Role of ^{18}F-FDG (fluro-deoxy-glucose) PET/CT in Patients with Differentiated Thyroid Cancer Who Present with Elevated Thyroglobulin and Negative ^{131}I Whole Body Scan

Thesis
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بسم الله الرحمن الرحيم

"قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ"

صدق الله العظيم

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Abstract

Serum Tg appears to be the most sensitive test in follow up of differentiated cancer thyroid while other imaging methods as ultrasound and CT may be helpful with limited sensitivity. Rising thyroglobulin levels are generally a reliable indicator of recurrent thyroid cancer.

This study aimed to detect the ability of 18F-FDG with PET/CT to explain the elevated Tg levels in patients with DCT and negative 131-I WBS. Correlation of 18F-FDG PET/CT with other diagnostic methods was done.

This study included 20 patients (13 males and 7 females) with pathologically proven differentiated cancer thyroid. All patients were subjected to near total thyroidectomy.

In our study we found an overall high sensitivity of PET/CT for detecting and localizing recurrent or metastatic differentiated thyroid cancer on 18F-FDG PET/CT.

Neck US detected 7 lesions in 6 patients, all of them confirmed to be positive by PET/CT with 13 additional neck lesions were detected by PET/CT in 15 patients. CT chest detected 8 patients, 6 of them confirmed by PET/CT while 2 of the lung lesions were negative. 8 additional mediastinal LNs metastatic lesions were detected by PET/CT.

Key Words :

5-Flurouracil - PET/CT – DTC .

List of Abbreviations

5-Fu	5-Flurouracil
ACS	American cancer society
ATC	Anaplastic thyroid cancer
CT	Computed tomography
DTC	Differentiated thyroid cancer
F18	Flourine 18
FDA	Food and Drug Association
FDG	FluoroDeoxyGlucose
FOV	Field of view
FWHM	Full width at half maximum
GCSF	Growth Colony Stimulating Factor
IMA	Immuno-metric assay
IMC	International Medical Center
IV	Intra venous
LN	Lymph node
LOR	Line of response
MRI	Magnetic resonance imaging
OSEM	Ordered Subsets – Expectations Maximization
PET	Positron Emission Tomography
PMT	Photo Multiplier Tube
RAI	Radio active iodine
RIA	Radio-Immunoassay
SUV	Standard uptake volume
Tg	Thyroglobulin
TgAb	Thyroglobulin Antibody
US	Ultrasound
WBS	Whole body scan

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Introduction

Differentiated thyroid cancer (Papillary and follicular) represents approximately 80%-85% of thyroid carcinoma. Both have an excellent prognosis, with a 20 years survival of 90%–95% and 75%, respectively (**Kumar et al.,** 2010).

The standard surgical treatment is total (or near-total) thyroidectomy. This procedure decreases the risk of local recurrence and facilitates post-surgical radioiodine ablation and adequate follow up (**Pacini et al.,** 2007).

A diagnostic scan with radio-active iodine 131 is usually obtained 4-6 weeks after surgery to demonstrate residual functioning thyroid remnant and/or metastases. The diagnostic ^{131}I dose typically ranges from (2–5 mCi), and scanning is performed 72 hours later (**Schlumberger et al.,** 2006).

Serum TG appears to be the most sensitive test in follow up of differentiated cancer thyroid while other imaging methods as ultrasound and CT may be helpful with limited sensitivity (**Girelli et al., 2010**).

The lacking of ^{131}I trapping by metastatic tissue does not allow whole body scintigraphy to visualize metastatic spread as well as the use of it in therapy to cure such metastatic spread. In this view, a high sensitive localizing imaging different form ^{131}I whole body scintigraphy is required and more favorable results have been reported with ^{18}F-FDG with PET/CT tomographs. The PET/CT fusion imaging systems provide good anatomical localization of the hyper metabolic metastatic lesions (**Alavi et al.,2009**).

Aim of the work

- To detect the ability of ^{18}F-FDG with PET/CT to explain the elevated Tg levels in patients with negative ^{131}I WBS after administration of diagnostic dose.

- Correlation of ^{18}F-FDG with PET/CT with other diagnostic methods and final diagnosis.

REVIEW OF LITERATURE

PATHOLOGY OF DCT

Virtually all malignant neoplasms of the thyroid gland are epithelial in origin and hence are carcinomas. The papillary and follicular carcinomas (differentiated) are arising from the follicular epithelium (**Headinger et al., 2000**).

Classification of DCT:

1- Papillary carcinoma.

2- Follicular carcinoma.

1-Papillary carcinoma

In most series, carcinoma that is either purely or predominantly papillary in structure is the most common; between 80-90% of the differentiated thyroid cancers are classified as papillary. They occur as a broad age range with a mean of about 45 years. Women are affected two to three times more common than men. Young patients with this disease sometimes give a history of having radiation therapy during childhood for cervical lymphadenitis or thymic enlargement, suggesting that radiation of the thyroid gland may play a pathogenic role. In general, papillary carcinoma is the most slow-growing of all thyroid carcinomas, often remaining localized to the thyroid gland for many years. It tends to spread via the intra-glandular lymphatics from its primary sites to other parts of the thyroid and to the pre-capsular and regional lymph nodes. Hematogenous spread to distant sites such as lung is uncommon. The growth of papillary carcinoma is thought to depend partially on TSH stimulation, this view stems from the observation that administration of suppressive doses of thyroid hormones sometimes leads to regression of metastases from a primary lesion that was predominantly papillary in type.

However, most papillary carcinomas contain follicular elements, and the metastases may be composed predominantly of the later. Papillary carcinoma has a tendency to become more malignant with advanced age. In patients diagnosed at the age of 50, thyroid cancer is more aggressive with an increase in the

incidence of metastases outside the neck and progressive increase in the risk of death (**Hay, Mazzaferri and Jihan, 2005**).

Clinically papillary carcinoma usually appears as an asymptomatic nodule in an otherwise normal thyroid or as an enlargement of the regional lymph nodes, sometimes without a palpable thyroid nodule. Invasion of adjacent structures and distant metastases are late manifestations (**Ezaki et al., 2009**).

Grossly, the carcinoma varies in size and is usually un-capsulated. On histo-pathological examination, it is composed of columnar epithelium that is thrown into folds, forming papillary projections with connective tissue stalks, there is frequently a mixed papillary and follicular pattern, which has the biologic behavior of papillary carcinoma, and should therefore be classified as papillary carcinoma. This classification is used because the prognosis for thyroid cancer with any papillary features differs from that of pure follicular cancers (Fig. 1 and 2)(**Robbins et al.,2008**).

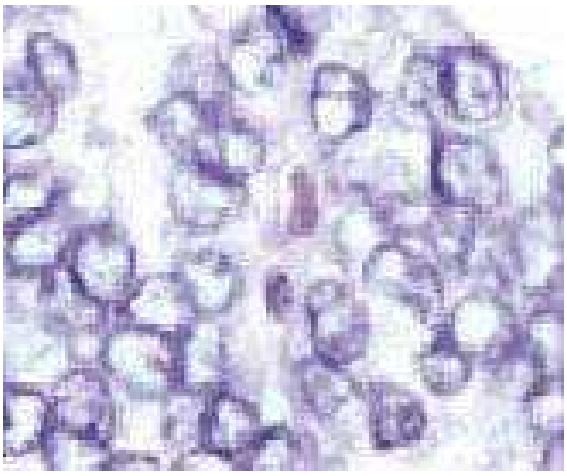

Fig. (1): Microscopic picture of papillary cancer thyroid (Robbins et al.,2008).

Fig. (2): Gross picture of papillary cancer thyroid.
(Robbins et al.,2008).

- **Variants of papillary carcinoma:**

The following morphological variants of papillary carcinoma have been described:

a. Papillary micro-carcinoma.

This is defined as papillary carcinoma measuring 1 cm or less in diameter. There is no evidence that these cancers affect health or life span as long as they remain clinically undetectable **(Sampson, 2000).**

b. Encapsulated variant.

Papillary cancers totally surrounded by a capsule and may be associated with nodal metastasis, but the incidence of distant metastasis or tumour death is nearly zero **(Vickery, 2008).**