CLINICALLY UNDETECTABLE OCCULT THYROID PAPILLARY CARCINOMA PRESENTING WITH CERVICAL LYMPH NODE METASTASIS

E. Tastekin^{1,*}, N. Can¹, S. Ayturk², M. Celik², F. Ustun³, S. Guldiken², A. Sezer⁴, H. Celik², M. Koten⁵

Trakya University, Faculty of Medicine, ¹Department of Pathology, ²Department of Endocrinology, ³Department of Nuclear Medicine, ⁴Department of General Surgery, ⁵Department of Otorhinolaryngology, Edirne, Turkey

Abstract

Background. Occult papillary thyroid carcinoma presented as isolated cervical lymphadenopathy without clinical and radiologic findings has been rarely reported.

Case report. A 47 years old female patient admitted to otorhinolaryngology clinic with 4X3 cm sized cervical mass. Physical examination of the patient was noted as a nontender, firm, mobile lymph node at right lateral cervical region. There was no inflammatory or infection disease in the history of patients anamnesis and no abnormal value on laboratory tests. Ultrasound screening of the neck detected a lymph node with suspicious features for malignancy. Head and neck examination was normal and there is no evidence of a tumoral mass or nodule in the thyroid gland. Whole body scan of MRI showed no pathologic sign both in the neck and body. Excisional biopsy was performed and revealed a carcinoma with papillary morphology. Immunohistochemical staining features of the tumor confirmed a papillary carcinoma derived from the thyroid gland. Second look USG of the neck and thyroid was performed but it revealed no tumoral mass. The patient underwent total thyroidectomy with right functional and central lymph node dissection. Histological examination of the thyroid gland showed multicentric 2 mm sized, three foci of papillary carcinoma located in bilateral thyroid lobes and metastatic lymph nodes in the right side of the neck.

Conclusion. A metastatic cervical lymph node can be evidence of a clinically undetected occult papillary thyroid carcinoma. Specific immunohistochemistry staining of specimen may lead to appropriate surgery and progression of carcinoma may be hindered by application of additional RAI therapy.

Key words: Thyroid, papillary carcinoma, papillary micro-carcinoma, occult carcinoma.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common tumor of the thyroid. The subgroup of PTCs

named as occult/micropapillary tumors are less than 10 mm sized, usually indolent and have good prognosis over 20 years survival at a rate of 90% or better (1, 2). But, sometimes, especially multifocal carcinomas can exhibit aggressive behavior (1-4). Retrospective surgical series reported the highest incidence of occult carcinomas at 49.9% of 860 cases (5). PTCs most often do metastasis initially via lymphatic to the regional lymph nodes (LN) (6).

CASE REPORT

A forty seven-year-old female patient admitted with painless swelling on the right side of the neck. A nontender, firm, mobile LN was noted as at lateral cervical region. There was no inflammatory disease in the anamnesis and no abnormal value on laboratory tests. Ultrasonography detected a LN with suspicious features for malignancy but no evidence of a mass/nodule in the thyroid. Nasopharyngeal videoendoscopic examination revealed no mass. Ultrasonography detected a 4X3 cm sized, spherical, hypoechogenic, cervical LN including indistinct hilus and microcalcification, on the right cervical region which indicates suspicion for malignancy. The entire neck ultrasonography showed no evidence of a tumor mass/nodule in the thyroid gland. Thoracic, abdominal and pelvic CT showed no pathologic sign such as another lymphadenopathy or tumoral focus. Cervical lymphadenectomy was performed by Otorhinolaryngology Department due to these findings. Macroscopically, a 4X4 cm sized LN with white colored, heterogeneous cut surface was detected. Parafine tissue blocks were prepared after fixation and routine processing steps. Slides were stained with haematoxylin eosin. Histologically, the architecture of LN was completely destroyed by an infiltrating tumor with complex branching papillary morphology

*Correspondence to: Ebru Tastekin, Assist. Prof., MD, Trakya University, Faculty of Medicine, Department of Pathology, 22030, Edirne, Turkey, E-mail: ebrutastekin@hotmail.com

(Fig. 1A). Fibrovascular stalks were lined by cuboidal epithelial cells. The tumor cells had nuclear crowding and overlapping with finely dispersed optically clear chromatin, micro nucleoli and nuclear grooves.

Careful examination and anamnesis of the patient demonstrated an oophorectomy performed 18 years ago and diagnosis was not known. In order to exclude tumors which may make metastases to cervical LN

Figure 1. Carcinoma metastasis in lymph node (A) and occult papillary carcinoma focus in the thyroid (H&EX12.5).

Figure 2. Carcinoma metastasis with papillary morphology in lymph node (red arrow: pseudoinclusion, blue arrow: groove) (H&E, AX50,B:X200). Immunoperoxidase stainings supported the papillary carcinoma metastasis arised from the thyroid (c: thyroglobuline abX400, d:TTF-1 abX200).

with papillary features, immunohistochemical stains were applied. Tumor showed positive reaction with cytokeratin-7, cytokeratin-19, TTF-1, thyroglobulin, HBME-1 and galectin-3 (Fig. 2); but it did not stain with WT-1, CA125 and p53 antibodies. The LN was diagnosed as “metastasis of papillary carcinoma; primarily compatible with PTC accompanied by immunohistochemical results”. After, the patient was referred to second look USG of the neck and thyroid was performed but revealed no tumoral mass. Laboratory findings were compatible with euthyroidism (fT4: 1.5 (0.8-1.8 ng/dL) fT3 3.1 (2-4.2 pg/mL) TSH: 1.2 (0.55-4.78 uIU/mL) ATPO: 24 (0-60IU/mL) ATGL: 30.5 (0-60 IU/mL). Tc-99m-pertechnetate-scintigraphy showed a normal thyroid gland and MRI investigation was performed. The screening modalities could not be able to detect a mass in scanning of neck or entire body. Total thyroidectomy central LN and right sided level 2-5 LN dissection were performed and evaluated in

pathology laboratory. Three foci of multicentric 2 mm sized PTCs were detected, two of them in the left lobe and one in the right lobe. One tumor in the left lobe was an encapsulated follicular variant and others were a locally invasive classical variant (Fig. 1B). These tumor foci revealed characteristic nuclear features of PTC as pseudoinclusions, grooves, clearing etc. and stained with mesotel cell and galectin antibodies (Fig. 3). All foci had free surgical margins without evidence of extrathyroidal extension. Twenty-one LNs were dissected from lateral level 2-5 neck. 10 of 21 LNs were metastatic in levels 2 and 4. The pathological stage was determined as pT1aN1bMx. The patient was discharged on postoperative 3rd day uneventfully. Whole body scan revealed no residual thyroid tissue and metastatic foci on postoperative 4th week. The patient underwent RAI ablation therapy (100 millicuries) 3 and 6 weeks after surgery and lifelong thyroxine suppression therapy was planned (dose

Figure 3. Histomorphologic appearance of papillary carcinoma in the thyroid. Typical nuclear features of papillary thyroid carcinoma (red arrow: pseudoinclusion, blue arrow: groove)(A,B:H&EX400). Tumor was shown diffuse strong membranous staining with Mesotel cell (AX400) and nuclear-cytoplasmic staining Galectin 3 ab (C:X200).

adjusted as TSH suppression to below 0.1 mU/L). The patient was classified as high risk group according to the American Joint Committee on Cancer (AJCC) [Stage 4a (T1a N1b M0)]. She was followed with Thyroglobuline and ATGL measurements and neck USG at every 6 months with the recommendation of American Thyroid Association (ATA) (7). Diagnostic ¹³¹-iodine whole- body scan was planned, following thyroid hormone withdrawal (6–12 months after adjuvant RAI therapy).

DISCUSSION

Thyroid nodules are common lesions in general population and approximately 70% of them can be detected only by ultrasound (8). Less frequently, these tumors can be presented as cervical lymphadenopathy without palpable/radiological detectable thyroid nodule (9). It should be kept in mind that generally they cannot be detected since they are generally ≤ 10 mm sized microcarcinomas.

The majorities of palpable metastatic cervical LNs are located at the jugular region, as in our patient. Cervical lymphadenopathy as a sole presenting sign of metastatic PTC has been reported as much as 13.4% (10) and it is usually uncommon.

In some reports, the incidence of cervical lymphadenopathy at the time of diagnosis is estimated at 20-25% for all sized tumors (11, 12). Even PTC metastasis in cervical LN with absence of tumor in the thyroid was reported (9). In this condition, to exclude other primary malignancies of head and neck region is absolutely very important. In 2015 ATA Management Guidelines (7) refers to BRAF V600E mutation identifies 65-77% of patients with PTMC in some studies (13, 14) and specific molecular profiles, such as the coexistence of BRAF with other oncogenic mutations (such as PIK3CA, AKT1), TERT promoter or TP53 mutations may serve as more specific markers of less favorable outcome of papillary thyroid cancer. Future studies are expected to establish the impact of molecular profiling involving multiple mutations or other genetic alterations on clinical management of patients with PTMC. If other foci cannot be detected with full-body-scan and immunohistochemical stains supported that primary focus is arising from the thyroid, most probably a millimetric occult PTC is overlooked (inadequate sampling/over shaving/serial sections/inexperienced evaluation, etc.).

Enlarged cervical LN can be evaluated with ultrasound, radionuclide scans, CT and/or MRI, but

25% of patients with PTC may have normal thyroid imaging (10-12, 15).

Ultrasonographic features which supported metastatic papillary carcinoma in cervical LNs are cystic masses with thickened-irregular inner lining (16). If a suspicious LN was detected, FNA can be performed as a first step. FNA is a useful method for determining of typical diagnostic cytopathologic features of PTC, but if pathologist cannot obtain cell block and cannot perform immunohistochemical stains; it is impossible to comment about primary site of tumor. LN excision is an unavoidable end of the diagnostic process. Due to the tumors originated from some parts of body have specific antigenic features, immunohistochemistry is an important diagnostic method for determining the primary site of metastatic tumors. TTF-1 and thyroglobulin immunostains can be used for supporting the primary tumor site as thyroid. Additionally Mesothel cell and Galectin antibodies are diagnostic markers for PTC.

The proposed treatment for patients diagnosed as PTC with metastasis to cervical LN is total thyroidectomy and appropriate ipsilateral and/or contralateral modified radical neck dissection. Prognosis of tumor is usually good if disease management is planned properly, radionuclide scanning following surgery and lifelong thyroid supplementation are recommended (17, 18).

In conclusion, PTC initially presenting with cervical LN metastasis is a rare entity. When a metastatic LN is present but clinical/radiological exams reveal a normal appearing thyroid, the best choice as the first diagnostic step is FNA of LN. FNA may exhibit diagnosis of papillary architecture carcinoma but do not detect primary site. Generally, performing LN excision and immunostains are useful processes in detection of primary site. Thyroidectomy should be performed for definitive diagnosis and treatment of metastatic PTC. When it is followed up by postoperative radionuclide scan and lifelong suppressive thyroxin, outcome is usually good.

The interesting feature of the present patient is the presence of large sized metastatic cervical LNs although the primary PTC foci are small sized as they cannot be detected with radiological methods and diagnostic confusion generated by history of oophorectomy.

Conflict of interest

The authors declare that they have no conflict of interest concerning this article.

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