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FDG PET/CT Negative Medullary Thyroid Carcinoma Patient With Elevated CEA Level: Case Report and Review of Literature

FDG PET/BT Negatif Yükselmiş CEA Değerleri Olan Medüller Tiroid Karsinomu Hastası; Literatür Derlemesi ve Vaka Sunumu

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Abstract

The tumor markers are considered reliable in follow up of Medullary Thyroid carcinoma (MTC) as an adjunct with other imaging methods like ultrasonography. In some circumstances imaging of thorax or whole body imaging may be necessary in these patients in the follow up. Calcitonin levels in combination with carcinoembryonic antigen is markers that we use in the follow up of MTC patients which elevation indicates recurrence and the recurrence cite may be described by means of Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (FDG PET/CT) imaging which was negative in our case. In this case we report a patient with exceptionally high carcinoembryonic antigen (CEA) and low calcitonin level in one month postoperative follow up who was diagnosed as having false positive CEA elevation and discuss the diagnostic methods and tumor markers in detection of the Medullary Thyroid carcinoma.

Key Words: Fluorodeoxyglucose F18; positron-emission tomography; carcinoembryonic antigen; thyroid cancer, medullary; calcitonin

Özet

Tümör markerları Medüller tiroid karsinomu hastalarında diğer ultrasonografi gibi görüntüleme metodlarına ek olarak güvenilir olduğu kabul edilerek kullanılmaktadır. Bazı durumlarda bu hastalarda takipte toraks ve tüm vücut görüntüleme de gerekli olabilir. Kalsitonin ve karsinoembryonik antijen birlikte medüller tiroid karsinomu takibinde güvenilir

olarak kullanılır ve yükselmeleri nüksü gösterir ve rekürrens alanı FDG PET/BT gibi tetkiklerle tanımlanabilir ki bizim hastamızda bu negatifti. Biz bu vaka ile nadiren görülen düşük kalsitonin düzeyine karşılık yüksek karsinoembryonik antijen yüksekliği ile tanı alan yanlış CEA pozitifliğini raporluyor ve medüller tiroid karsinomunda tanısal metodların ve tümör markerlarının yerini tartışıyoruz.

Anahtar Kelimeler: Fluorodeoksiglukoz F18; pozitron emisyon tomografi; karsinoembriyonik antijen; medüller tiroid kanseri; kalsitonin

Introduction

Recurrent or metastatic MTC is usually presents with high calcitonin and CEA as well. There is some several case reports in the literature incidentally firstly recognized with F-18 FDG PET/CT with suspicion of elevated CEA levels with metachronous colon carcinoma.[1, 2] Elevated tumor markers (calcitonin and CEA) usually refer to either metastasis or recurrence in patients with MTC. There are several imaging methods in identification of recurrence or metastasis in these kinds of patients which are conventional morphological imaging methods which do not yield a high accuracy and sensitivity and several Nuclear Medicine methods. These methods are DMSA V scintigraphy, F-18 FDG PET, F-18 DOPA PET and peptide receptor imaging. The latest studies have shown that the F-DOPA PET might show the extend of disease most accurately and F-18 FDG PET shows more aggressive lesions of patients with higher marker levels and lower marker doubling times and receptor scintigraphies may be considered for decision of treatment.[3-5] Among this nuclear medicine imaging methods previous studies have pointed that F-18 FDG PET might be more helpful in patients with elevated or unstable CEA doubling time rather than elevated calcitonin levels.[2, 6] However there is no report of a similar case with isolated CEA elevation with normal calcitonin levels. We wanted to present F-18 FDG PET results of a case with MTC and only CEA elevation.

Case Report

A seventy three years old male patient who has history of diabetes mellitus and hypertension attended hospital for complaint of tinnitus. He had a thyroid nodule in physical examination and underwent bilateral total thyroidectomy operation due to suspicion of malignancy in fine needle aspiration result (suspicion of papillary carcinoma follicular variant). Postoperative pathology results revealed medullary thyroid carcinoma in the right lobe (3 cm in size) confined to the lobe without any finding of invasion. One month after the operation he had persistent CEA levels 40 ng/mL (1-5 ng/mL:normal limits) despite low calcitonin levels. Further diagnostic work-up by F-18 FDG PET revealed focal small area with increased uptake adjacent to trachea in the midline of the neck with SUVmax level of 2.6 indicating inflammatory changes due to operation otherwise normal (Figure 1). Although there was no metastatic lymph node involvement in the pathology results the control CEA levels were completely decreased (1,62 ng/mL) after two months from the operation. According to preoperative results prior to the first surgery it was indicated that the patient had mild uremia (58 mg/dL) probably because of diabetes mellitus. After three months follow up the plasma CEA and calcitonin levels were in normal range and neck ultrasound was normal.

Discussion and Literature Review

The MTC is one of the neuroendocrine tumors (NET's). The identification and detection of NET's consist different imaging modalities like previously I-131 MIBG, Tc-99m V DMSA and recently somatostatine receptor imaging, anti-CEA antibody imaging and F-18 DOPA PET imaging.[7] In a review it has been highlighted that Tc-99m V DMSA imaging considered the most sensitive, MIBG most specific method additionally MIBG or SR imaging serves for therapeutic considerations.[8] Also FDG PET may provide prognostic information about bad prognosis and SR imaging about better prognosis.[8] FDG PET has acceptable sensitivity

especially for detection of metastatic lymph nodes and according to a review analysis has the highest sensitivity compared to the other imaging methods. [9, 10] However in a previous study post-RIT (anticarcinoembryonic antigen pretargeted radioimmunotherapy) scintigraphy has been considered more sensitive compared to FDG PET. [11] FDG PET is a valuable tool in the identification of occult residual or metastatic disease and guide for surgery.[12] The FDG PET imaging is more valuable in patients with elevated and rapidly increasing tumor markers (calsitonine and especially CEA) and points out aggressive disease.[13] F-18 DOPA has higher lesion detection for MTC metastases compared to F-18 FDG.[14]

Theoretically there are no indications for I-131 treatment or diagnostic I-131 imaging due to undifferentiated phenotype of this tumor group.

The disease usually is presented with metastatic lymph nodes in nearly half of the patients and in 10-15% patients distant metastasis may be present at the time of diagnosis usually involvement of lung, liver, bone and brain as multiple organ disease.[15, 16] The disadvantage in the detection of MTC metastases is tendency of the small volume of metastatic sites especially in liver which may cause low sensitivity for diagnostic tests.[5] In a previous study 40% of the patients with suspicion of recurrence or metastasis who were referred to FDG PET/CT remain unidentified but these patients were a selected group who do not have any identified tumor by conventional imaging modalities as well.[4] Additionally the sensitivity and mean SUV max values of the lesions decreases for indolent types of MTC like the ones associated with MEN syndromes.[17]

The most important advantage in the follow up of MTC is the presence of informative tumor markers like CEA and calcitonin. The completely normal level of calcitonin is the goal of surgical treatment and those patients are considered surgically cured.[18] Recurrence or metastases may be easily detected by elevation of those markers. Especially calcitonin is the

most accurate tumor marker in follow up of MTC.[4] CEA elevation usually represents more aggressive and dedifferentiated type of tumor.[4] The standard surgical approach includes bilateral total thyroidectomy and neck dissection for MTC.[19, 20] Elevation of the markers requires further tests in order to detect the site of recurrence. In a multicenter study Diehl et al. have suggested FDG PET because of higher sensitivity compared to Tc-99m V DMSA, Tc-99m sestamibi, In-111 SR scintigraphy and CT and MR.[21] However Ong et al. have observed that the sensitivity may be reasonable when calcitonin level is above 1000 pg/ml while limited while calcitonin level is below 500 pg/ml.[22] However other researchers have suggest that >30 pg/ml levels should be evaluated.[19] In a previous study it has been documented that detection rate will increase in patients with calcitonin and CEA levels higher than 1000 pg/mL and 5 ng/mL respectively and doubling time of <12 months for calcitonin and <24 months for CEA.[23] Additional to indication of residual or metastatic disease elevation of these markers are found to be reflecting the volume of disease.[24, 17] The calcitonin levels turns to normal levels after several months from the surgery and those patients with normal calcitonin levels and patients with normal pentagastrin stimulation test are considered to be in complete remission who has 3% risk of recurrence and 97.7% 10 year survival rates.[25, 26]

Recently new radiopharmaceuticals and methods are preferred for detection of MTC like Ga-68 labeled peptide imaging. Bogsrud et al. have highlighted that Ga-68 DOTANOC has high sensitivity in biochemically recurrent MTC compared to FDG PET but not as sensitive as it is compared to the other NE tumors.[19] The tumor markers have important role in the follow up of MTC. Calcitonin is more specific marker but CEA might contribute in special circumstances.[27] Additionally short doubling time of these tumor markers might indicate progression.[28] Also there are cut off values for these tumor markers above which might point out positivity might be expected in imaging modalities like FDG PET and FDOPA PET.[29]

However there is a study that showed no significant difference between sensitivities of FDG PET studies of patients with calcitonin values higher or lower than 150 pg/ml limits showing a high sensitivity value (93%) for PET.[30] CEA which is considered as another important tumor marker in follow up of MTC patients has some handicaps and questions about its sensitivity and specificity.[31] As it is in our case; there are some false positivity reasons related to CEA but this is the first report showing a false positivity in the literature as far as we know.

Previously Bogsrud et el. have shown that FDG PET might be informative even in case of positive or negative calcitonin levels.[19] It is suggested to evaluate imaging modalities besides calcitonin and CEA levels which cannot replace each other.[32] In our case the imaging revelaed no residual tissue but false positive elevation of one of the tumor markers was the problem. There are some false positivity causes of CEA which generally is between the levels of 5-15 ng/mL for detection of colorectal cancer where over 35 ng/mL has reported to be associated with recurrence.[33] Sousa et al. have reported false positive elevation of CEA after bowel cleaning.[34] Previously a physiologically expressed CEA splice variant has been identified.[35] As in our case it has been previously reported to be another important situation to be remembered in false positive elevation of CEA is uremia and renal failure.[36] Additionally CEA levels might be elevated in several conditions including smoking, pancreatitis, obstruction of biliary system, peptic ulcer and hypothyroidism. [37] The patient was questioned regarding other false positivity reasons and uremia was considered as the only cause.

This case report remembers us to consider the diagnostic markers with caution and in conjunction with each other and diagnostic methods especially FDG PET/CT.

Authorship contributions/Yazar Katkıları,

All the authors contributed sufficiently to the work.

Conflict of interest/Çıkar Çatışması

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Figure 1. Transaxial fusion image of F-18 FDG PET/CT from the neck region; slight activity accumulation in thyroid bed indicating inflammatory changes due to recent surgery.