as trucut biopsy or frozen section can be considered in order to plan the type of surgery and palliative therapies.

To conclude, we report two cases of PSCCT, coexisting with TCVPTC. The first case is unique in the way that TCVPTC and PSCCT are separate tumors and the second case demonstrates an original co-occurrence of PSCCT and metastatic TCVPTC, without evidence or history of PTC in thyroid.

### *Source of Finance*

*During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.*

### *Conflict of Interest*

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

### *Authorship Contributions*

***Idea/Concept:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan;* ***Design:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan, Günter Hafız, Sina Ercan, Ferda Özkan;* ***Control/Supervision:*** *Günter Hafız, Sina Ercan, Ferda Özkan;* ***Data Collection and/or Processing:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan;* ***Analysis and/or Interpretation:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan, Günter Hafız, Sina Ercan, Ferda Özkan;* ***Literature Review:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan, Günter Hafız;* ***Writing the Article:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan;* ***Critical Review:*** *Günter Hafız, Sina Ercan, Ferda Özkan-* ***References and Fundings:*** *Zeynep Alkan, Günter Hafız;* ***Materials:*** *Ezgi Hacıhasanoğlu, Zeynep Alkan, Günter Hafız.*

## REFERENCES

1. Lloyd RV, Osamura RY, Klöppel G, Rosai J, World Health Organization, International Agency for Research on Cancer. WHO Classification of Tumours of Endocrine Organs. 4th ed. Lyon: IARC; 2017. [Link]
2. Lam AK. Squamous cell carcinoma of thyroid: a unique type of cancer in World Health Organization Classification. Endocr Relat Cancer. 2020;27(6):R177-R192. [Crossref] [PubMed]
3. Cho JK, Woo SH, Park J, Kim MJ, Jeong HS. Primary squamous cell carcinomas in the thyroid gland: an individual participant data meta-analysis. Cancer Med. 2014;3(5):1396-403. [Crossref] [PubMed] [PMC]
4. Morris LG, Shaha AR, Tuttle RM, Sikora AG, Ganly I. Tall-cell variant of papillary thyroid carcinoma: a matched-pair analysis of survival. Thyroid. 2010;20(2):153-8. [Crossref] [PubMed] [PMC]
5. Bronner MP, LiVolsi VA. Spindle cell squamous carcinoma of the thyroid: an unusual anaplastic tumor associated with tall cell papillary cancer. Mod Pathol. 1991;4(5):637-43. [PubMed]

6. Kleer CG, Giordano TJ, Merino MJ. Squamous cell carcinoma of the thyroid: an aggressive tumor associated with tall cell variant of papillary thyroid carcinoma. Mod Pathol. 2000;13(7):742-6. [Crossref] [PubMed]
7. Gopal PP, Montone KT, Baloch Z, Tuluc M, LiVolsi V. The variable presentations of anaplastic spindle cell squamous carcinoma associated with tall cell variant of papillary thyroid carcinoma. Thyroid. 2011;21(5):493-9. [Crossref] [PubMed]
8. Evans WD. De-differentiation of papillary thyroid carcinoma into squamous cell carcinoma. A case of coexistence within an excised neck lesion. BMJ Case Rep. 2012;2012:bcr 201 2007 707. [PubMed] [PMC]
9. Basnet A, Pandita A, Fullmer J, Sivapiragasam A. Squamous cell carcinoma of the thyroid as a result of anaplastic transformation from BRAF-positive papillary thyroid cancer. Case Rep Oncol Med. 2017;2017:4276435. [Crossref] [PubMed] [PMC]
10. Kallel S, Kallel R, Ayadi S, Ghorbel A. Primary squamous cell carcinoma of the thyroid associated with papillary thyroid carcinoma and Hashimoto's thyroiditis. Eur Ann Otorhinolaryngol Head Neck Dis. 2018;135(4):291-3. [Crossref] [PubMed]
11. Gadde R, Tafe LJ, Tsapakos MJ, Liu X. A case report of papillary thyroid carcinoma dedifferentiated to squamous cell carcinoma presenting as a lung metastasis: A potential diagnostic pitfall. Diagn Cytopathol. 2020;48(6):581-5. [Crossref] [PubMed]
12. Saunders CA, Nayar R. Anaplastic spindle-cell squamous carcinoma arising in association with tall-cell papillary cancer of the thyroid: A potential pitfall. Diagn Cytopathol. 1999;21(6): 413-8. Erratum in: Diagn Cytopathol 2000; 22(2):136. [Crossref] [PubMed]
13. Sutak J, Armstrong JS, Rusby JE. Squamous cell carcinoma arising in a tall cell papillary carcinoma of the thyroid. J Clin Pathol. 2005;58(6):662-4. [Crossref] [PubMed] [PMC]
14. Ashraf MJ, Azarpira N, Khademi B, Peiravi M. Squamous cell carcinoma associated with tall cell variant of papillary carcinoma of the thyroid. Indian J Pathol Microbiol. 2010;53(3): 548-50. [PubMed]
15. Patten DK, Ahmed A, Greaves O, Dina R, Flora R, Tolley N. Anaplastic spindle cell squamous carcinoma arising from tall cell variant papillary carcinoma of the thyroid gland: a case report and review of the literature. Case Rep Endocrinol. 2017;2017:4581626. [Crossref] [PubMed] [PMC]