

# The reason of high level of thyroglobulin in papillary thyroid microcarcinoma patient: Mediastinal thyroid tissue

## Papiller tiroid mikrokarsinomlu hastada yüksek tiroglobulin değerinin nedeni: mediastinel tiroid dokusu

Zeynep Gozde Ozkan<sup>1</sup>, Yasemin Sanli<sup>1</sup>, Berker Ozkan<sup>2</sup>, Artur Salmaslioglu<sup>3</sup>, Ferihan Aral<sup>4</sup>, Seher Nilgun Unal<sup>1</sup>

<sup>1</sup>Specialist of Nuclear Medicine. Istanbul University, Istanbul Medical Faculty, Nuclear Medicine Department, Istanbul, Turkey

<sup>2</sup>Specialist of Thoracic Surgery. Istanbul University, Istanbul Medical Faculty, Thoracic Surgery Department, Istanbul, Turkey

<sup>3</sup>Assoc. Professor of Radiology. Istanbul University, Istanbul Medical Faculty, Radiodiagnosics Department, Istanbul, Turkey

<sup>4</sup>Professor of Endocrinology and Metabolism Disorders. Istanbul University, Istanbul Medical Faculty, Internal Medicine Department, Division of Endocrinology and Metabolism Disorders, Istanbul, Turkey

### Abstract

Thyroglobulin (Tg) which is used as a tumor marker in differentiated thyroid carcinoma (DTC) patients can be secreted from benign tissues, along with malignant tissues due to DTC. We present a young female patient with papillary microcarcinoma of thyroid who, after total thyroidectomy, had unexpectedly high level of Tg. After diagnostic work out, the source of Tg came out to be thyroid tissue, located in mediastinum instead of a malignant focus. After resection of this tissue, Tg level diminished which led to the decision of omitting radioactive iodine (RAI) treatment which would be an unnecessary treatment option for this patient.

**Key words:** Differentiated thyroid carcinoma, thyroglobulin, radioactive iodine treatment, mediastinal thyroid tissue

### Özet

Diferansiye tiroid kanser (DTK) hastalarında tümör belirteci olarak kullanılan tiroglobulin (Tg), DTK'e bağlı malign dokuların yanında benign dokulardan da sentezlenir. Yazımızda, total tiroidektomi sonrası beklenilmeyen düzeyde yüksek Tg değeri saptanan, papiller mikrokanserli genç, kadın hastayı anlatmaktayız. Titiz bir çalışma sonucunda, hastadaki yüksek Tg değerinin, malign bir odak yerine mediasten yerleşimli rezidüel tiroid dokusundan salgılandığı saptanmıştır. Bu dokunun rezeksiyonu sonucu Tg değerinin önemli oranda düşmesi sonucu, hastada radyoaktif iyot tedavisinin gerekliliği de ortadan kalkmıştır.

**Anahtar kelimeler:** Diferansiye tiroid kanseri, tiroglobulin, radyoaktif iyot tedavisi, mediastinal tiroid dokusu

### Introduction

Total thyroidectomy, followed by remnant tissue ablation with radioactive iodine (RAI) and thyroid stimulating hormone (TSH) suppression therapy are the main treatment modalities which provide differentiated thyroid carcinoma (DTC) patients with favorable prognosis. The patient must be evaluated thoroughly in order to decide for the best possible treatment scheme.

After the operation, the residual thyroid tissue and

presence of pathologic lymph nodes should be evaluated with neck ultrasound (USG). TSH, thyroid hormones triiodothyronine (T3) and thyroxine (T4), thyroglobulin (Tg), and anti-Tg antibody (Tg Ab) levels must be measured. At initial staging just before RAI ablation treatment is given, Tg value above 30 ng/ml has been shown to be a bad prognostic factor<sup>1</sup>. Usually there is a concordance with high Tg levels and either with large remnants, remaining cervical lymph nodes, or distant metastases. When evaluations are not done

**Yazışma Adresi | Correspondence:** Zeynep Gozde Ozkan, MD  
Istanbul University, Istanbul Medical Faculty, Nuclear Medicine Department,  
Millet Cad. 34390, Capa-Fatih, Istanbul, Turkey  
e-posta: zgozdeozkan@yahoo.com

**Başvuru tarihi | Submitted on:** 14.10.2015

**Kabul tarihi | Accepted on:** 25.11.2015

well, the patients can receive unnecessary RAI treatments, have unnecessary operations, or even left untreated properly. Here, we present a case of young, female papillary thyroid microcarcinoma patient with high level of Tg after total thyroidectomy which could be explained after meticulous evaluation that led to the best possible treatment scheme for the patient.

### Case report

Thirty-one years old female patient had a total thyroidectomy, after the detection of multiple thyroid nodules in USG. Her pathology report revealed a papillary microcarcinoma follicular variant, 3mm in diameter with no invasion. She was given T4 suppression treatment immediately after the operation. She was referred to nuclear medicine department to be evaluated for RAI treatment, 2 months after the operation.

On her admittance to the out-patients' clinic, TSH level was 0.3mIU/L, Tg level was 122.7 ng/ml, and Tg Ab level was 207.6 IU/ml. Her postoperative USG report revealed no remnant tissue or cervical lymph nodes. There was a serious discrepancy between USG findings and laboratory results. Also the tumoral features (small size, non-aggressive variant, no invasion) could not explain a possible dissemination of the disease.

Knowing that a papillary thyroid carcinoma, even the tumors smaller than 1cm, make metastasis firstly to cervical lymph nodes, a new neck USG from an experienced radiologist in USG evaluation was ordered. In new USG evaluation, there was no residual tissue on the location of right lobe, but there was a remnant tissue on the location of left lobe, measured 7.5 x 4.6 x 7.7 mm. There were 2 other spherical nodular lesions, 2.6 x 2.5 mm and 4 x 2.2 mm in size, which were reported also as remnant thyroid tissues. There were also many, subcentimetric lymph nodes which were described as reactive in nature. Interestingly, caudally to right lobe location, there was a nodular lesion, 29.1 x 16.5 mm, located just cranially to jugulum with heterogenous intensity. In order to discriminate between residual thyroid tissue and pathologic lymph node, a biopsy was planned from this suspicious lesion, but the patient did not accept. Therefore, to be able to evaluate this lesion, T4 suppression therapy was withdrawn.

One month later, TSH level was 48.35 mIU/L, free T4 level was 9 pmol/l, free T3 level was 3.7 pmol/l, Tg level was 210.7 ng/ml, and Tg Ab level was 152.6 IU/ml. High levels of T4 and T3 in an athreotic patient made the lesion that was located in jugulum more likely to be residual thyroid tissue. In the RAI uptake study with 50  $\mu$ Ci iodine-131, the uptake values, measured in 1.-2.-24.hours, were 7.47%, 9.35%, 26.79%, respectively. On

thyroid scintigraphy, there were 2 faint foci of RAI in the location of left lobe and an intense focus, located caudally in right lobe location (**Fig. 1**). With these findings, the lesion, located in the jugulum was thought to be a remnant thyroid tissue, but in order to eliminate any distant metastasis of papillary thyroid cancer due to very high Tg level, a fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) imaging was ordered.

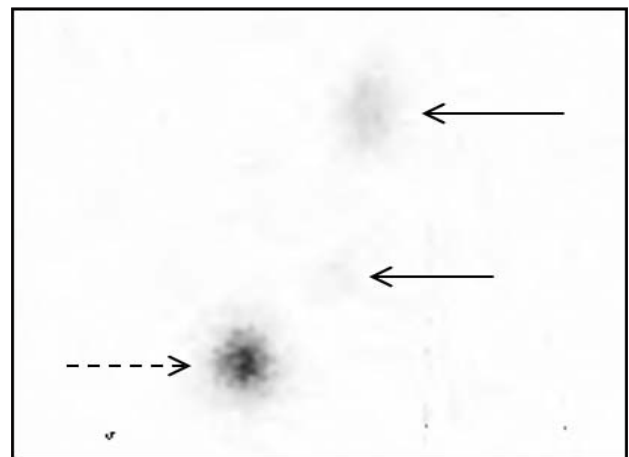
On FDG PET-CT, the only pathological uptake (SUVmax: 5.2) was seen in the lesion, 3.2 x 2 x 4.5 cm in size, located in right paratracheal region on the level of jugulum and extended inferiorly to arcus aorta (**Fig. 2**). This lesion, located in anterior mediastinum was determined to be the only macroscopic foci which produced Tg. The resection of this lesion was planned.

In the operation, after partial upper sternotomy, the lesion located in anterior mediastinum was resected. The histopathologic evaluation revealed benign thyroid tissue. 2 weeks after the operation, TSH level was 59.22 mIU/L, Tg level was 11.18 ng/ml, Tg Ab level was 42.93 IU/ml.

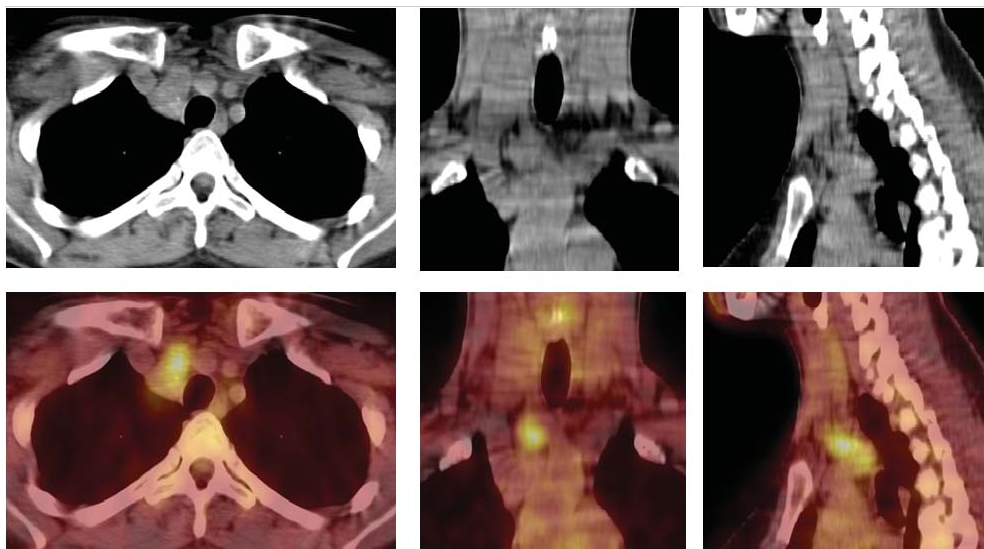
As the result, the tumor of our patient was 3mm in diameter with no invasion or metastasis. Therefore we decided to omit RAI and follow the patient with TSH suppression treatment.

### Discussion

High level of Tg values point out metastatic disease or unsuccessful ablation of the thyroid remnant in a DTC patient. Although these are malignant causes of high Tg levels, there are also some benign causes. Ectopic thyroid tissues and TSH-stimulated thymus may be reasons for high Tg level in a patient with no pathologic



**Figure 1.** In the location of left lobe there are 2 faint foci of RAI (arrows), whereas there is an intense focus, located caudally in right lobe location (dashed arrow) in iodine-131 thyroid scintigraphy of the patient



**Figure 2.** Axial (left column), coronal (middle column), sagittal (right column) images of FDG PET-CT show the lesion, 3.2 x 2 x 4.5 cm in size which is located in right paratracheal region on the level of jugulum and extended inferiorly to arcus aorta with high FDG uptake (SUVmax: 5.2).

foci of Tg production<sup>2</sup>. High level of Tg due to thyroglobulinemia, normally seen in early postoperative period, is a transient rise which usually lowers in couple of weeks. Another benign reason for high Tg level is laboratory error that occurs on the presence of Tg Ab, depending on the immunoassay method used in the laboratory<sup>3</sup>. Although there are benign reasons for high Tg values, the exclusion of malignant reasons must be done in order to perform best treatment scheme in a DTC patient. At the initial stage, before RAI ablation therapy is given, high Tg level, such as above 30 ng/ml, is just not a bad prognostic factor<sup>1</sup>, but also arise suspicion for more disseminated disease as in our case.

In our patient, the histopathologic evaluation of thyroidectomy revealed a papillary microcarcinoma, 3 mm in diameters, without any aggressive component. Neither in the preoperative nor in the postoperative neck USG reports, there was any comment on metastatic lymph nodes. Normally, such a patient who can be classified as having low-risk disease, has low level of Tg, after thyroidectomy. When in our patient, Tg level was measured as 122.7 ng/ml under TSH suppression therapy, the discrepancy between laboratory results and USG findings should have been resolved. Repetition of USG imaging which is very operator-dependant showed us a nodular lesion which could be related with residual thyroid tissue or metastatic lymph node both of which could explain high Tg level in our patient. Both in the initial evaluation and also in the follow-up of DTC patients, USG evaluation should be done by a specialist who is experienced in this field. American Thyroid Association (ATA) guidelines for DTC suggests FDG

PET-CT for initial evaluation of patients with high Tg levels which cannot be explained by radiologic modalities for determining possible metastatic spread of the disease<sup>4</sup>. We also performed FDG PET-CT which revealed no such foci to exclude any other pathologic sites that could not be shown by USG imaging in our patient.

When USG, iodine uptake test, thyroid scintigraphy, T3-T4 levels, and FDG PET-CT results of our patient were evaluated, high Tg level was correlated with residual thyroid tissue in anterior mediastinum. Although big remnant tissues which produce high level of Tg that will hamper the follow-up of DTC patient can be ablated with multiple RAI treatments, the best possible treatment modality seems to be the resection of this remnant tissue, especially in a patient like ours with low-risk disease who normally does not require RAI ablation treatment.

Thyroid tissue, located in mediastinum, can either be primary ectopic thyroid tissue or extension of cervical goiter. Primary ectopic thyroid tissue is very rare, accounting less than 1% of goiters<sup>5</sup>. It is usually located in anterior mediastinum, although 10-15% of these tissues may be located in the posterior mediastinum<sup>6</sup>. In the literature, there are many case reports about mediastinal primary ectopic thyroid tissues with no anatomical connection to normally located cervical thyroid tissues<sup>5,7-12</sup>. The mediastinal thyroid tissue that was resected in our patient was probably an ectopic thyroid tissue, located in anterior mediastinum because there was not any information about extension of cervical thyroid tissue towards mediastinum in the surgery report of total thyroidectomy.

As a conclusion, initial evaluation of DTC is important which requires a team work that combine the findings of radiologic (especially USG evaluation, performed by an experienced radiologist) and scintigraphic modalities with laboratory data. Discrepancies between these data must be solved before preceeding with important therapeutical decisions.

Conflict of interest: The authors declare no conflict of interest.

## References

1. Toubeau M, Touzery C, Arveux P, et al. Predictive value for disease progression of serum thyroglobulin levels measured in the postoperative period and after 131I ablation therapy in patients with differentiated thyroid cancer. *J Nucl Med* 2004;45:988-94.
2. Zanotti-Fregonara P, Keller I, Calzada-Nocaudie M, et al. Increased serum thyroglobulin levels and negative imaging in thyroid cancer patients: are there sources of benign secretion? A speculative short review. *Nucl Med Comm* 2010;31:1054-8.
3. Ma C, Kuang A, Xie J, Ma T. Possible explanations for patients with discordant findings of serum thyroglobulin and 131I whole-body scanning. *J Nucl Med* 2005; 46: 1473-80.
4. Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1-48.
5. Lee WS, Kim YH, Chee HK, et al. A 7.3×5.3×3.5-cm heterotopic thyroid in the posterior mediastinum in a patient with situs inversus totalis. *J Thorac Dis* 2014;6:E39-42.
6. Madjar S, Weissberg D. Retrosternal goiter. *Chest*. 1995;108:78-82.
7. Karapolat S, Bulut I. Ectopic posterior mediastinal thyroid: a case report. *Cases J* 2008;1:53.
8. Demirhan R, Onan B, Oz K, Keser SH, Gul AE, Onan IS. Posterior mediastinal ectopic thyroid: an unusual cause for dysphagia. *Ann Thorac Surg* 2009;88:656
9. Mace AD, Taghi A, Khalil S, Sandison A. Ectopic sequestered thyroid tissue: an unusual cause of a mediastinal mass. *ISRN Surg* 2011;2011:313626.
10. Abdel Aal M, Scheer F, Andresen R. Ectopic mediastinal thyroid tissue with a normally located thyroid gland. *Iran J Radiol* 2015;12:e7054.
11. Wang J, Fang J. Ectopic thyroid mass in the left lateral neck and anterior mediastinum: a case report. *J Med Case Rep* 2014; 8: 351.
12. Kamaleshwaran KK, Rajan F, Asokumar P, Mohanan V, Shinto AS. Mediastinal ectopic benign colloid goiter detected using iodine-131 whole body scintigraphy and single-photon emission computed tomography-computed tomography. *Ind J Nucl Med* 2015; 30: 180-2.