Whole-body $^{18}$F-FDG PET/CT in primary non-Hodgkin’s lymphoma of the thyroid associated with Hashimoto’s thyroiditis and bilateral kidney infiltration


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Abstract.—An 82-year-old female patient with hypothyroidism and Hashimoto’s thyroiditis noted three years ago to have a small asymmetric goiter (left > right). Nevertheless, a rapid growth of the thyroid over 3-6 months caused dysphagia and shortness of breath. Ultrasound and a thyroid gammagram showed an image consistent with a multinodular goiter with a hyperfunctioning nodule in the right lobe. Due to the history of Hashimoto’s thyroiditis and a rapid increase in size of the thyroid gland, diagnoses of thyroid lymphoma and anaplastic thyroid cancer were considered. Thyroidectomy was attempted at an outside facility to relieve compressive symptoms. Fine needle aspiration was insufficient for diagnosis, and the product of thyroidectomy confirmed the diagnosis of diffuse large-cell lymphoma. A positron emission tomography/computed tomography scan was performed in our institution for staging, revealing nodal and extranodal metastasis. Chemotherapy using cyclophosphamide, vincristine and dexamethasone (COP modified) led to a dramatic response of the tumor and a complete resolution of compressive symptoms.

KEY WORDS: fluorodeoxyglucose $^{18}$F, diffuse large-cell lymphoma, thyroid gland, thyroid neoplasms, thyroiditis, positron emission tomography.

$^{18}$F-FDG PET/TC DE CUERPO COMPLETO EN LINFOMA NO HODGKIN PRIMARIO DE LA TIROIDES ASOCIADO CON TIROIDITIS DE HASHIMOTO E INFILTRACIÓN RENAL BILATERAL

Resumen.—Paciente mujer de 82 años con hipotiroidismo y tiroiditis de Hashimoto, observado desde hace tres años la presencia de un bocio asimétrico pequeño (izquierdo > derecho). Sin embargo, un crecimiento rápido de la glándula en un periodo de 3-6 meses causó disfagia y respiración corta. La ecografía y la gammagrafía tiroidea mostraron imágenes consistentes con bocio multinodular con un nódulo hipofuncionante en el lóbulo derecho. Por la historia de tiroiditis de Hashimoto y el aumento rápido en el tamaño de la glándula tiroidea, se consideró un diagnóstico de linfoma tiroideo y cáncer tiroideo anaplásico. Se realizó tiroidectomía en un hospital externo para aliviar los síntomas compresivos. La aspiración con aguja fina fue insuficiente para el diagnóstico, y en la pieza de la tiroidectomía se confirmó el diagnóstico de un linfoma difuso de células grandes tipo B. En nuestro centro se realizó un rastreo con FDG-PET/CT para estadificación, mostrando metástasis intra y extraganglionares. La quimioterapia con ciclofosfamida, vincristina y dexametasona (COP modificado), produjo una respuesta dramática del tumor y una resolución completa de los síntomas compresivos.

KEY WORDS: fluorodesoxiglucosa $^{18}$F, linfoma de células grandes, glándula tiroides, neoplasia tiroides, tiroiditis, tomografía por emisión de positrones.

INTRODUCTION

Primary non-Hodgkin lymphoma (NHL) of the thyroid is an uncommon disease. The incidence has been estimated to be 3.4% among primary thyroid malignancies1. $[^{18}$F$]$fluoro-2-deoxy-D-glucose positron emission tomography ($^{18}$F-FDG PET) is recently proposed as the imaging method of choice for the detection and staging of lymphoma2.

An special feature of this disease includes the association with Hashimoto’s thyroiditis3, the frequent-ly isolated gastrointestinal relapse4 and controversy regarding the extent of surgical management5.
Elderly women are most commonly affected. The disease arises in association with chronic lymphocytic thyroiditis (Hashimoto’s disease) in 40-80% of cases\(^1\). Histologically, NHL of the thyroid tends to present as a poorly differentiated lesion. However, there may be a subgroup of patients with characteristics of mucosa-associated lymphoid tissue (MALT)\(^1\). These lymphomas remain localized for an extended period of time, which accounts for the high prevalence of early disease, stages IE (confined to the thyroid gland) and IIE (local lymph node involvement), at initial presentation\(^3\). Recognition of the thyroid as a component of the MALT system warrants attempts at identification and eradication of antigenic stimulation of B-cell MALTomas. We present the \(^18\)F-FDG PET/computed tomography (CT) findings in a case of thyroid lymphoma with complete kidneys infiltration at presentation; to the best of our knowledge a patient with these imaging features has not been previously reported.

**CASE REPORT**

We report the case of an 82-year-old female patient who was initially evaluated at an outside facility, she noted three years ago to have a non-tender growing asymmetric goiter (left > right). Rapid growth of the thyroid over the last 6 months caused pressure symptoms consisting in dyspnea and hoarseness. Past history included a hysterectomy, she did not have any family history of diabetes or thyroid disease and she was not receiving any specific medications. On physical examination the neck revealed a hard and fixed non-tender swelling on both sides; other findings were unremarkable.

Blood tests showed a normal full blood count, erythrocyte sedimentation rate, calcium, renal and liver function. A thyroid profile showed a free thyroxine concentration of 22.4 pmol/l (normal range 9.6-26.5 pmol/l) and thyroid stimulating hormone of 6.6 mU/l (normal range 0.6-4.8 mU/l) indicative of “compensated euthyroidism”. The thyroperoxidase antibody level was strongly positive. She was started on thyrroxine and ultrasound (US) and thyroid gammagram were requested.

US showed an enlarged thyroid gland mimicking a multinodular diffuse goiter (fig. 1A-B). The median largest diameter of the tumor was 6.5 cm, without any apparent involvement of adjacent soft tissues. An additional thyroid gammagram showed an extensive cold area of the left and right lobes with a hot spot in the last one (fig. 1C-D). The initial diagnosis was a hyperfunctioning nodular goiter, possibly in relation with a neoplastic tumor of the right lobe.

A thyroidectomy was performed in an outside hospital to relieve compressive symptoms. At surgery, both lobes were involved without infiltration to soft tissues or cervical vessels. A frozen section study revealed a diffuse large B-cell lymphoma of the thyroid gland. In addition, Hashimoto’s thyroiditis was reported in the thyroid tissue adjacent to the B-cell lymphoma. For treatment and staging purposes the patient was referred to our institution. A whole-body \(^18\)F-FDG PET/CT scan was scheduled; the PET/CT fused images showed at the neck level just below and to the left of the thyroid cartilage, a clump of lymph nodes with a maximum standardized uptake value (SUV) of 31.5, this mass extended to the upper mediastinum with a mean maximum diameter of 3.5 cm (fig. 2A-B). Other lesions were identified in posterior or mediastinum at both sides of the carina with a maximum SUV of 23. Another lesions with variables sizes were found in both lungs with maximum SUV of 45.1 (figs. 2A-C and 3A-B).

In the stomach, at the level of the antrum there was a thickening of the gastric wall with a maximum SUV of 36.6. Both kidneys presented enlarged size with diffuse appearance on the CT suggestive of tumor infiltration, PET/CT fused images showed tumor infiltration with a mean maximum SUV of 35.6 in both kidneys (figs. 2C-D and 3A).

Additional areas with abnormal \(^18\)F-FDG uptake were observed in the ileum (SUV max 14.1) and jejunum (SUV max 3.6) wall, abdominal wall (SUV max 2.5), lymph nodes of the left iliac fossa (SUV max 5.2), hypophysis gland (SUV max 14.9) (fig. 3C-D); and pelvic floor (SUV max 24.6) (fig. 2D).

Chemotherapy using cyclophosphamide (500 mg/m\(^2\)), vincristine (1.4 mg/m\(^2\)) and dexamethasone (40 mg/day × 4 days) led to a dramatic response of the tumor, follow-up is continued.

**DISCUSSION**

Hashimoto’s thyroiditis is a well established risk factor for the development of thyroid lymphoma\(^2\), making the incidence higher in patients with this entity\(^3,4\). Thyroid lymphoma tends to occur most
commonly in women during the sixth and seventh decades of life. Most patients present with a single neck mass; other symptoms are most commonly related to local compressive symptoms associated with acute thyroid enlargement. Other symptoms as fever, night sweats or weight loss are not usually reported.

A relatively rapid growth of the thyroid gland should lead one to consider lymphoma or an anaplastic thyroid cancer as a differential diagnosis. Diagnosis can be made with fine needle aspiration or core needle biopsy, however larger amounts of tissue (obtained by performing an incisional biopsy) may be required for flow cytometry and confirmation of diagnosis.

The more common subtype, comprising up to 70% of cases, is diffuse large B-cell lymphoma. This subtype appears to have the most aggressive clinical course with almost 60% of these tumors diagnosed with disseminated disease. Up to 40% of all diffuse large cell lymphomas have been observed that undergone transformation from a MALT lymphoma, but they behave in a similar fashion to diffuse large B-cell lymphomas.

The association between Hashimoto’s disease (chronic lymphocytic thyroiditis) and non-Hodgkin’s lymphoma has been widely debated. It is sometimes difficult to distinguish between the two entities histologically, and it is presumed that the chronic inflammatory response elicited in Hashimoto’s disease will eventually lead to malignant degeneration. Progression can be identified by monoclonal antibody identification of light chain restriction.

The transformation may require chronic antigenic stimulation similar to that seen with *H. pylori* and B-cell associated MALToma of the stomach. In fact, several authors consider non-Hodgkin’s lymphoma of the thyroid to represent lymphomatous
transformation of MALT. Arising within the stomach, thyroid, lung, and salivary glands, these tumors enjoy a prolonged period of localized disease.

Chemotherapy and radiation are the mainstays of treatment. However, the potential aggressiveness of this disease requires adequate follow-up and multimodality treatment of recurrent or persistent disease. The 5-year survival rate in diffuse large B-cell lymphoma has been reported of 44%.

Palliative thyroidectomy is occasionally required. Imaging evaluation in non-Hodgkin’s lymphoma helps in accurate staging and prognostic information and can guide therapeutic management; in this patient lymphoma was reported as a stage IV which required systemic treatment.

Sometimes a residual increased uptake of $^{18}$F-FDG in the thyroid mimicking disease is linked to regeneration processes related to tumor necrosis or local inflammatory process. In these cases, a fine-needle aspiration of the residual mass is indicated. In our patient the size of the mass, and the intensity of SUV left no doubts it was a residual mass. Performance of $^{18}$F-FDG PET/CT has also been reported in a patient with MALT lymphoma and known Hashimoto’s thyroiditis.

No biopsies of the kidneys or stomach were required, according to Cotswold’s modification of the Ann Arbor classification for describing the stage of Hodgkin’s disease; the CT is currently included as a technique for evaluating intrathoracic and infradiaphragmatic lymph nodes; the criteria for clinical involvement of the spleen and liver are modified to include evidence of focal defects with two imaging techniques and the abnormalities of liver function may be ignored. Besides, the patient presented with 6 mg of serum creatinine on admission; this value was normalized after chemotherapy, which indirectly supports the kidney infiltration.
Until recently, a chest x-ray, CT scan of the abdomen, and bone marrow biopsy had been the most important investigations in ruling out disseminated disease. Nowadays, PET/CT scan is considered the imaging method of choice for the detection and staging of lymphoma, which may have an impact on definitive therapy. Under staging of patients may result in less than optimal treatment for disease which has extended beyond the thyroid gland or the regional lymphatics.

This is specially important as after treatment, residual masses may call in question the possibility of residual disease. Indeed, it has been shown that in many cases lack of reduction of such tumoral masses after chemotherapy does not necessarily mean persistence of the disease. In this case, fused images from PET/CT, let us detect residual disease in the neck, total infiltration of the kidneys, multiple metastasis in lungs, as well as the hypophysis and pelvic floor, these findings allowed an initial diagnosis of stage IV NHL on admission.

REFERENCES


Roldán-Valadez E et al. Whole-body 18F-FDG PET/CT in primary non-Hodgkin’s lymphoma of the thyroid associated with Hashimoto’s thyroiditis and bilateral kidney infiltration


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