

# Lymphatic Metastasis of Papillary Thyroid Carcinoma Involving Submandibular Lymph Node in a Skip Pattern: Case Report

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## ÖZET

Papiller tiroid karsinomun submandibüler lenf nodunu içeren skip tarzda lenfatik metastazı: Olgu sunumu

**Amaçlar:** Submandibüler lenf nodlarını içeren servikal lenf nodu skip metastazı yapan papiller tiroid karsinom (PTK) olgusu sunumu.

**Gereç ve Yöntem:** Ümraniye Eğitim ve Araştırma Hastanesinde takip edilen PTK olgusunun sunumu ve literatürel değerlerle tartışması.

**Bulgular:** 20 yaşında bayan hasta mobil, semisolid ve 3x3cm'lik boyun kitlesi şikayetiyle polikliniğe başvurdu. Boyun USG'sinde; sol süpraklaviküler bölge ve sol juguler zincir boyunca multipl lenfadenopatiler (LAP) ve sol submandibüler bez arkasında (bölge IB) tek bir lenfadenopati gözlemlendi. En belirgin LAP'sinden yapılan ince iğne aspirasyon biyopsisi PTK metastazı olarak sonuçlandı. Hastaya genel anestezi altında, horizontal T insizyonu ile total tiroidektomi ve sol fonksiyonel boyun diseksiyonu yapıldı. Patoloji sonucuna göre sol tiroid lob üst kısmında ekstrakapsüler ve ekstratiroidal invazyon gösteren iyi diferansiyeli PTK kitlesi raporlandı. Ayrıca submandibüler bölgede (bölge 1B) ekstrakapsüler PTK metastazlı iki adet lenf nodu; bölge III'te iki adet ve bölge IV'te beş adet ekstrakapsüler yayılım göstermeyen lenf nodu tutulumu skip tarzda gözlemlendi. Santral kompartmanda (bölge VI) herhangi bir metastatik lenf nodu görülmedi. TNM evrelemesi T4N1M0 (ekstratiroidal invazyon ve lenf nodu metastazı mevcut fakat uzak metastaz yok) olarak belirlendi. Hastaya postoperatif 1. ayında bir kez 150 mci RAI-131 terapisi verildi ve sonrasında günde tek kullanımlık Levotiron tedavisi başlandı.

**Sonuçlar:** İnce iğne aspirasyon biyopsisi boyun kitleleri için kabul edilebilir bir tanı yöntemidir. PTK skip tarzda bir servikal boyun metastazı yapabilir. Literatürün tersine, olgumuzda santral kompartmanda (bölge VI) lenf nodu metastazı gözlemlenmedi. Literatürdeki hiçbir çalışmada henüz submandibüler üçgende lenf nodu metastazıyla karşılaşılmaışken bizim olgumuzda bölge IB'de ekstrakapsüler yayılımı olan iki adet lenf nodu metastazı ve bölge III-IV'de multipl lenf nodu tutulumu gözlemlenmiştir. Bu sebeple, bu klinikteki hastalara bölge I-VI arasında içeren bir fonksiyonel boyun diseksiyonu yapılmalıdır.

**Anahtar kelimeler:** Papiller tiroid karsinom; ince iğne aspirasyon biyopsisi; fonksiyonel boyun diseksiyonu; submandibüler bez; skip metastaz.

Ümraniye Tıp Dergisi 2009;2:113-118

## ABSTRACT

Lymphatic metastasis of papillary thyroid carcinoma involving submandibular lymph node in a skip pattern: Case report

**Objectives:** We report a case of papillary thyroid carcinoma (PTC) with cervical lymph node metastasis involving submandibular lymph node (LN) in a skip pattern.

**Study Design and Methods:** A case of PTC which was followed in Ümraniye State Hospital for Research and Training and discussed with the knowledge of literature.

**Results:** 20 years old female patient applied to outpatient clinic with a complaint of mobile, painless, semisolid and 3x3 cm sized neck mass. Multiple lymphadenopathies (LAP) were imaged at left supraclavicular region and along left jugular chain; and a LAP was observed behind the left submandibular gland (level IB) at her neck USG. The fine needle aspiration biopsy (FNAB) of the properly marked lymph node resulted as PTC metastasis. Under the general anesthesia and with a horizontal T incision, total thyroidectomy and left functional neck dissection (FND) were performed. According to pathology report: there was a well-differentiated PTC mass at the superior part of left thyroid lobe. There was extracapsular and extrathyroidal invasion. PTC metastasis in two LN at the level 1B (submandibular region) with extracapsular invasion; in two LN at the level III and in five LN at the level IV without extracapsular invasion were seen in a skip pattern. There was not any metastatic lymph node at central compartment. The TNM staging system was T4N1M0 (extrathyroidal invasion, lenf nodu metastazı and not distant metastazı). The patient had 150 mci RAI-131 therapy once at postoperative first month. After then the patient began to take Levotiron once a day.

**Conclusions:** FNAB is an acceptable diagnostic method for a neck mass. The PTC may have a cervical lymph node metastasis in a skip pattern. On the contrary to the literature, we did not observed any LN metastasis in central compartment (level VI). LNs metastasis in submandibular triangle have not yet seen in any study. In opposition to these results, we observed two submandibular LNs (level IB) metastasis with extracapsular invasion accompanied to involvement of the nodes of lateral neck (level III-IV). Therefore the patients should undergo FND, including level I-VI.

**Key words:** Papillary thyroid carcinomas; fine needle aspiration biopsy; functional neck dissection; submandibular gland; skip metastasis

Ümraniye Tıp Dergisi 2009;2:113-118

## INTRODUCTION

Thyroid neoplasms are uncommon in the general population. They occur with a frequency of

1-1.5%. These ratios include only the clinic cases, but if micropapillary carcinomas are also considered, there will be an increase in their prevalence. The thyroid gland neoplasms can be classified as well-differentiated thyroid cancer (90%), medullary carcinoma (7%), anaplastic carcinoma (3%) and the others. The well-differentiated thyroid cancer may also be subclassified as papillary (80%), follicular (10%), papillary microcarcinoma and Hurtle cell carcinoma. Papillary thyroid carcinomas (PTC) arise from hormone secreting cells of thyroid gland.

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Kabul tarihi / Date of acceptance:  
17 Temmuz 2009 / July 17, 2009

They are not inheritable. Their prevalence increase with radiation exposure. PTC are the common (60-80%) and well prognosed type of thyroid neoplasm. They are especially seen in female patients over 35 years old. PTC are usually multifocally located and generally unencapsulated or pseudocapsulated. They have intraglandular invasion (1).

Thyroid fine needle aspiration biopsy (FNAB) is the gold standard diagnostic modality for evaluating patients with a thyroid nodule. The majority of FNAB today is performed in the outpatient clinic, freehand by palpation. There are, however, limitations to the palpation guided approach, including difficulty sampling nodules that are small or non-palpable, indistinct, posterior or deep in location, and cystic. These factors lead to an unsatisfactory cytology rate that is between 5% and 43.1% (2,3,4) Recently, the use of ultrasonography (USG)-guided FNAB has facilitated the detection and diagnosis of papillary carcinomas, even when the tumor measures 10 mm or less in its maximal diameter (5).

Many studies have shown a high percentage of metastatic lymph nodes in well-differentiated thyroid cancer (WDTC) ranging from 30% to 80% (6,7). Papillary thyroid carcinoma (PTC) tends to metastasize through the lymphatic system. Cervical lymph node (LN) metastasis is found in 40% to 60% of patients at the time of diagnosis (8). Several researchers have addressed the question of whether there is a correlation between cervical metastatic disease and survival. While previous studies failed to show any association, recent publications have shown that positive lymph nodes have a prognostic value. Nodal involvement is currently considered as indicative for poor prognosis (9). Male gender, over 40 years in male, over 50 years in female, under 20 years in both gender and tumor size <4cm are other poor prognostic factors.

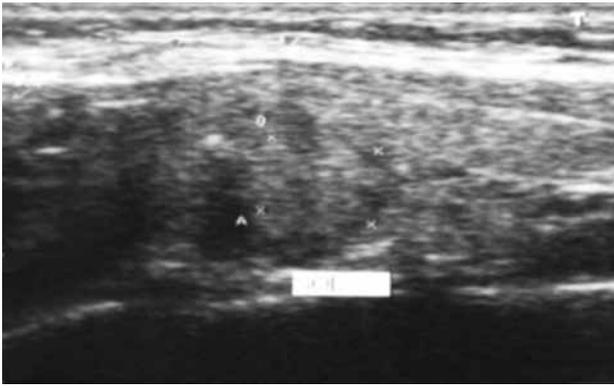
PTC has an excellent prognosis with 10-year survival rate of over 90% of patients. These outstanding results have raised a question regarding the extension of surgical intervention in the neck with clinical findings of metastases. Several options have been suggested addressing positive lymph nodes in the neck, ranging from refrain from any surgical

intervention, through random lymph node biopsy, i.e., "berry picking" (removal of gross metastatic nodes that could be found at the surgical bed of the thyroid), sentinel lymph node biopsy, and neck dissection. Neck dissection (ND) was proposed at a variety of extensions, including radical ND, modified ND, and various selective ND (10,11,12,13). The pattern of regional metastasis spread from WDTC is crucial to determine the extent of neck dissection needed to be performed in patients with clinical regional metastasis (14,15,16). In many cases, these lymph nodes do not appear abnormal by inspection or radiologic imaging. The highest incidence of metastases occurs in the central neck, but the lateral neck is often involved as well (17,18,19). For this reason; many surgeons recommend systematic central neck dissection (level VI) or modified neck dissection (levels II-V) as opposed to "berry picking" of grossly involved nodes, given the high rate of microscopic metastases (20) and the increased surgical morbidity of subsequent re-operation. Mitigating against a more aggressive approach, surgical risks may increase with the extent of surgery. This is particularly true in the central neck because of the location of the parathyroid glands and recurrent laryngeal nerves (21,22). But there are still few studies that address this issue and insufficient data regarding the pattern of spread of cervical metastasis in PTC (14,15,16).

In this case report, we evaluated the pattern of spread to regional lymph nodes metastasis of PTC in patients presenting with clinically positive nodes.

## CASE REPORT

20 years old woman referred to outpatient clinic of otorhinolaryngology department at Ümraniye State Hospital For Education and Training with a complaint of neck mass. This mass has grown in 7-8 months period. There was a mobile, painless, semisolid, 3x3 cm sized mass at the left side of neck and 2 cm below the mandibular angle in physical examination. There were also multiple palpable lymph nodes along jugular chain. The physical examination of other organs were in normal pattern. Than a neck USG was ordered; multiple lymphadenopathies (LAP),

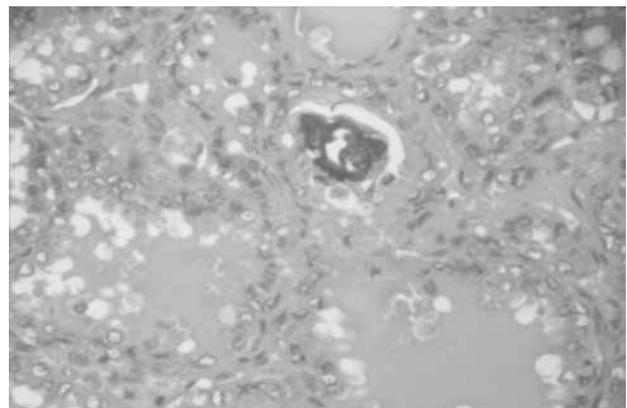


**Figure 1: Lymph nodes at the posterior of left submandibular gland (level 1B)**

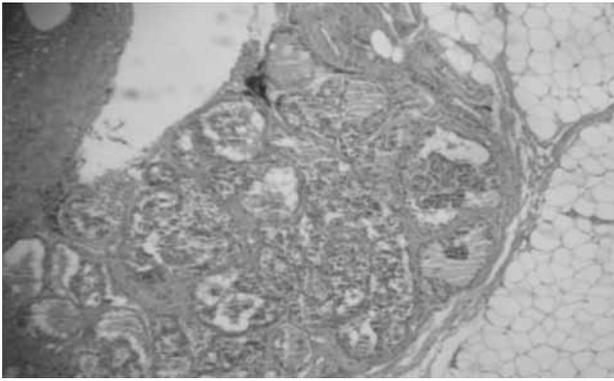
whose biggest was 26x24 mm sized, were imaged at left supraclavicular region and along left jugular chain. A 29x15mm sized LAP was observed behind the left submandibular gland (level 1B) (Figure 1). A few hypoechoic milimetric nodules were imaged at lower pole of left thyroid lobe. After that, a neck computerised tomography (CT) with intravenous contrast scanned to obtain details about lesion's location and size. CT resulted as: a lobulated, cystic and 38x40x56mm sized mass at left carotid region and at anterolateral side of internal carotid artery (ICA) and external carotid artery (ECA). A USG guided FNAB of the properly marked LN was done to make approximate diagnosis. FNAB resulted as papillary thyroid carcinoma metastasis. The patient has hospitalised to prepare to the operation.

Under the general anesthesia, the horizontal T incision was made from left mastoid process and clavicular median part to the thyroid lobe. During total thyroidectomy, recurrent nerves and parathyroid glands were meticulously identified and preserved in situ. Metastases to the neck were further evaluated with respect to the levels of the neck as described by Robbins et al. (23). For the purposes of operative planning, the neck was considered to have four compartments: the left lateral compartment consisting of the lymph nodes along the jugular vein from the level of the hyoid superiorly to the level of the clavicle inferiorly (levels II, III and IV), the left central compartment consisting of the paratracheal nodes from the carotid artery laterally to the midline of the trachea and the cricoid

superiorly to the innominate artery inferiorly (level VI), the left posterior triangle (level V) and the left submandibular area (level 1B). This has included some of the upper portion of level VII in some instances, but sternotomy was never performed nor necessary to achieve this inferior limit of dissection. During neck dissection, the lymphatic tissues at the level 1B, 2, 3, 4, 5, 6 and superior mediastine and the fascia of jugular vein are dissected and the FND was completed by conserving the SKM, IJV and SAN. Patient remained hospitalized for 2 night to monitor for hypocalcemia but there was not any pathology about blood Ca level. The specimen send to pathology department in two pieces: total thyroidectomy part and FND part. The neck dissection specimens were separated during surgery into levels and also sent to pathology as separate specimens. This provided an accurate description of the nodal disease in the neck according to the levels of the neck. According to pathology report: there was a 2x1.5x0.6mm sized, well-differentiated thyroid papillary carcinoma mass at the superior part of left lobe with view of pathologic psammomatous calcification (Figure 2). There was extracapsular and extrathyroidal invasion (invasion to perithyroidal fatty tissue and strap muscles) but there was not any central tumoral necrosis (Figure 2). The mean nodal yield (total number of nodes that were removed at ND) was 25 nodes and the mean number of pathologic nodes in ND specimen was 9; papillary carcinoma metastasis in two LN at the level 1B



**Figure 2: View of psammomatous calcification in the papillary thyroid carcinoma (Hematoxylin-eosine staining (H+E); 200X).**



**Figure 3: Lymph node metastasis of papillary thyroid carcinoma at Level 1B with pericapsular invasion (H + E ;100X).**

(submandibular region) with extracapsular invasion (Figure 3), papillary carcinoma metastasis in two LN at the level 3 and in five LN at the level 4 without extracapsular invasion. There was not any metastatic lymph node at central compartment. There was reactive hyperplasia in other LNs. The primary tumor size according to the TNM staging system for thyroid cancer of the American Joint Commission on Cancer (24) was T4N1M0 (extrathyroidal invasion, lenf node metastasis and not distant metastasis). There was not any postoperative complications like hypocalcemia, hematoma or bleeding. The patient had 150 mci RAI-131 therapy once at postoperative first month. After then the patient began to take Levotiron once a day.

## DISCUSSION

The guidelines of the American Association of Clinical Endocrinologists indicate that LN involvement in PTC generally begins with the LNs of the central compartment of the neck followed by the nodes of the lateral neck and superior mediastinum . Therefore, it is important to determine whether central LN metastasis is present (25).

Wang T.S. et al.(26) reported that the incidence of central compartment LN metastasis in cases of well-differentiated thyroid carcinoma between 20 and 90%. They described that the reasons for this wide range of metastatic disease are unclear, and controversy remains regarding whether elective central compartment LN dissection should be performed at the time of thyroidectomy.

In a prospective study reported by Hisham et al. (27), central compartment selective lymphadenectomy at the time of the primary thyroidectomy has been shown to be safe and without a higher morbidity rate compared with thyroidectomy alone (28, 29). However, elective central compartment LN dissection may induce unnecessary complications such as hypocalcemia and recurrent laryngeal nerve palsy. Thus, it will be reasonable to perform elective central compartment LN dissection after predicting the presence of metastasis to central compartment LN.

On the contrary to these studies, there was not any LN metastasis in central compartment (level VI) in our case report.

It is generally accepted that prognosis depends on LN involvement, tumor multifocality, capsular or vascular invasion, and tumor size. Ozaki et al. (30) and Sampson et al.(31) reported that there were clinical correlations between central LN metastasis and capsular invasion. The size of the tumor in PTC is a significant predictive factor for central compartment LN metastasis. Despite the thyroid capsular invasion and 2x1.5x0.6mm tumor size, we did not encounter any LN metastasis in central compartment in our case.

Sang- Hyuk Lee et al. (32) emphasized that the relationship between lateral LN involvement and central compartment metastasis would be expected because LN metastasis begins with the central compartment of the neck and is followed by involvement of the nodes of the lateral neck and the superior mediastinum. They suggested that lateral LN metastasis may be accompanied by central compartment LN metastasis. As we did not get any LN metastasis in central compartment beside our predictive involvement of the nodes of the lateral neck, our findings are not compatible to these studies.

Kupferman et al. (14) studied the pattern of thyroid cancer metastasis and they examined neck dissection specimens of 39 patients and showed that there was a high rate of metastases to the lateral neck, of which level III had the most prominent involvement (57%), and the posterior neck had high involvement as well (20%). There is no report regarding the extent

of metastasis in the central compartment or in the submandibular triangle at that study. Pingpank et al. (16) showed a similar pattern of distribution to the lateral and posterior neck; however, the rates of metastasis were higher: level III, 76%; level IV, 59%; level IIa, 43%, and level V, 28%. They did not observe any LN metastasis in submandibular triangle. In opposition to these results, we observed two submandibular LNs (level IB) metastasis with extracapsular invasion accompanied to involvement of the nodes of lateral neck (level 3-4).

Yoav Yanir et al.(33) demonstrated that patients with clinical evidence of regional metastasis in the posterolateral neck have high rates of metastases to the central compartment (95%). Their data also demonstrated significant involvement of the lateral neck, especially to level III and IV, with 68% and 57%, respectively, followed by 54% of level II. The amount of metastasis at level II in the that study, 54%, was found to be significant and similar to previous data. While most of the disease was found at level IIa, there were two patients (7%) who had metastasis at level IIb, above the spinal accessory nerve. It is interesting to note that one of the patients had metastasis in level IIb with no disease at level IIa. Pingpank et al.(16) also reported a high rate of lymph nodes metastasis at level IIb (21%) of whom three patients out of seven had disease above the accessory nerve with no metastasis below the nerve. Additionally, in 7 out of 38 patients, there was an intervening node level without disease, they called it "skip metastasis." Thus the author recommends anterior and posterolateral neck dissection for patients with lateral neck metastases of PTC. The skip metastasis

may also be acceptable for our case because there were LNs metastasis only in level 1B, III and IV which were not correlated with suitable order of LNs metastasis.

The size of the primary thyroid tumor had been previously studied as a prognostic factor (34,35,36). Reddy et al. (34) showed that lymph node metastasis does not correlate with tumor size in T1 differentiated thyroid carcinoma. Machens et al.(36) found that the cumulative risk of lymph node metastasis increased linearly with increasing tumor diameter. Moreover, a correlation was found between the tumor size and the risk for distant metastasis. Our findings are in agreement with Machens et al. who suggested a correlation between primary tumor size and number of metastatic node.

According to Wada et al. (18) and Ito et al. (37), tumors located at the superior portion of the thyroid gland are likely to metastasize to the lateral neck LN. The same result was also observed in our case that there was lateral neck's LNs metastasis accompanied to superior location of thyroid papillary carcinoma.

## CONCLUSIONS

- 1) Patients with PTC and not clinical positive nodes metastasis at level IB.
- 2) The rate of metastases is also high at the lateral neck (level III-IV).
- 3) The skip metastasis including level 1B, III and IV involvement.
- 4) Therefore these patients should undergo FND, including level I-VI.
- 5) FNAB is an acceptable diagnostic method.

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