CASE REPORT

**Medical Journal of Western Black Sea**
Batı Karadeniz Tıp Dergisi

Med J West Black Sea 2022;6(3): 410-416
DOI: 10.29058/mjwbs.1164665

# Difficulty in Follow-Up of Papillary Thyroid Cancer Co-Existent with Hypopituitarism: Case Report and Review of the Literature

## Hipopitüitarizm ile Birlikte Olan Papiller Tiroid Kanserinin Takibinde Zorluk: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

**Ömercan TOPALOĞLU[1], Güldeniz Gizem SÜREN[2], Sakin TEKİN[1], Barkın MALKOÇ[3], Esin KAYMAZ[3], Güldeniz KARADENİZ ÇAKMAK[4], Taner BAYRAKTAROĞLU[1]**

[1]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Endocrinology, Zonguldak, Turkey
[2]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Internal Medicine, Zonguldak, Turkey
[3]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of Pathology, Zonguldak, Turkey
[4]Zonguldak Bülent Ecevit University Faculty of Medicine, Department of General Surgery, Zonguldak, Turkey

**ORCID ID:** Ömercan Topaloğlu 0000-0003-3703-416X, Güldeniz Gizem Süren 0000-0002-0254-4269, Sakin Tekin 0000-0002-1408-1249, Barkın Malkoç 0000-0002-2073-0188, Esin Kaymaz 0000-0003-4127-6559, Güldeniz Karadeniz Çakmak 0000-0001-5802-4441, Taner Bayraktaroğlu 0000-0003-3159-6663

**Cite this article as:** Topaloğlu Ö et al. Difficulty in follow-up of papillary thyroid cancer co-existent with hypopituitarism: case report and review of the literature. Med J West Black Sea. 2022;6(3):410-416.

*The abstract of our article was accepted and presented as an "Electronic Poster" with a heading of "Difficulty in Follow-up of Papillary Thyroid Cancer Co-Existent with Hypopituitarism: Case Report" in 9th (Online) Congress of Thyroid Diseases of Türkiye, 2021.*

**Corresponding Author**
Ömercan Topaloğlu

**E-mail**
drhomercan@hotmail.com

**Received**
20.08.2022

**Revision**
28.08.2022

**Accepted**
31.08.2022

This work is licensed by "Creative Commons Attribution-NonCommercial-4.0 International (CC)".

## ABSTRACT

**Aim:** We present an interesting case of papillary thyroid cancer co-existent with hypopituitarism.

**Case:** Fortysix-year-old female was applied with a complaint of painful palpabl lump in the right side of the neck, difficulty swallowing, cough and dyspnea. The patient was diagnosed with type 2 diabetes mellitus 8 years ago, underwent craniotomy for nonfunctioning pituitary adenoma 15 years ago, and received gamma knife 10 years ago. She had been taking insulin glargine and lispro, prednisolone, and levothyroxine (LT4). Physical examination was unremarkable. Pituitary MRI revealed partial empty sella. A solid nodule of 33x27x30 mm with irregular borders and containing microcalcifications in the right thyroid lobe was detected on sonography. Fine needle aspiration cytology revealed "strongly suspicious features for malignancy". Papillary thyroid carcinoma (PTC) was detected after right lobectomy and then complementary thyroidectomy. Follow-up sonography performed 14 months later than radioactive iodine (RAI) showed an avascular solid area of 30x14x15 mm in the right. We decided to monitor free thyroxine (fT4), thyroglobulin and anti-thyroglobulin levels. LT4 dose was adjusted to keep fT4 level closer to the upper limit of normal. No complications or recurrences were detected.

**Conclusion:** Studies on the follow-up of PTC cases with hypopituitarism are limited. We performed RAI after total thyroidectomy, and treated the patient with LT4 by adjusting fT4 level.

**Keywords:** Thyroid cancer, Pituitary insufficiency, Pituitary, Thyroid, Hypopituitarism

## ÖZ

**Amaç:** Papiller tiroid kanserinin hipopitüitarizm ile birlikte görüldüğü ilginç bir olgu sunuyoruz.

**Olgu:** Kırkaltı yaşında kadın hasta boyun sağ kısmında ele gelen ağrılı sertlik, yutkunma güçlüğü, öksürük ve boğaz ağrısı şikâyeti ile başvurdu. Hastanın 8 yıldır tip 2 diyabet tanısı mevcuttu, 15 yıl önce nonfonksiyone hipofiz adenomu sebebiyle kraniyotomi, 10 yıl önce gamma knife alma öyküsü mevcuttu. Hasta insülin glarjin ve lispro, prednizolon, levotirosin (LT4) kullanmaktaydı. Fizik bakısında önemli bir özellik bulunmadı. Hipofiz MR görüntülemede parsiyel "empty sella" izlendi. Tiroid sonografisinde sağ


© 2022 Zonguldak Bulent Ecevit University, All rights reserved.

lob orta kesimde 33x27x30 mm, düzensiz sınırlı, mikrokalsifikasyon içeren solid nodül izlendi. İnce iğne aspirasyon sitolojisinde "malignite yönünden kuvvetli şüpheli yaymalar" saptandı. Öncelikle sağ lobektomi, sonrasında tamamlayıcı tiroidektomi uygulanan hastanın patolojik analizinde papiller tiroid kanseri (PTK) saptandı. Postoperatif radyoaktif iyot (RAİ) tedavisinden 14 ay sonra kontrol sonografisinde sağ tiroid lojunda 30x14x15mm vaskülaritesi kodlanmayan solid alan izlendi. Serbest T4 (sT4), tiroglobulin ve anti-tiroglobulin düzeylerini takip etmeye karar verdik. Komplikasyon veya nüks izlenmedi.

**Sonuç:** Hipofiz yetmezliğinde PTK takibi ile ilgili çalışmalar kısıtlıdır. Biz total tiroidektomi sonrasında RAİ uyguladık ve sT4 düzeyine göre LT4 tedavisi verdik.

**Anahtar Sözcükler:** Tiroid kanseri, Hipofiz yetmezliği, Hipofiz, Tiroid, Hipopituitarizm

## INTRODUCTION

Papillary thyroid carcinoma (PTC) accounts for 85% of well-differentiated thyroid malignancies (1). Most PTCs are identified in the early stages and have an excellent prognosis (2,3). For patients at high risk for recurrence, bilateral surgery allows administration of radioiodine (RAI) for remnant ablation (4,5). Serum Tg is a sensitive marker of residual/recurrent thyroid cancer after ablation of the post-surgical residual thyroid tissue. Because the vast majority of PTC recurrences are in cervical lymph nodes, neck sonography, together with serum Tg and anti-thyroglobulin (anti-Tg) measurements, should be performed about 6 months after thyroid ablation in a patient followed-up with levothyroxine (LT4) suppression. Little has been known regarding the follow-up of the cases with PTC co-existent with hypopituitarism. We present follow-up a case of PTC co-existent with hypopituitarism.

## CASE REPORT

A 46-year-old-female patient presented to our clinic with a complaint of palpabl painful lump in right side of the neck in October 2018. She had a diagnosis of type 2 diabetes mellitus for 8 years. The patient underwent pterional craniotomy surgery due to nonfunctioning pituitary adenoma in 2003 and received gamma knife treatment in 2008. The patient then developed visual loss in the left eye due to left optic atrophy, and also hypopituitarism. She had been taking insulin glargine 1x40 unit/day, insulin lispro 3x16 unit/day, prednisolone 1x5 mg/day and LT4 25 mcg/day. On physical examination, blood pressure was 140/80 mmHg, heart rate 75 beat/min, respiratory rate 20/min, $SPO_2$ 98%, temperature 36$^{o}$ C, height was 165cm and weight was 75kg, body mass index was 27.55. System examinations were unremarkable. Neck examination revealed nodular goiter. EKG showed normal sinus rhythm.

In laboratory analysis, TSH was 0.691 mIU/L, fT4 0.957 ng/dL, free triiodothyronine (fT3) 2.47 pg/mL, anti-Tg negative. Other baseline laboratory findings were demonstrated in Table 1. On thyroid sonography, a solid nodule of 33x27x30 mm with irregular borders and containing microcalcifications in the central part of the right lobe was detected. Strongly suspicious features for malignancy were detected on fine needle aspiration cytology of the nodule. We then referred the patient for thyroidectomy under glucocorticoid protection in November 2018. Pathological analyses were as followings: A thyroid lobectomy material containing a right lobe measuring 4.8x3.6x2.8 cm. A solid nodule with a size of 2.3x2.2x1.6 cm, partially uniformly limited, dirty cream color was observed, located on the upper surface with a mark on the sections. The tumor was located in the upper right lobe and had a diameter of 2.3 cm. There were no capsules around the tumor. The tumor had infiltrated into the thyroid tissue and perithyroid tissue. There was no tumor on the surgical border, but the tumor was closer than 0.1cm to the surgical border. There was no perineural and lymphovascular invasion around the tumor. A positive reaction was observed in tumor cells with CK19, HBME1 and no reaction was observed with CD56. Diagnosis was PTC (Figure 1). Because the patient had bilateral multicentric tumor and the resected tumor was closer than 0.1cm to the surgical border, we decided in multidisciplinary thyroid council to proceed with total thyroidectomy. The patient was then referred for a complementary total thyroidectomy in November 2018. Pathology results of the left lobe came back as classical subtype papillary thyroid microcarcinoma. The tumor had a diameter of 0.2 cm and it was properly limited and encapsulated. There was no tumor at the thyroid surgical border, but the tumor was located 0.2 cm away from the surgical border. There was no perineural and lymphovascular invasion around the tumor. LT4 was continued after complementary thyroidectomy. RAI ablation was decided based on multidisciplinary thyroid council. We cessated LT4 for 3 weeks before RAI, but TSH was elevated just to 5.56 mUI/L probably due to central hypothyroidism. We could not attain recombinant human TSH (rhTSH) before RAI ablation. The patient underwent RAI ablation with 100 mCi oral $^{131}$I in April 2019, 5 months after second surgery. 24$^{th}$ hour radiation dose was <30 microsievert/hour. Whole body scan after $^{131}$I showed accumulations of activity on residual tissue of varying intensity in the middle or even in two foci on the sternal notch in the neck region. We followed up with the patient every 3 months with LT4 dose of 150 mcg/day prescribed after RAI ablation. In the next follow-up in July 2019, laboratory analysis showed TSH<0.01 mUI/L, fT4 2

ng/dL, fT3 3.66 pg/mL, Tg 0.32 ng/dL, and anti-Tg negative. Thyroid sonography showed that bilateral parotid and submandibular glands had a normal sonographic appearance, the thyroid gland was enlarged, and a non-bloody homogeneous solidified appearance with a size of 35x17x16 mm was observed in the right thyroid bed. The finding was considered as a collection of liquids with a dense content. Thyroid residual tissue could not be ruled out. Also, a small number of reactive lymph nodes were observed in the bilateral submandibular area and the upper-middle jugular chain (the largest of which was 15x6 mm in size in the right submandibular region). We then decided to continue the treatment and follow-up with thyroid sonography and LT4 treatment. We adjusted LT4 dosage based on the fT4 level in the patient because she has hypopituitarism. We tried to keep the fT4 in the upper range of normal limits. TSH was already suppressed due to hypopituitarism (Figure 2).

In our last follow up in January 2022, 37 months after surgery, 22x14mm hypoechoic avascular lesion in the right lobe and another 28x12mm hypoechoic avascular lesion in the right lobe was detected in thyroid sonography (Figure 3). FNA was not performed because we thought the lesions to be postoperative soft tissue-fluid collection. Pituitary magnetic resonance imaging (MRI) performed in November 2021 revealed partial empty sella and 21x17x15 mm heterogeneous contrast enhancing mass, diffusely surrounding the left optic nerve and filling the left internal carotid artery (ICA) cavernous segment which is considered to be recurrence/residue (Figure 4).

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Table 1:** Laboratory parameters during the follow-up.

| Parameters | Preoperative | 3rd month | 6th month | 12th month | Reference range |
|---|---|---|---|---|---|
| TSH (mIU/L) | 0.59 | 5.56 | <0.01 | 0.001 | 0.27-4.2 |
| fT4 (ng/dL) | 0.97 | 3.78 | 2.24 | 1.61 | 0.93-1.7 |
| FfT3 (ng/dL) | 2.53 | 3.2 | 3.48 | 3.04 | 2-4.4 |
| Tg (ng/dL) | - | 0.32 | 0.37 | 0.26 | 3.68-64.15 |
| Anti-Tg (IU/mL) | - | neg | neg | neg | 0-150 |
| Total Cortisol (ug/dL) | 1.78 | 2.74 | 4.98 | 1.69 | 6.2-19.4 (morning)<br>2.3-11.9 (afternoon) |
| Prolactin (ng/mL) | 3.68 | 3.4 | 3.6 | 2.9 | 4.79 - 23.3 |
| FSH (mIU/mL) | 6.42 | 5.2 | 5.5 | 5.89 | Mid-Follicular Phase: 3.5-12.5<br>Midcycle: 4.7-21.5<br>Midluteal Phase: 1.7-7.7<br>Postmenopause: 16.8-134.8 |
| LH (mIU/mL) | 1.71 | 2.69 | 2.92 | 2.18 | Follicular Phase: 2.4-12.6<br>Ovulatory Phase: 14-96<br>Mid-Luteal Phase: 1-11.4<br>Postmenopause: 7.7-59 |
| ACTH (pg/mL) | 32.8 | | | | 0-46 |
| Growth hormone (ng/mL) | 2.66 | | | | <8 |
| Estradiol (pg/mL) | <20 | <5 | 13 | <5 | midfolicular phase 12.5-166<br>pre-ovulation stage 85.5-498<br>midluteal phase 43.8-211<br>postmenopause 5-54.7 |
| Progesterone (ng/mL) | <0.05 | <0.05 | <0.05 | <0.05 | follicular stage: 0.2-1.5<br>luteal stage: 1.7-27<br>postmenopausal: 0.1-0.8 |
| HbA1C (%) | 8.6 | 7.4 | 8.4 | 8.4 | 4-5.9 |
| FBG (mg/dL) | 193 | 164 | 256 | 194 | |

**fT4:** Free T4, **fT3:** Free T3, **Tg:** Thyroglobulin, **Anti-Tg:** Anti-thyroglobulin, **FSH:** Follicule stimulating hormone, **LH:** Luteinizing hormone, **ACTH:** Adrenocorticotropic hormone, **FBG:** Fasting blood glucose

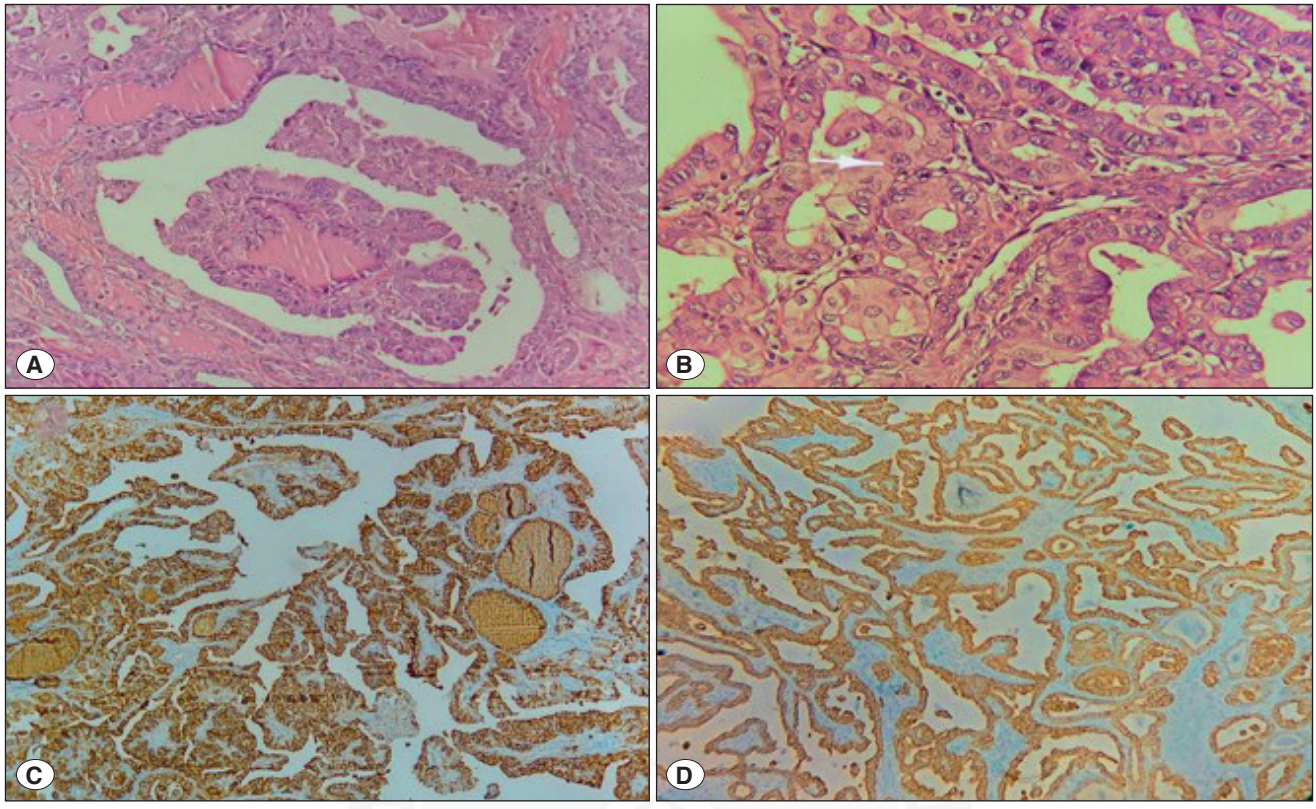


**Figure 1:** (Panels A-D) Histopathology of PTC at diagnosis: **A)** True papillae with fibrovascular cores with multipl branching (H&E, x200); **B)** A nuclear pseudoinclusion marked with white arrow, also chromatin clearing (Orphan Annie nuclei) and coffee bean nuclei changes are seen around (H&E, x400); **C)** Diffuse membranous and cytoplasmic staining in PTC (CK19, BSA, x200); **D)** Basolateral membranous staining with HBME1 in PTC (HBME1, BSA, x200).

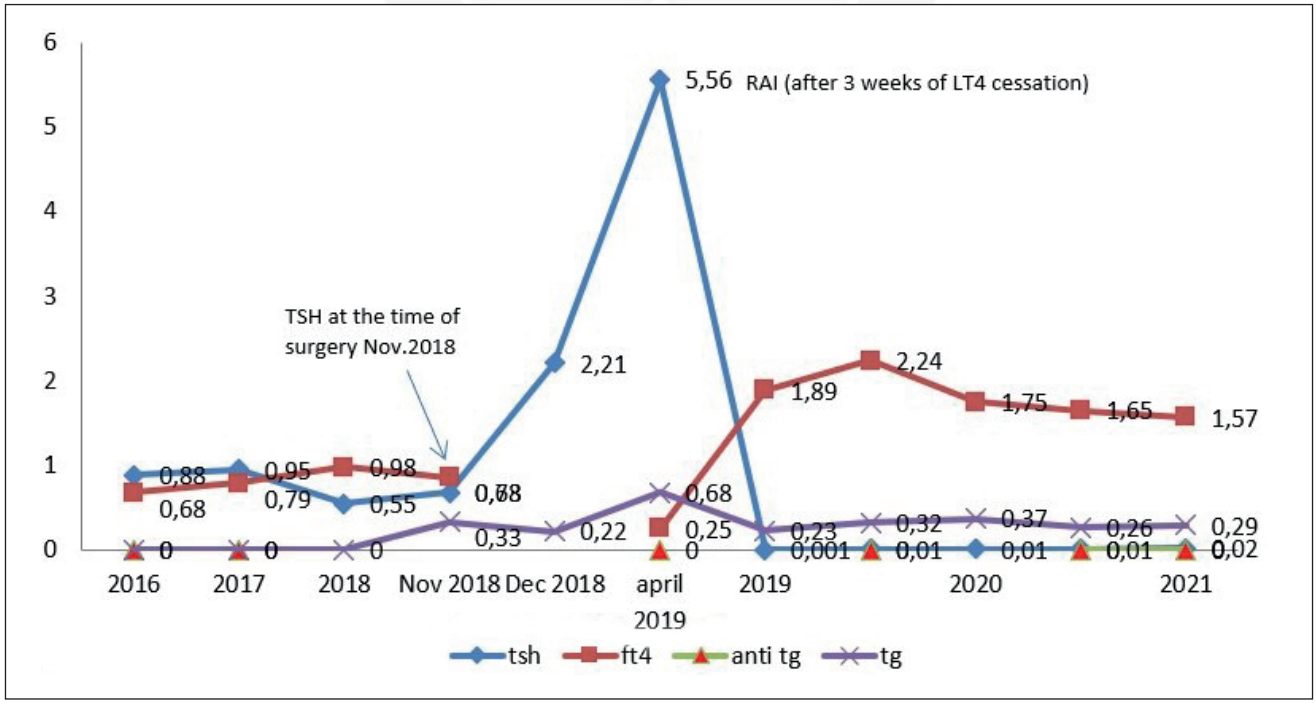


**Figure 2:** Temporary changes in TSH, fT4, anti-Tg, Tg levels.

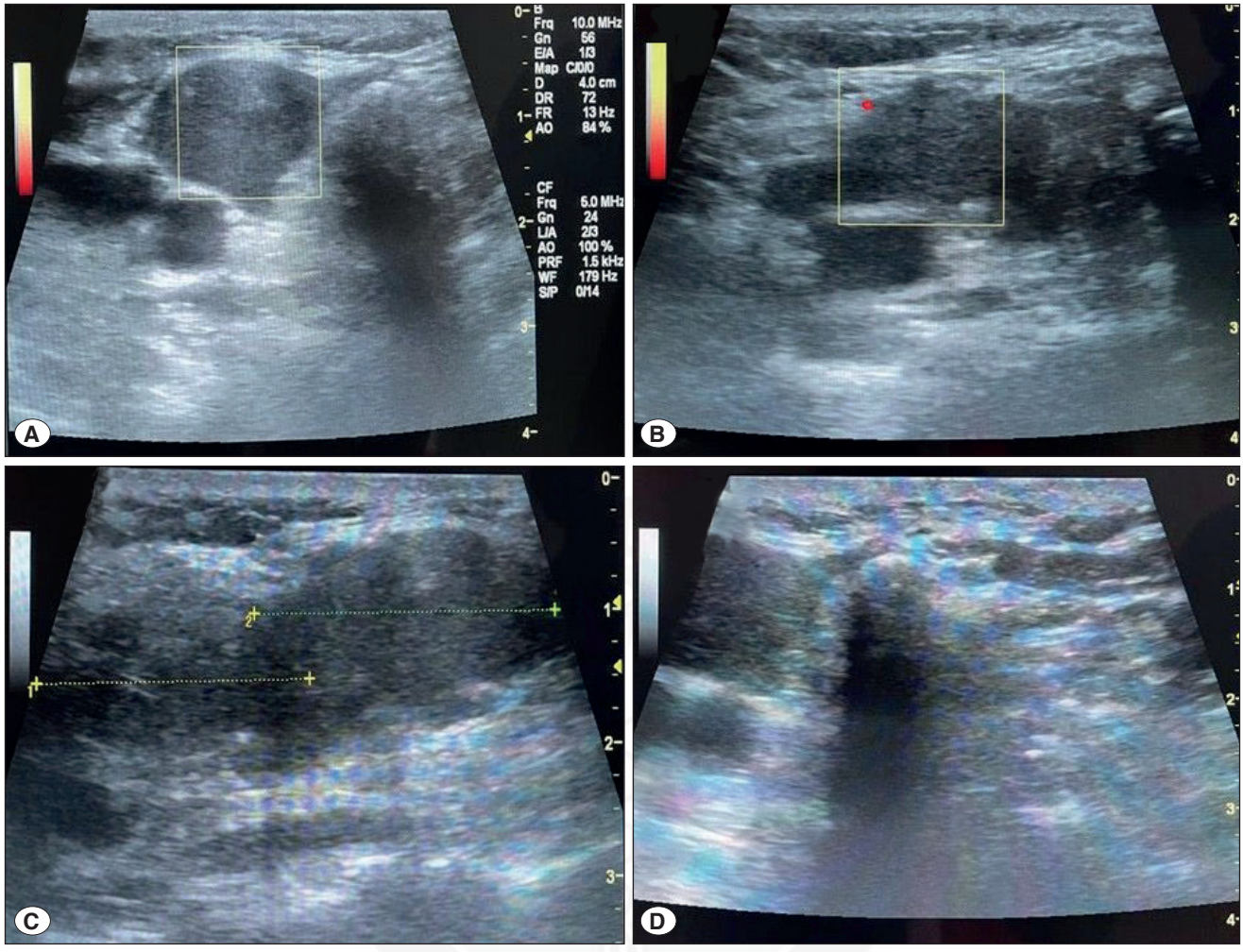


**Figure 3:** Panels (A-D) **A)** 22x14mm hypoechoic avascular lesion in right lobe similar to prior sonography images. **B)** 28x12mm hypoechoic avascular lesion in the right lobe. **C)** Longitudinal imaging of the lesions in the right lobe. **D)** No residue was detected in left lobe.

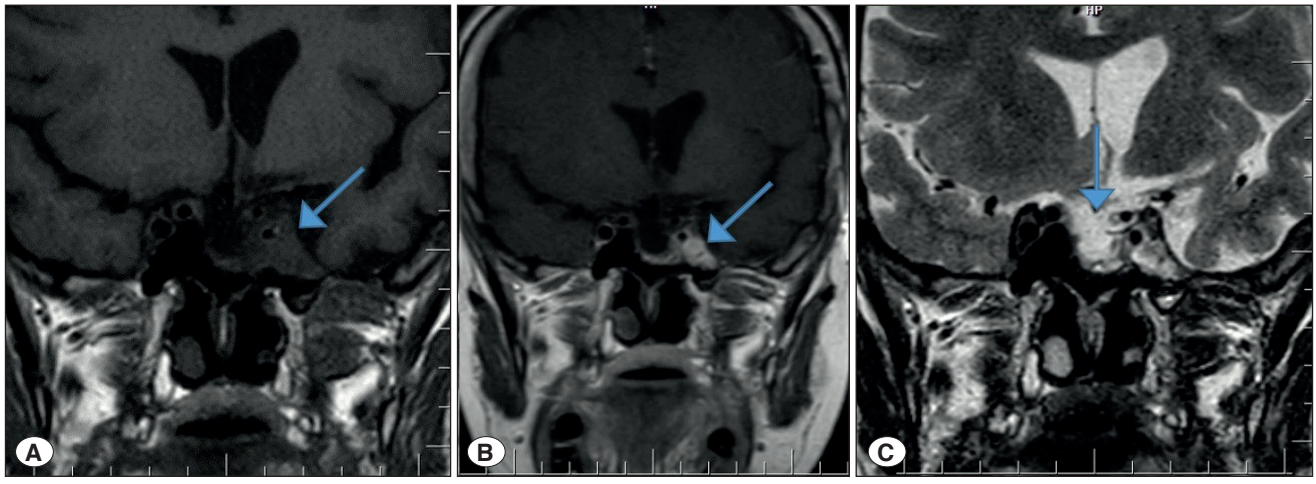


**Figure 4: A)** MRI image (T1-weighted 21x17x15mm heterogeneous contrast enhancing mass, diffusely surrounding the left optic nerve and filling the left ICA cavernous segment which is considered to be recurrence/residue. **B)** MRI image (T1-contrast enhanced heterogeneous contrast enhancement in the mass. **C)** MRI image (T2-weighted Empty sella in the right part of the pituitary gland.

## DISCUSSION

We report clinical follow-up of a patient with PTC co-existent with hypopituitarism. Our patient had preexisting pituitary insufficiency. To our knowledge, there have only been cases of thyroid cancer and hypopituitarism due to metastasis to pituitary gland or concomitant pituitary tumor.

In a case report by Vianello et al. (6) a 61-year-old woman presenting with visual field deficits and pain to the right orbit was found on MRI to have a large mass involving the pituitary gland. A transnasal biopsy confirmed metastatic follicular thyroid carcinoma. Anterior pituitary function tests showed hypopituitarism. There was no adrenocorticotropic hormone (ACTH) and cortisol response, or TSH response, after corticotropin-releasing hormone and TSH-releasing hormone administration, respectively. They used rhTSH as preparation for a series of RAI treatment and achieved a decrease in serum Tg levels accompanied by substantial clinical improvement. Despite the fact that our patient was in the low risk group according to ATA(4) guidelines, in multidisciplinary thyroid council we decided to proceed with complementary resection due to tumor being closer than 0.1 cm to the surgical border. We continued the treatment with RAI after complementary thyroidectomy but could not obtain rhTSH in our country. Since waiting for TSH to rise after LT4 reduction was not an option due to central hypopituitarism, RAI might have been ineffective in our patient.

In another case report by Gut et al. (7), a 71-year-old patient with PTC, after thyroidectomy and subsequent ablative $^{131}$I treatment was tested for TSH stimulation. Despite the 4-week LT4 withdrawal, TSH stimulation could not be achieved. There was no TSH response in the thyrotropin-releasing hormone(TRH) stimulation test, and reduced serum levels of FSH and LH, normal levels of ACTH and growth hormone (GH), and elevated level of prolactin(PRL) (1026 µIU/ml). Pituitary MRI confirmed the presence of a 34x18x16 mm tumor, growing into the sella turcica and infiltrating both cavernous sinuses. Control tests were done with the use of exogenous stimulation by rhTSH giving two doses of rhTSH, each one 0.9 mg, at an interval of 24 hours. Whole-body scintigraphy showed no pathological tracer accumulation foci, with low concentrations of Tg and anti-Tg. Much like our patient, lack of TSH stimulation was due to partial hypopituitarism caused by tumor of the pituitary gland. After total thyroidectomy due to differentiated thyroid cancer, the next step of the treatment is mostly treatment by RAI. TSH stimulation is needed to increase the uptake and accumulation of the isotope in the tumor. That is why 3–4 weeks of LT4 withdrawal is planned before the therapy. Since our patient had preexisting hypopituitarism, there was no TSH stimulation. We tried to perform an effective follow-up by keeping the fT4 level close to the upper range of normal limits in our patient.

Kuo et al. (8) reported a case of advanced PTC with pituitary ACTH-secreting tumor. A 58-year-old male patient had thyroid cancer in 1991 and presented with headache caused by pituitary tumor with apoplexy in 1993. The patient underwent RAI ($^{131}$I) for detection and treatment of PTC after the use of rhTSH in 2000, due to hypopituitarism. During follow-up for thyroid cancer, $^{201}$thallium scan proved to be an effective tool for detecting metastatic PTC in the patient without pituitary TSH reserve. Pituitary ACTH-secreting tumor was confirmed in 2001 based on the high serum ACTH level and positive immunohistochemical stain for ACTH. The patient had no cushingoid features. Moreover, serum ACTH levels were 337 and 232 pg/mL with normal serum cortisol and urine-free cortisol. Although the patient underwent three surgeries and a total of 370 mCi $^{131}$I therapy for recurrent thyroid cancer, the cancer continued to progress. Our patient had low levels of Tg so we did not scan for metastases.

In another case report by Risse et al. (9) published in 1999, a patient with PTC and hypopituitarism required rhTSH for $^{131}$I scanning with respect to subsequent therapy. The thyroid cancer had been unknown until central neurological symptoms developed, leading to the diagnosis of a huge metastasis to the sella that was the only manifestation of metastatic spread. The failure to generate endogenous TSH was overcome by the use of rhTSH for performing a $^{131}$I test. Unfortunately, the $^{131}$I uptake was not sufficient for therapy. Unfortunately, there was not sufficient RAI uptake in patient's sella tumor. Fortunately, the disease was stable after external photon beam therapy, and the Tg level had even decreased. Unfortunately, we could not use rhTSH before RAI due to lack of simple access in our country.

As mentioned above, despite our patient having low risk according to ATA (4) guidelines, we decided to follow through with complementary resection because tumor was closer than 0.1 cm to surgical border. We could not wait until TSH level rises because there was no endogeneous TSH secretion due to panhypopituitarism. When TSH reached 5 mUI/L, RAI was used without prior rhTSH supplementation. RhTSH was not easily accessible in our country. RAI might not have been effective in our patient but we tried to treat the patient to the best of our circumstances with success thus far. ATA (4) guideline also recommends rhTSH to be used in patients with underlying comorbidities making iatrogenic hypothyroidism potentially risky, in patients with pituitary disease whose serum TSH cannot be raised, or in patients in whom a delay in therapy might be harmful such as our patient. To our knowledge, we report the first patient to have RAI without TSH elevation in case of co-existence of PTC and hypopituitarism.

There is not much literature regarding thyroid cancer follow up and treatment alongside panhypopituitarism. Further research is needed, especially regarding thyroid tumorigenesis independent of TSH stimulation which is the case with our patient. The genetic alterations of PTC activate the mitogen-activated protein kinase (MAPK) pathway that promotes cell division (10). Rearrangements of the genes

coding for RET and NTRK1 tyrosine kinases, activating mutations of BRAF, and activating mutations of RAS are sequential components leading to activation of MAPK. Additional drivers include anaplastic lymphoma kinase (ALK) rearrangements, EIF1AX mutations, and mutations of the promoter region of the telomerase reverse transcriptase gene (TERT) (10). In general, any given PTC carries only a single one of these genetic changes (11). Approximately 9 percent of PTC harbor both a TERT promoter mutation plus either a BRAF or RAS activating mutation. These are more aggressive than those carrying only a single driver (12).

Despite limited literature, we closely monitor the patient and managed successfully so far with no recurrences. She had no complications as of yet. Our patient might not have an indication for complementary thyroidectomy or RAI ablation based on the previous guidelines, but we decided to do so in multidisciplinary thyroid council. Due to inadequate elevation of TSH levels both because of panhypopituitarism and lack of access to rhTSH, RAI might not have been effective in our patient. Our patient is the first patient in the literature to have RAI without TSH elevation in case of co-existence of PTC and hypopituitarism.

In summary, we report a case of PTC which was developed without TSH stimulation due to panhypopituitarism. Our patient had low risk thyroid cancer and after thyroidectomy, disease was well managed with a combination of RAI and LT4 replacement therapy. We tried to perform an effective follow-up by keeping the fT4 level close to the upper limit in our patient. Studies on the follow-up of PTC in pituitary insufficiency are limited. Complications regarding cardiovascular system like arrythmias and osteroporosis especially in elderly patients must be taken into account when adjusting fT4 levels. As mentioned before, data is limited, and there is no guideline about the management of PTC in patients with central hypothyroidism. LT4 replacement doses should be decided case by case in our opinion. More studies are needed in patients with PTC and panhypopituitarism.


## Acknowledgment

We thank to all authors for contribution to design, concept, data collection, interpretation, writing and preparing the manuscript.


## Author Contributions

Author's contributions are equal.

## Conflicts of Interest

There is no conflict of interest.


## Financial Support

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.


## Ethical Approval and Consent

Not Available.

## Review Process

Extremely peer-reviewed and accepted.

## REFERENCES


1. Jameson J, Weetman AP. Thyroid Cancer. In: Longo DL. editors. Harrison's Hematology and Oncology. 2nd ed. McGraw Hill; 2013.
2. Perez-Montiel MD, Suster S. The spectrum of histologic changes in thyroid hyperplasia: A clinicopathologic study of 300 cases. Hum Pathol 2008;39(7):1080-1087.
3. LiVolsi VA. Papillary thyroid carcinoma: An update. Mod Pathol 2011;24 Suppl 2:S1-9.
4. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26(1):1-133.
5. Casey MB, Lohse CM, Lloyd RV. Distinction between papillary thyroid hyperplasia and papillary thyroid carcinoma by immunohistochemical staining for cytokeratin 19, galectin-3, and HBME-1. Endocr Pathol 2003;14(1):55-60.
6. Vianello F, Mazzarotto R, Taccaliti A, Lora O, Basso M, Servodio O, Mian C, Sotti G. Follicular thyroid carcinoma with metastases to the pituitary causing pituitary insufficiency. Thyroid 2011;21(8):921-925.
7. Gut P, Matysiak-Grześ M, Fischbach J, Klimowicz A, Gryczyńska M, Ruchała M. Lack of TSH stimulation in patients with differentiated thyroid cancer - possible causes. Contemp Oncol (Pozn) 2012;16(3):273-275.
8. Kuo SF, Chen JY, Chuang WY, Jung SM, Chang YC, Lin JD. Concurrent papillary thyroid cancer with pituitary ACTH-secreting tumor. J Formos Med Assoc 2007;106(4):330-335.
9. Risse JH, Grünwald F, Bender H, Schüller H, Van Roost D, Biersack HJ. Recombinant human thyrotropin in thyroid cancer and hypopituitarism due to sella metastasis. Thyroid 1999;9(12):1253-1256.
10. Cancer Genome Atlas Research Network. Integrated genomic characterization of papillary thyroid carcinoma. Cell 2014;159(3):676-690.
11. Kimura ET, Nikiforova MN, Zhu Z, Knauf JA, Nikiforov YE, Fagin JA. High prevalence of BRAF mutations in thyroid cancer: genetic evidence for constitutive activation of the RET/PTC-RAS-BRAF signaling pathway in papillary thyroid carcinoma. Cancer Res 2003;63(7):1454-1457.
12. Hen X, Liu R, Xing M. A six-genotype genetic prognostic model for papillary thyroid cancer. Endocr Relat Cancer 2017;24(1):41-52.