18F-fluorodeoxyglucose-avid Thyroid Incidentalomas in Patients with Lymphoma

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Positron emission tomography, using 18F-fluorodeoxyglucose, has become a major whole-body non-invasive imaging modality for screening a variety of malignant tumors that show increased glucose utilization compared with normal tissues. There is ample evidence suggesting the superiority of 18F-FDG-PET for staging and follow-up of lymphoma patients, with a higher specificity compared with that of gallium-67 scintigraphy and 96% positive predictive value when combined with conventional imaging, thus affecting treatment and prognosis.

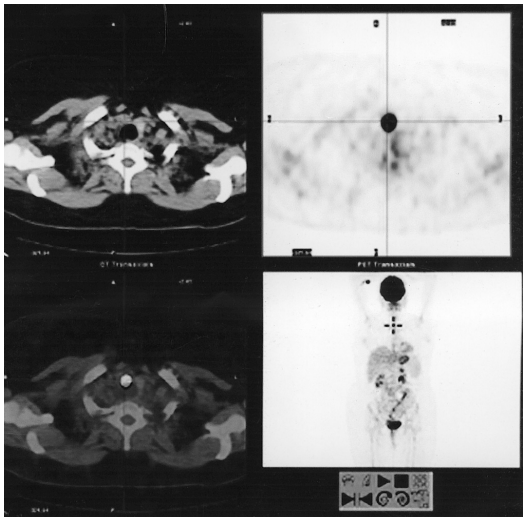
Since FDG-PET scan identifies metabolic processes in various tumors, it may reveal even occult, otherwise non-suspected second lesions (incidentalomas) in the lung, thyroid, colon, breast, esophagus, and bile duct, when utilized for staging or response to therapy of other tumors [1]. Fusion of PET data with computed tomography improves the localization and specificity of the FDG-avid sites.

We present two patients diagnosed with clinically occult thyroid cancer while undergoing FDG-PET/CT scanning for staging and follow-up of previously diagnosed and treated lymphoma.

Patient Descriptions

Patient 1

A 47 year old woman had been diagnosed with follicular grade III non-Hodgkins lymphoma (with large B cell component), based on biopsy of a painful left thigh mass. CT scanning identified tumor also in the left femur, dorsal spine at the level of T11, and in abdominal and pelvic lymph nodes. At the time of diagnosis, FDG-PET/CT showed multiple FDG-avid tumor sites, one of them located in the right lobe of the thyroid gland. The patient was treated with six cycles of chemotherapy. Following treatment, a follow-up whole-body PET/CT demonstrated focal FDG uptake (SUV 47.9) only in the right thyroid lobe, with complete response of all other lesions [Figure]. Ultrasound of the neck with fine-needle aspiration of a solid thyroid nodule revealed papillary carcinoma of the thyroid gland. The patient underwent total thyroidectomy, and histopathologic examination revealed a 1.4 cm papillary carcinoma in the right lobe with additional tumor foci scattered throughout both lobes of the gland.



PET/CT for follow-up of follicular lymphoma. Coronal PET maximal intensity projection image (lower right) and transaxial slice (upper right) show focal uptake in the right neck that is confined to the right lobe of the thyroid gland on PET/CT fusion image (lower left). The focal uptake overlaps a low attenuation area on the non-enhanced CT (upper left) of the PET/CT. FNA of the FDG-avid focus disclosed the presence of papillary carcinoma of the thyroid gland.

Patient 2

A 56 year old man had been diagnosed and treated for a primary cutaneous T cell lymphoma (mycosis fungoides) involving the skin over the left thigh, 3 years prior to the present disease. Staging of the lymphoma included a PET/CT scan that demonstrated increased FDG uptake in the left thyroid lobe. Subsequent ultrasound-guided FNA of the lesion showed no signs of malignancy. The patient was successfully treated with radiotherapy to the left thigh with no evidence of systemic disease to date. A repeat ultrasound and FNA of the thyroid lesion showed tumor cells compatible with papillary carcinoma. The patient underwent total thyroidectomy. Histopathology revealed papillary carcinoma, 1 cm in diameter, in the left thyroid lobe invading the surrounding soft tissues, with two additional tumor foci (0.3 cm in diameter) at the isthmus.

Comment

FDG-PET scan is not considered a primary imaging tool for the diagnosis of thyroid pathology, as the normal thyroid gland shows low grade FDG uptake and is usually not visualized on whole-body FDG-PET scan. Occasionally, diffuse FDG uptake will indicate the presence of chronic thyroiditis. Thus, PET scan is not part of the primary evaluation of suspected thyroid tumors, and there is no established role for FDG-PET in the diagnosis of cold thyroid nodules. This modality, however, was able to detect occult thyroid cancer and to diagnose recurrent and metastatic

FDG = fluorodeoxyglucose
PET = positron emission tomography
FNA = fine-needle aspiration

disease with a sensitivity of 94% and specificity of 95% in the presence of negative 131I scans. When 131I scans are negative, whole-body FDG-PET may not only identify tumor sites, thus sparing patients unnecessary aggressive local curative maneuvers, but may also serve as a prognostic indicator of the disease.

As the use of FDG-PET scans is gaining popularity, incidental uptake in the thyroid gland, diffuse and focal, is more frequently encountered on FDG-PET scans performed for staging and follow-up of various other malignancies. The reported frequency ranges from 1.2% to 4.3% for thyroid incidentalomas discovered by 140–4803 FDG-PET studies performed for staging of other cancers, such as lung, colon, breast, esophagus, bile duct, and head and neck tumors [1], or for cancer screening of healthy subjects [2].

The FDG images are usually interpreted qualitatively, and an area of abnormality is identified by comparison with background activity. Using attenuation-corrected images, a semi-quantitative parameter termed SUV (standardized uptake value) is a widely used index in clinical FDG-PET studies to differentiate malignant from benign tumors and to assess the efficacy of therapy. SUV is calculated as follows:

SUV = MBq/g [in tissue] / (injected dose [MBq]/patient's body weight [g])

Focal FDG activity in the thyroid has been associated with malignancy in several studies, with thyroid cancer detected in 27–47% of subjects who underwent biopsy of an incidental focal thyroid FDG-avid site. Furthermore, in the study of Kim et al. [3], cytologic diagnosis in 32 of 45 patients found malignant lesions in 16 (50%) patients, including 14 papillary thyroid carcinomas and 2 metastatic cancers of the thyroid. The true prevalence of cancer may have been higher, since surgery was not performed when cytology showed follicular neoplasm, indeterminate follicular cell lesion and nodular hyperplasia, and since cytologic or histologic verification was not available for all focal FDG-avid sites in the various studies described.

Increased focal uptake has also been described in benign thyroid lesions, however, patients with malignant lesions show significantly higher SUV compared to those with benign lesions. Mean and standard deviation of SUV in a group with malignant thyroid lesions were higher (6.92 ± 1.54) compared with benign thyroid lesions (3.37 ± 0.21, $P = 0.04$). In a second group of malignant thyroid incidentalomas SUV was 16.5 ± 4.7 compared to benign lesions with SUV of 6.5 ± 3.8. In the series of Chen et al. [2], of the 50 thyroid incidentalomas that underwent FNA and surgery, 14% (7/50) were found to be malignant, with SUV of 6.7 ± 3.66 versus 2.6 ± 1.01 in 43/50 benign lesions.

Since an overlap of SUVs between benign and malignant findings was documented by others [3], the conclusion was that a cytologic diagnosis of focal thyroid FDG-PET incidentaloma is required regardless of SUV values, considering the very high prevalence of thyroid malignancy. For now, lesions detected by FDG-PET scanning should be further evaluated by a detailed ultrasound examination and possibly FNA. Thus, focal FDG uptake may indicate the presence of thyroid cancer, as documented in 14–50% of nodules, which underwent biopsy or surgical excision.

Only four cases of incidental finding of papillary carcinoma of the thyroid in lymphoma patients have been published in the English-language medical literature. Blum and co-authors [4] presented a patient with aggressive non-Hodgkin's lymphoma who was found to have pathologic uptake at the base of the neck after completion of chemotherapy. FNA followed by surgery revealed carcinoma of the thyroid. A second patient, reported by Kim and team [5], was diagnosed and treated for grade III non-Hodgkin's lymphoma presenting as right cervical lymphadenopathy. FDG-PET scan performed for re-staging of suspected recurrence in this patient, revealed an area of increased uptake in the left neck and led to further workup and surgical removal of papillary carcinoma measuring 1.7 cm in diameter. Among 1912 patients studied, 2 additional patients with papillary carcinoma of the thyroid were diagnosed following the detection of focal FDG uptake in patients with follicular lymphoma and with diffuse B cell lymphoma [1].

In conclusion, FDG-PET scan does not routinely serve as a tool for detection of thyroid cancer. While the prevalence of detected thyroid nodules with this modality is not higher than 4.3%, it seems that this modality has a better specificity than other types of scans in predicting malignancy. An incidental focal thyroid lesion on FDG-PET scan performed for another malignancy should not be considered metastatic without tissue confirmation. Especially in the case of lymphoma, which may involve the thyroid gland, residual metabolically active tissue on PET scans after treatment does not necessarily indicate resistant primary or recurrent disease; thus, the likelihood of primary thyroid carcinoma should be entertained, especially in cases with high SUV values. Detection and treatment of thyroid malignancy may have significant clinical relevance, with subsequent impact on patient management.

SUV = standardized uptake value

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