Journal of
Surgical Procedures and Case Reports

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Case Report Open Access

Cutaneous and Liver Metastases of a Micropapillary Thyroid Carcinoma Evaluated by ^{18}F-fdg Pet/Ct: A New Case Report

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Received Date: March 28, 2022 **Accepted Date:** April 21, 2022 **Published Date:** April 23, 2022

Citation: Jemni Z, Sfar R, Nouira M, Charfi H, Chatti K (2022) Cutaneous and Liver Metastases of a Micropapillary Thyroid Carcinoma Evaluated by ^{18}F-FDG PET/CT: A New Case Report. J Surg Proce Case Rep 4: 1-7.

Abstract

Skin and liver metastases from differentiated thyroid carcinoma (DTC) are rare. This case report describes the occurrence of cutaneous and liver metastases in a patient with a history of papillary thyroid microcarcinoma that had previously recurred in cervical lymph nodes. The relevant literature is reviewed, and a discussion of the salient points of the case is provided.

Keywords: Oncology, Metastases, Micropapillary Carcinoma, Radioiodine, Thyroid Carcinoma

Abbreviations

PTC: Papillary Thyroid Cancer; DTC: Differentiated Thyroid Carcinoma; PTMC: Papillary Thyroid Microcarcinoma; STg: Stimulated Serum Thyrogolobulin Levels; TgAb: Thyroglobulin Antibodies Levels; ^{131}I: Iodine-131; SPECT: Single-Photon Emission Computed Tomography; CT: Computed Tomography; ^{18}F-FDG PET: ^{18}F-fluorodeoxyglucose Positron Emission Tomography Scan; FDG: ^{18}F-fluorodeoxyglucose; SUV Max: Maximum Standardized Uptake Value; RAI: Radioactive Iodine

Introduction

Papillary thyroid cancer (PTC) is the most common thyroid malignancy [1]. It is characterized by slow growth and an indolent biological behavior [2]. Distant metastases occur in fewer than 10% of patients with differentiated thyroid carcinoma (DTC). Half are present when the tumor is first diagnosed; the others are found later, sometimes decades after initial treatment [3]. Commonly DTC is well known for nodal metastases as well as lung and bone disease but metastases to the abdomen are rare. The most common sites are lungs and bones [4]. Papillary thyroid microcarcinoma (PTMC) is a thyroid cancer with small tumors that are 1.0 cm maximum in diameter; it is also the most common type of malignant thyroid tumor with an increasing prevalence, but an excellent prognosis [5].

However, some PTMC's exhibit aggressive behavior, including the development of regional and distant metastases [6].

Material and Methods

We report an unusual case of PTMC associated with diffuse metastases to the skin, liver and lungs eight years after diagnosis in a patient considered disease -free after total thyroidectomy and radioiodine treatment.

Case Report

A 65year old patient had a past medical and surgical history of PTMC classic variant, with a single cervical lymph node metastatic status post total thyroidectomy in 2012.

Features of initial histological diagnosis showed an encapsulated tumor (2mm), with follicular and papillary architecture, that presented nuclear features of PTC, with no vascular invasion. (pT1aN1aM0).

He initially received 200mCi of iodine-131 (^{131}I) with a good therapeutic response: Stimulated serum Thyroglobulin levels (STg) = 0 ng/ml, negative thyroglobulin antibodies (TgAb) and negative therapeutic whole-body iodine-131 scan (WBS) which classified him as a low risk of persistent or recurrent disease.

The patient did, however, present with local recurrence, five years later with positive TgAb (>1000 UI/ml) and negative STg. He underwent selective neck dissection and supraclavicular lymph node excision. The histopathologic findings showed a metastatic lymph node recurrence of vesicular variant of PTC. The patient received 200mCi of ^{131}I adjuvant therapy. The WBS showed a focal remnant uptake in the thyroid bed. The subsequent single-photon emission computed tomography/computed tomography (SPECT/CT) showed a residual focus of uptake in supraclavicular lymph nodes and in a laterotracheal soft tissue mass. On further follow, the biochemical response was incomplete with increasing TgAb (>1000 UI/ml) and false negative STg levels (1ng/ml).

After 3 years, he presented with some palpable sub-cutaneous nodules of the interscapular region with continuously increasing TgAb reaching 3540 UI/ml.

After excisional biopsy, the histopathological examination confirmed some cutaneous and intramuscular metastases of a poorly differentiated PTC with massive and insular pattern. Surgical margins were infiltrated. Screening for activating mutations of genes coding for RET or TRK tyrosine kinase receptors were not available.

After the diagnosis of skin metastases, we searched other possible lesions by ^{18} F-fluorodeoxyglucose positron emission tomography scan (^{18}F-FDG PET/CT).

The patient fasted for 12 hours before imaging. He received 221 MBq (6 mCi) of ^{18}F-FDG intravenously. PET/CT was initiated 60 min after the injection, and a dual-slice lutetium oxyorthosilicate PET/CT scanner (Siemens) was used.

^{18}F-FDG PET/CT showed an FDG avid cervical soft tissue mass with maximum standardized uptake value (SUV max) of 20,84 causing endotracheal and vertebral involvement. There was FDG uptake in the IIa and 2R levels lymph nodes. The scan also showed an FDG avid hypodense lesion in segment VII of the liver (SUV max = 6.2), multiple pulmonary nodules from those two are FDG avid (left posterior basal segment, and right medial lower lobe).

Three highly metabolic (SUV max = 20.75) additional cutaneous and subcutaneous lesions were found in the back with trapezius muscle infiltration (Figure 1).

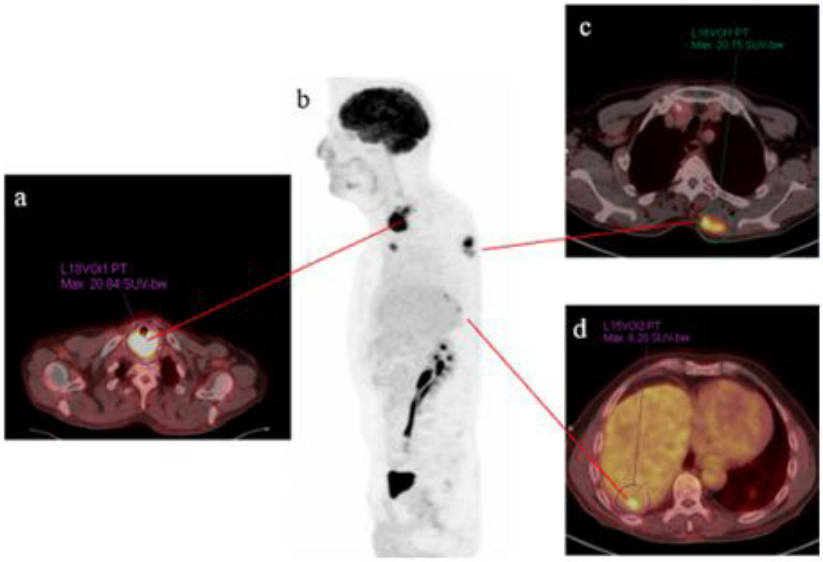

Figure 1: Baseline [18] F-fluorodeoxyglucose positron emission tomography scan ([18]F-FDG PET/CT): (a) High uptake in the cervical mass (SUVmax = 20.84), (b) cutaneous nodules in the back (SUVmax = 20.75), and (d) liver secondary nodule of segment VII (SUVmax = 6.20). (b) PET maximum intensity projection of the patient

The patient underwent a suboptimal resection of the cervical mass, a spine corpectomy followed by vertebral body reconstruction and an excision of cutaneous metastases.

We administrated a postoperative 100mCi of [131]I. The SPECT/CT showed multiple foci [131]I positive lesions in the latero-tracheal remnant mass, hepatic lesion, as well as the emergence of an upper left paratracheal metastatic lymph node (Figure 2). Both [131]I-avid and non-[131]I-avid pulmonary nodules were found.The patient was assigned to a locoregional palliative external beam radiotherapy before starting antiangiogenic multikinase inhibitor (MKI) therapy for a metastatic radioactive iodine (RAI) -refractory disease.

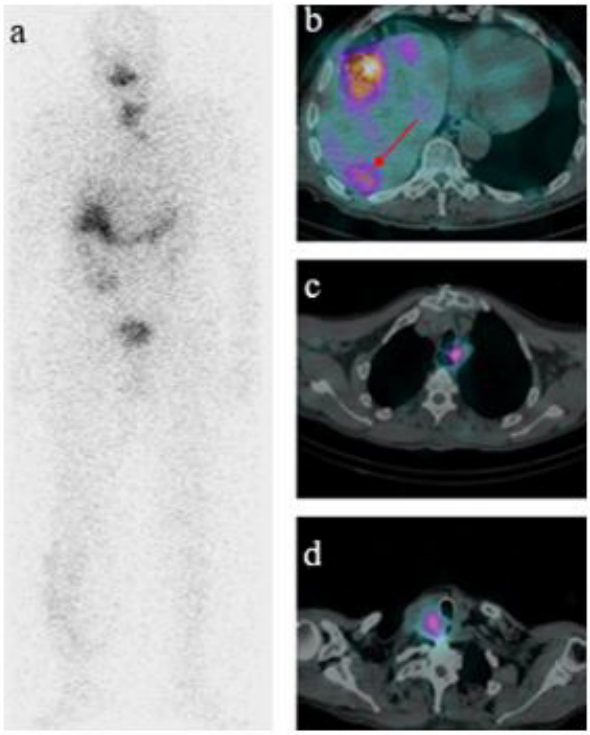

Figure 2: Post-operative whole body scan 131 iodine ([131]I) (a) showed residual uptake in the latero-tracheal remnant mass (d), hepatic lesion (b), as well as the emergence of an upper left paratracheal metastatic lymph node (c)

Discussion

Nearly 15% of the thyroid cancers undergo metastasis with 10-year survival rates of 42 % (4). However, the probability of hematogenous spread is less with PTC, as it commonly spreads through lymphatic's unlike follicular carcinoma thyroid, which has a propensity for vascular invasion and hematogenous metastases [7].

PTMC often have an indolent course but this may depend upon patient age: It may be more aggressive in young patients (< 40 years) than in older ones [8].

PTMC is associated with a high rate of central lymph node metastasis to ipsilateral and pretracheal subsites. The study of Roh and al. [9] found no clinicopathologic factor predicting nodal metastasis. Distant recurrence rates following surgery for a PTMC is 1-2% [9].

BRAF mutation-positive PTMC's were more likely to manifest aggressive characteristics, extrathyroidal extension and lymph node metastasis [10].

Zheng and al. [11] showed that extrathyroidal invasion, lymph node metastases, and the type of surgical procedures were significantly associated with tumor recurrences as for other DTC subtypes.

According to other authors, one of the risk factors for aggressive PTMC's is lymph node metastasis [5], while Choi and al. stated that no definite biological or clinical parameters currently exist to distinguish low-risk indolent PTMC from potentially aggressive one's.

Their results suggested that patients initially eligible for active surveillance who underwent delayed surgical intervention had more aggressive disease and unfavorable oncologic outcomes [12].

Presence of BRAF mutations are associated with high risk features, including extrathyroidal cancer extension and multifocality, and also predictive of an increased risk of lateral compartment nodal disease. Tumor size of PTMC (< 5 vs ≥ 5mm) has also been reported as being related to aggressive cancer behavior, with larger PTMC's being more likely to have high risk features and nodal metastasis [6].

In our case, the patient had initial involvement of one central lymph node metastasis with no other aggressive histological features that might be the cause of such a widespread disease; screening for BRAF mutation is not available in our country.

DTC's metastases to the solid organs of the abdomen (liver and kidney) are recognized but uncommon [4,13].

Metastatic liver involvement is generally multiple and found in patients with thyroid high-risk tumors, along with bone or lung metastases. It nearly always appears to be an advanced manifestation of the disease from follicular thyroid carcinoma.

It has a reported frequency of 0.5%, although at necropsy up to 25% of patients have liver involvement, most often with anaplastic carcinoma [14].

To our knowledge, there are only three reports in literature documenting a single liver metastasis from thyroid cancer [15,16].

Case reports of DTC's metastases to the adrenal gland [17] and spleen [18], bowel [19], pancreas [20] and pituitary gland [21] are also found in the literature.

The extension of PTC to cutaneous and subcutaneous tissue is also a rare phenomenon with a reported prevalence of 0.06-0.82% [22,23].

Concerning histological subtypes of DTC with skin metastasis the results are contradicting: One study of 50 patients reported follicular thyroid carcinoma as the most prevalent subtype while another study of 43 patients described PTC as the most common subtype with cutaneous metastasis [24,25].

PTC with cutaneous metastasis has been reported involving the thyroidectomy scar [26], but the majority of metastatic skin lesions involves the scalp owing to local vascular factors: rich dermal capillary network may initially trap tumor cell emboli from the systemic circulation.

The remainder generally involve the head and neck regions [24]

Our patient showed an uncommon location of skin metastases in the back along with visceral extension which is related to the aggressiveness of the disease relapse.

^{18}F-FDG PET/CT is useful for assessing the extent of disease and defining the prognosis.[3], and there is a well-defined situation where ^{18}F-FDG PET/CT plays an important role, so-called TENIS (Tg Elevated and Negative I-131 WBS) [27].

PET-FDG can also be indicated in cases of gradually increasing TgAb and / or when there is a doubt about a lesion in anatomical imaging.

Our case shows the importance of PET-FDG used as a first-line isotopic imaging technique in a RAI-refractory disease with increased TgAb.

Conclusion

In conclusion, from this case report and from the few previous cases documented in literature, aggressive surgeries, should be considered in selected patients with metastatic disease from PTC to alleviate the symptoms and prolong the survival.

Neither PTM size, nor the absence of high risk features, excludes the possibility of synchronous lymph node metastases.

Adjunct and multikinase inhibitors (sorafenib or sunitinib) may also slow down the disease progression, especially in patients with BRAF V600E mutation in tumor cell lines.

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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