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The widespread metastases at presentation in a patient with tall cell variant of papillary thyroid carcinoma : A case report and review of the literature

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ÖZET

Tall cell varyant papiller tiroid karsinomalı bir hastada tanı anında yaygın metastaz: olgu sunumu ve literatür taraması

Papiller tiroid kanserinin uzak metastazları nadirdir ve en sık akciğer ve kemiklerde görülür. Papiller tiroid kanserinin beyin ve mediastinal lenf nodu metastazlarının birlikte görülmesi ise oldukça nadirdir ve genellikle çok kötü prognoza sahiptir. Bu yazıda; papiller kanser tall cell varyantlı bir olguda FDG PET/BT ile isthmusta tespit edilmiş rezidüel tömörün yanı sıra, çok sayıda beyin, akciğer, kemik ve mediastinal / servikal lenf nodu metastazları sunulmaktadır. Tüm hastalık alanlarında tanı endobronşial ultrasonografi eşliğinde yapılan transbronşial iğne aspirasyonu (EBUS-TBIA) ve ince iğne aspirasyon biyopsisi (İİAB) ile histopatolojik olarak doğrulanmıştır.

Anahtar Kelimeler: *Tall cell varyant, uzak metastaz, 18F-FDG PET/BT, prognoz*

SUMMARY

Distant metastases of papillary thyroid carcinoma (PTC) are rare and usually involve the lungs or the bones. Brain and mediastinal lymph node metastases from PTC simultaneously in the same patient are extremely rare, and usually have a very poor prognosis. We report a case with residual tall cell variant of PTC in isthmus localization detected with fluorodeoxyglucose positron emission tomography/ computed tomography (FDG PET/CT) as well as multiple cerebral, lung, bone and mediastinal / cervical lymph node metastases. Histopathologic confirmation was accurately obtained by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and fine needle aspiration biopsy (FNAB) for all disease sites.

Key words: *Tall cell variant, distant metastasis, 18F-FDG PET/CT, prognosis*

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Introduction

Some variants of papillary thyroid carsinoma (PTC) have been associated with a worse prognosis such as the tall cell variant, columnar cell variant and insular pattern (1). Distant metastases of PTC are infrequent and usually occur in advanced stages of the disease, especially in lungs or bones. Unlike the good prognosis of PTC confined to the thyroid gland or cervical lymph nodes, distant metastases increase the mortality up to 50% in 1 year (2). Brain metastases from PTC are extremely rare, with a reported incidence of 0.4–1.2% (3). Radioiodine therapy is contraindicated in patients with cerebral metastases since, radioiodine crosses the blood-brain barrier and affects a metastasis in a manner similar to that of the primary tumor. Tumor cell destruction in a metastatic deposit often results in hemorrhage and edema, which may cause serious neurologic problems (4). Surgical resection and external beam radiotherapy traditionally have been the mainstays of therapy (4,5). When brain metastases are detected and treated early there may be a significant benefit in long-term survival. Despite its rarity, mediastinal lymph node metastasis from PTC is a well known clinical condition. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a rapid and accessible way to obtain a definite pathological diagnosis (6). This case illustrates the poor prognosis of distant metastases of PTC and emphasises the value of fluorodeoxyglucose positron emission tomography/ computed tomography (FDG PET/CT) in the management and detection of distant metastases in poorly differentiated variants.

Case Report

A 65-year-old man, with a history of tall cell variant of PTC diagnosed after right thyroid lobectomy, presented with vertigo and mild cognitive impairment. No other symptoms were reported. The patient's past medical history was limited to hypertension and uncontrolled diabetes mellitus. Further physical examination was unremarkable. Ultrasonographic examination showed intact left thyroid lobe, suspicious hypoechoic residual tumor in isthmus localization and most likely metastatic left cervical lymph nodes. Because of the poor prognostic variant and intact left lobe, FDG PET/CT was decided to perform in order to detect distant metastases prior to I-131 whole body scan (WBS). After the injection of 10 mCi (370 MBq) FDG, imaging was performed 45-60 min later on a PET/CT scanner (GE Discovery 690 PET/CT). FDG PET/CT showed focal incrased uptake in the isthmus consistent with residual tumor and multiple enlarged metastatic cervical lymph nodes which was confirmed by fine needle aspiration biopsy (FNAB) (Figure 1).

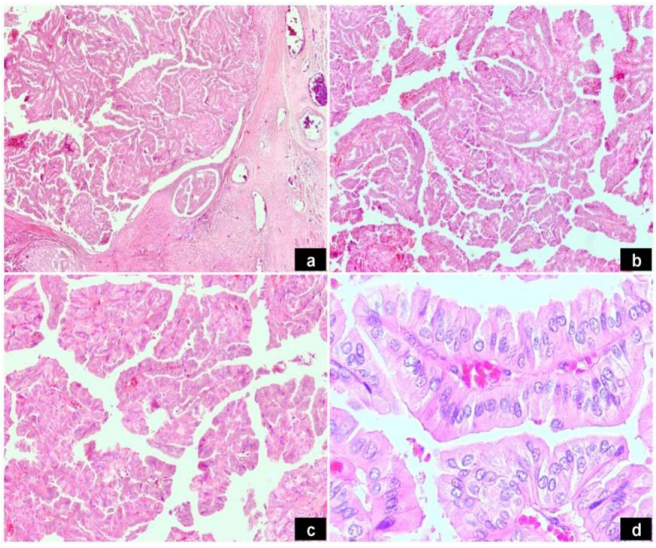

Figure 1: Under low power magnifications (a and b) invazive carcinoma forming papillary structures, which is next to the thyroid capsule, is seen. Higher power magnifications (c and d) revealed that the tumor is composed of atypical epithelial cells with abundant eosinophylic cytoplasms and distinctively tall-cuboidal in appearance. Based on these morphological evidences, it is reported as tall-cell variant papillary thyroid carcinoma (Hematoxylen & Eosin, a:X20, b:X40, c:X100 d:X400 magnifications).

PET CT also showed multiple focal increased foci in brain, mediastinal and hilar lymph nodes, lung nodules and lytic bone lesion with markedly increased maximum standardized uptake values (SUVmax) consistent with distant metastasis (Figure 2). Cerebral metastases were confirmed with following Magnetic Resonance Imaging (MRI). Metachronous lung cancer with widespread metastases other than solely thyroid cancer was suspected at first glance. But EBUS-TBNA revealed papiller carsinoma metastases in hilar and paratracheal lymph nodes.

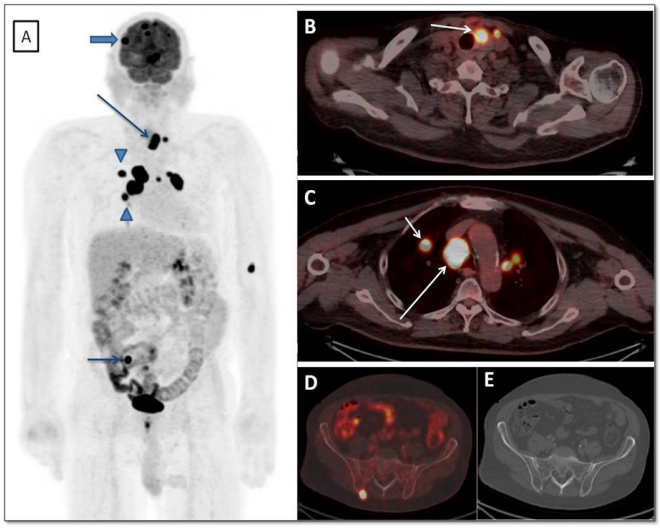

Figure 2: Maximum intensity projection (MIP) image (A), showing intense FDG uptakes in residual tumor (long arrow), multiple brain metastases (thick arrow), cervical, mediastinal and hilar lymph nodes (SUVmax:57.3), lung nodules (SUVmax:23.6) (arrow heads), and right iliac metastasis (SUVmax:30.0) (thin arrow). FDG PET/CT fusion image (B) showing focal FDG uptake in residual tumor in isthmus localization (SUVmax:22.9) (arrow) and left cervical metastatic lymph node. FDG PET/CT fusion image (C) showing focal FDG uptake in right lung nodule (short arrow), right paraaortic (SUVmax:56.9) (long arrow) and left hilar lymph nodes. FDG PET/CT fusion (D) and corresponding CT (E) images showing focal FDG uptake of lytic bone metastasis in posterior right iliac bone.

Surgery was not considered and histopathologic confirmation was not made for unresectable numerous brain metastases due to ethical considerations. Before complementary total thyroidectomy and radioactive iodine ablation, the patient was referred for cranial external beam irradiation. He was planned to receive fractionated whole brain radiotheraphy. A day prior to starting radiotheraphy, concomitant glucocorticoid therapy (4 mg every 6 hours) was given to the patient by radiation oncologist in order to minimize hemorrhagic, inflammatory and edematous effects of the irradiation and decrease mass effect symptoms. But in the fifth day of glucocorticoid therapy, the patient's blood glucose rose abruptly and he got into diabetic ketoacidosis coma. He was hospitalized, anti-diabetic and supporting theraphy was started immediately, but despite all efforts the patient died because of uncontrolled diabetes within two days.

Literature Review and Discussion

PTC has the highest incidence among all thyroid malignancies, compared to follicular, medullary or anaplastic histologic subtypes. PTC is a well-differentiated malignancy and usually presents in an early stage. It's characterized by an excellent overall prognosis with long-term survival. But some variants such as diffuse sclerosing, columnar cell and tall cell variants (TCV) are associated with a less favorable outcome (7).

The tall cell variant maintains the papillary architecture but in addition, the cells have abundant cytoplasm, which makes the cells at least twice as tall as they are wide. The mean age at diagnosis is higher than that for the classic form of papillary carcinoma. Tall cell carcinoma usually concentrates radioiodine well enough to be visualized on a total body radioiodine scan, but less than classic form of papillary carcinoma and usually produces thyroglobulin unless it contains foci of undifferentiated (anaplastic) carcinoma in addition to the tall cell component (4).

In our opinion, the tumor became dedifferentiated in time and included anaplastic foci in this patient. We had two reasons for such a thought. Firstly, there were multiple distant metastases including rare localizations (brain, mediastinum). Secondly, primary tumor and metastatic foci showed very high FDG avidity and SUVmax values.

The risk of locoregional recurrence and distant metastasis were found four times greater in patients with tall cell carcinoma than in patients with well differentiated tumors and affects survival (8). In patients with tall cell variant, CT, MRI, or PET/CT scan must be obtained in addition to I-31 WBS if symptoms suggest the possibility of a distant metastasis, or in a patient with markedly elevated thyroglobulin (4).

PET/CT is suggested to use for thyroid carcinoma, especially in cases in which iodine 131 (I-131) scan is negative. As well-differentiated thyroid cancers become less differentiated, they may lose their iodine avidity resulting, I-131 scanning less effective. At the same time, less differentiated thyroid cancers may have increased metabolic activity, enhancing glucose uptake and leading to PET positivity as in our patient (9). Although we planned the patient to have complementary total thyroidectomy followed by I-131 ablation after completing whole brain radiotheraphy, we didn't have time because of

his sudden death. To best of our knowledge, even if we had chance to perform, I-131 scan would be negative because of high FDG avidity of metastases and poorly differentiated tumor. But it would be still considered as a treatment option, since I-131 and PET/CT scans may not capture the same foci of papillary thyroid carcinoma. In addition, the size and consistency of residual or recurrent disease, location of metastases and cell differentiation may affect the sensitivity, specificity and accuracy of PET/CT evaluation (9).

The presence of distant metastases is the most significant poor prognostic factor for survival. Lung is the most common site of distant metastasis, followed by bone, whereas the brain, breast, liver, kidney, muscle, and skin are rarely involved (10). Lung metastases from PTC are potentially curable. But lung metastases larger than 1 cm in patients over age 45 years have a less favorable prognosis. Since thyroid tissue usually concentrates radioiodine much more avidly than metastatic cancer, it is not possible to effectively treat lung metastases with I-131 in a patient with a large thyroid remnant as in our patient. When lung metastases are detected prior to ablation of the thyroid remnant, a minimum activity of 200 mCi I-131 therapy is recommended after complementary thyroidectomy in adults (4,11).

The first treatment approach to patients with tall cell variants should be radioiodine therapy unless it is clear that tumor sites do not accumulate radioactive iodine. The general rule is to destroy brain metastases with either surgery or external beam radiotherapy prior to delivering radioiodine therapy for other sites of disease. Radioiodine therapy is not the first choice of treatment in patients with cerebral metastases. Because it may lead hemorrhage and edema. The choice depends on the number and size of the metastases. If there is solitary metastasis smaller than 3 cm, radiosurgery is the treatment option. Solitary metastasis larger than 3 cm must be treated by surgical resection followed by radiotherapy. In case of more than 3 metasteses, whole brain radiotherapy should be the useful approach. If radioiodine therapy is given to a patient with brain metastases, it's recommended to treat the patient with dexamethasone 4 mg every 6 hours for a minimum of 5 days following radioiodine administration (4,12).

Bone metastases are usually from poorly differentiated variants and the most common sites of metastases were: vertebrae (29%), pelvis (22%), ribs (17%), and femur (11%). FDG-PET/CT scans may be the best way to identify bone metastases form all types of PTC. Because radioiodine can deliver very high local radiation doses specifically targeted to metastatic lesions, it is the primary treatment modality for unresectable disease. Surgical resection of metastatic deposits in addition to radioiodine and/or external beam radiotherapy may improve survival (4).

Mediastinal lymphadenectomy has only sporadically been mentioned in patients with thyroid cancer (13). Lymph node involvement of the mediastinum in papillary thyroid carcinoma is usually confined to the superior mediastinum. The nodes of the superior mediastinum seem distinct from the nodes in the rest of the mediastinum, since these nodes are closely linked to the lymph nodes of the central neck. Surgical approch is possible for these nodes unlike the rest of mediastinal lymph nodes that are free of disease. On the other hand, lower mediastinal lymp node metastases from PTC are rarely described in the literature. It may lead to the invasion of surrounding organs and upper airway obstruction. The primary treatment method is surgery if possible and radiation therapy afterwards (6).

In our patient, we planned to treat brain metastases first. The next step would have been complementary thyroidectomy in order to reduce tumor burden and try to get some benefit from radioiodine therapy for other disease sites if they are proven to be iodine avid.

As conclusion, older age, extrapulmonary metastases, and undifferentiated component in pathology were significant predictors of the poor outcome (14). The use of PET/CT is a useful tool in the management of patients with undifferentiated thyroid cancer to show disease extension with precise anatomic localization for having a better treatment strategy.

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