Comparison of FDG-PET and ^{99m}Tc-MIBI Scintigraphy in Detecting Metastatic Well Differentiated Thyroid Carcinoma with Negative ^{131}I-Whole Body Scan

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Objectives. The aim of this study was to evaluate the effectiveness of ^{99m}Tc methoxysiobutyl isonitrile (^{99m}Tc MIBI) scintigraphy and 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) in detecting metastatic lesions in well differentiated thyroid carcinoma (DTC) after nearly total thyroidectomy and ^{131}I treatment in patients who presented with elevated serum human thyroglobulin (hTg) levels but negative ^{131}I whole body scintigraphy (WBS).

Methods. This study comprised 23 patients (15 women and 8 men; age, 22 to 71 years) with DTC (20 papillary and 3 follicular type) who underwent nearly total thyroidectomy and either radioiodine ablation or radioiodine therapy. All research subjects had negative ^{131}I WBS and elevated hTg levels (hTg ≥ 2.0 μgIU/mL) under thyroid-stimulating hormone (TSH) stimulation (TSH ≥ 30 μgIU/mL). Both ^{99m}Tc MIBI scintigraphy and FDG-PET were performed for comparison.

Results. FDG-PET detected abnormal hypermetabolic lesions in 20 patients while ^{99m}Tc MIBI scintigraphy revealed lesions in only 11 patients. Both FDG-PET and ^{99m}Tc MIBI scintigraphy failed to demonstrate miliary pulmonary metastasis in 2 patients. One patient did not show any lesion via FDG-PET, ^{99m}Tc MIBI scintigraphy, chest CT or other imaging techniques and he has remained disease-free for 10 months.

Conclusions. This study demonstrated that FDG-PET is more sensitive than ^{99m}Tc MIBI scintigraphy in detecting metastatic lesions in DTC patients with elevated hTg but negative ^{131}I WBS. FDG-PET is ^{99m}Tc MIBI scintigraphy capable of detecting smaller lesions, especially in the small mediastinal lymph nodes. However, miliary pulmonary metastasis may be missed by both techniques. **(Mid Taiwan J Med 2004;9:44-9)**

Key words

^{18}Fluoro-2-deoxyglucose, positron emission tomography, ^{99m}Tc MIBI scintigraphy, well differentiated thyroid carcinoma

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INTRODUCTION

Serum human thyroglobulin (hTg) measurement and ^{131}I whole body scintigraphy

Table 1. FDG-PET and ^{99m}Tc MIBI scintigraphy results

Case	Sex	Age	Histopathology	Metastatic foci	FDG-PET	^{99m}Tc-MIBI scintigraphy
1	M	58	Papillary	Left lower neck lesion	Positive	Negative
2	F	29	Papillary	Miliary lung meta	Negative	Negative
3	F	68	Papillary	Right mediatinual lesion	Positive	Positive
4	F	70	Papillary	Multiple lung & bone lesions	Positive	Positive
5	F	52	Papillary	Bilateral lower neck lesions	Positive	Positive
6	M	65	Papillary	Bilateral thoracic inlet & mediastinum	Positive	Positive
7	M	65	Papillary	Bilateral mediastinal lesions	Positive	Positive
8	F	31	Papillary	Miliary lung meta	Negative	Negative
9	F	41	Papillary	Bilateral mediastinal tiny LNs	Positive	Negative
10	F	71	Papillary	Bilateral mediastinal LNs	Positive	Negative
11	F	71	Papillary	Right mediastinal LN	Positive	Positive
12	F	47	Papillary	Bilateral mediastinal tiny LNs	Positive	Negative
13	M	40	Papillary	-	Negative	Negative
14	F	53	Follicular	Multiple lesions at left thoracic inlet	Positive	Positive
15	F	41	Papillary	Thyroid bed recurrent	Positive	Positive
16	M	29	Papillary	Thyroid bed recurrent	Positive	Positive
17	F	64	Papillary	Left neck LN Right parotid area	Positive	Negative
18	F	39	Papillary	Left neck tiny LN	Positive	Negative
19	M	51	Follicular	Left submandibular LN Multiple small LNs in mediastinum	Positive	Negative
20	F	29	Papillary	1 tiny LN at left neck	Positive	Negative
21	M	22	Papillary	1 LN at right neck	Positive	Negative
22	F	37	Papillary	2 tiny LNs at right lower neck	Positive	Positive
23	M	32	Papillary	Left submandibular 4 LNs at right neck	Positive	Positive

(WBS) have been widely used for follow-up of patients with well differentiated thyroid carcinoma (DTC) after nearly total thyroidectomy and ^{131}I treatment [1-4]. Although ^{131}I WBS has a very high specificity of 99% to 100%, ^{131}I recurrences in WBS-positive cases is about 50% to 60% in papillary and 64% to 67% in follicular thyroid cancer [2,5-6]. Patients with elevated hTg levels but negative ^{131}I WBS, are not usually treated with high-dose ^{131}I. Accurate localization of metastatic lesions is therefore very important since they need to be removed surgically or treated with external radiotherapy. Non-specific radiopharmaceuticals, such as ^{201}Tl chloride, ^{99m}Tc methoxysiobutyl isonitrile (^{99m}Tc MIBI) and positron emission tomography (PET) with 2-[^{18}F]fluoro-2-deoxy-D-glucose (FDG) have been shown to be valuable [7-19]. This study was designed to assess the clinical usefulness of ^{99m}Tc MIBI scintigraphy and FDG-PET in the follow-up of patients with differentiated thyroid cancer who present with increased hTg levels and negative ^{131}I scans.

PATIENTS AND METHODS

Patients

The study group was composed of 23 patients (15 women, 8 men; age 22-71, median 47 years) with DTC (20 papillary-type and 3 follicular-type) who underwent nearly total

Table 2. Diagnostic values of FDG-PET and ^{99m}Tc-MIBI scintigraphy

	Sensitivity (%)	Specificity (%)	Accuracy (%)
FDG-PET	90.9	100	91.3
^{99m}Tc-MIBI scintigraphy	50.0	100	52.2

thyroidectomy and radioiodine ablation therapy. All had negative ^{131}I WBS scans and elevated hTg levels (hTg ≥ 2.0 ng/mL) under thyroid-stimulating hormone (TSH) stimulation (TSH ≥ 30 μgIU/mL).

^{99m}Tc MIBI Scan and FDG-PET

Ten minutes after a bolus injection of 740 MBq (20 mCi) ^{99m}Tc MIBI, whole body scan and SPECT of the head and chest were performed. The images were recorded by a dual-head gamma camera and a low-energy high-resolution collimator appropriate for low (less than 180 keV) energy levels. All patients fasted for at least 6 hours prior to the whole-body FDG-PET study. The FDG-PET study was performed 45 minutes after a bolus injection of 370 MBq (10 mCi) of FDG by either a Siemens-CTI EXACT HR + PET scanner (Siemens Medical systems, Iselin, NJ, USA; CTI Knoxville, TN, USA) or a GE Advance PET system (General Electric, Milwaukii, WI, USA).

Interpretation of FDG-PET and ^{99m}Tc MIBI scans was based on visual analysis by two experienced nuclear medicine physicians without prior knowledge of the results of the other examinations. Lesions showing ^{99m}Tc MIBI uptake or FDG metabolism greater than the radioactivity of the neighboring background were considered to be positive.

RESULTS

FDG-PET and ^{99m}Tc MIBI scintigraphy results and the patients' characteristics are summarized in Table 1. FDG-PET detected abnormal hypermetabolic lesions in 20 patients. In 11 patients, all of the lesions detected by ^{99m}Tc MIBI had also been detected by FDG-PET. There were 9 patients whose FDG-PET scans were positive but whose ^{99m}Tc MIBI scintigraphy scans were negative. However, in one patient (patient 17) ^{99m}Tc MIBI scintigraphy demonstrated a lesion on the left side of the neck but missed the lesion in the right parotid region.

Both FDG-PET and ^{99m}Tc MIBI scintigraphy failed to demonstrate any lesion in 3 patients. However, X-ray computed tomography (CT) showed miliary pulmonary nodules in two of these patients (patient 2 and patient 8). No lesions were detected by chest CT or any other imaging studying in the other patient (patient 13). Close follow-up over the past 10 months has shown that the patient has remained disease free. The diagnostic values of these two imaging modalities are listed in Table 2.

DISCUSSION

A combination of ^{131}I WBS and the determination of serum hTg levels has been suggested for the follow up care of differentiated thyroid carcinoma patients treated by total or nearly total thyroidectomy followed by ^{131}I plus thyroid hormone therapy [1-4]. A positive ^{131}I scintigraphy also indicates that ^{131}I is useful in the treatment of recurrent or metastatic lesions. However, for those patients with elevated hTg levels but negative ^{131}I scintigraphy, early determination of metastatic lesions is difficult, but very important. Radical surgery, external radiotherapy or redifferentiation therapy can be performed if the lesions can be identified. In these cases, the metastatic foci lose the ability to take up ^{131}I because of dedifferentiation of the cancer cells. Both ^{99m}Tc MIBI scintigraphy and FDG-PET have been demonstrated to be useful in these situations.

^{99m}Tc MIBI has been found to accumulate in various tumor cell types, including DTC. The cationic charge and lipophilicity of ^{99m}Tc MIBI, the mitochondrial and plasma membrane potentials of the tumor cells, and the cellular mitiochondrial content are all considered to play significant roles in the mechanism of tumor

uptake of this agent [20]. FDG-PET has also been found to be a valuable imaging modality in detecting metastatic lesions in patients with DTC who present with elevated hTG and negative ^{131}I WBS levels [11,13,21].

For the detection of metastatic DTC, studies have found that ^{99m}Tc MIBI [7] and FDG [11,21] accumulated more often in lesions in which ^{131}I had failed to accumulate. It was suggested that FDG uptake and concomitant loss of ^{131}I uptake is a sign of dedifferentiation of the cancer cells [11,15,21,22]. In this study, we observed that FDG-PET was more sensitive than ^{99m}Tc MIBI scintigraphy in these cases. The FDG-positive/MIBI-negative lesions tended to be small-sized including tiny lesions in the mediastinum in 4 patients. Our results are understandable since PET scanners have a higher spatial resolution than SPECT images from a dual-head gamma camera. Moreover, ^{99m}Tc MIBI scintigraphy missed 2 lesions (patient 17 at right parotid and patient 19 at left submandibular) close to the salivary glands. This could have been due to interference by the physiological uptake of ^{99m}Tc MIBI in these glands.

Both ^{99m}Tc MIBI scintigraphy and FDG-PET were performed in this study without TSH stimulation. Although the influence of TSH on ^{99m}Tc MIBI and FDG uptake in DTC cells remains to be determined, Mueller et al [23] reported that the uptake of ^{99m}Tc MIBI in thyroid carcinoma was independent of TSH stimulation while higher sensitivity of FDG-PET under high TSH levels was not observed [18,21].

In our study, 2 patients with miliary pulmonary metastases were verified by spiral CT. Neither FDG-PET nor ^{99m}Tc MIBI SPECT were able to differentiate the region of elevated uptake from normal lung background. In these circumstances, spiral CT should be included in the follow-up protocol.

This study showed that FDG-PET is more sensitive than ^{99m}Tc MIBI scintigarphy in detecting metastatic lesions in DTC patients with elevated hTg but negative ^{131}I WBS. FDG-PET can detect smaller-sized lesions than ^{99m}Tc MIBI sintigarphy can, especially in the mediastinal lymph nodes; however, both modalities may miss miliary pulmonary metastasis.

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氟-18去氧葡萄糖正子造影於碘131全身閃爍掃描為陰性者對偵測良好分化的轉移性甲狀腺癌之比較

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目的　此研究主要在比較鎝99m-MIBI閃爍掃描與氟-18去氧葡萄糖正子造影在偵測分化良好的甲狀腺癌病人在甲狀腺完全切除手術並接受碘-131清除治療後，且碘131全身閃爍掃描爲陰性，因病人血清中的甲狀腺球蛋白值升高而疑似有轉移病灶的靈敏度。

方法　在這個研究中共有23個甲狀腺癌病人(其中15個爲女性，8個爲男性，年齡在22到71歲之間，20個爲乳突型，3個爲濾泡型)，這23個病人都經過甲狀腺完全切除手術及放射性碘清除治療。在此研究中的病人其碘131全身閃爍掃描均爲陰性，而且病人經過甲狀腺刺激荷爾蒙(TSH ≥ 30 μIU/mL)刺激後，血清中的甲狀腺球蛋白值升高(hTg ≥ 2.0 μIU/mL)。病人同時做鎝99m-MIBI閃爍掃描與氟-18去氧葡萄糖正子造影，並加以比較。

結果　氟-18去氧葡萄糖正子造影在23個病人中發現20個病人有代謝過高的部位，而鎝99m-MIBI閃爍掃描只發現11個病人有異常，此外，鎝99m-MIBI閃爍掃描與氟-18去氧葡萄糖正子造影皆無法偵測出其中2個病人有肺部細粒狀的癌轉移。在23個病人中，有一個病人在鎝99m-MIBI閃爍掃描、氟-18去氧葡萄糖正子造影、肺部斷層掃描或其他造影技術均無任何發現，且此病人在10個月內沒有復發或轉移的情形。

結論　當碘131全身閃爍掃描爲陰性且血清中的甲狀腺球蛋白值升高時，氟-18去氧葡萄糖正子造影在偵測分化良好的甲狀腺癌病人的癌轉移比鎝99m-MIBI閃爍掃描更爲敏感。氟-18去氧葡萄糖正子造影能比鎝99m-MIBI閃爍掃描能偵測到更小的轉移，尤其是在小縱隔淋巴結轉移，但鎝99m-MIBI閃爍掃描與氟-18去氧葡萄糖正子造影可能均無法偵測到肺部細粒狀的癌轉移。（**中台灣醫誌 2004;9:44-9**）

關鍵詞

氟-18去氧葡萄糖，正子造影，鎝99m-MIBI閃爍掃描，分化良好甲狀腺癌

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