Disseminated Lung Metastases in Thyroid Cancer

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A 23-year-old female suffered from a locally invasive well-differentiated thyroid papillary carcinoma with cervical lymph nodes metastases and disseminated lung metastases 16 years ago (in 1989). After undergoing a surgical operation, she had received subsequent accumulated therapeutic dose of 13 GBq (350 mCi) of ^{131}I in the following two years. Thereafter, she delivered two healthy babies in 1993 and in1996, respectively. Ten years later (in 1999), persistent disseminated lung metastases were identified with a 7.4 GBq ^{131}I post-therapy scan. Meanwhile, FDG-PET study was negative. In 2005, she received FDG-PET study, ^{131}I therapy, and post-therapy ^{131}I scan using the injection of recombinant human TSH instead of thyroxin withdrawal. The result showed nearly resolution of the metastatic lesions. The establishment of diagnostic/treatment guideline, the introduction of metabolic imaging modality, and the invention and production of recombinant human TSH in the past decade, this patient is able to receive accurate diagnosis, therapy and follow-up.

Key words: thyroid cancer, disseminated lung metastases, FDG-PET

Ann Nucl Med Sci 2005;18:247-252

Differentiated thyroid carcinoma (DTC) accounts for 90%~95% of thyroid cancers and roughly 1% of all newly developed malignant disease. Patients with DTC have excellent prognoses, particularly in young females. Locoregional invasion and metastasis are poor prognostic factors. Pulmonary metastases are the most common distant lesions of DTC. Functioning pulmonary metastasis presenting with positive ^{131}I uptake and negative chest X-ray accounted for about 30-50% of the metastatic cases. Most of them revealed disseminated military spreading on post-therapeutic ^{131}I whole body scan [1-3].

Case Report

In 1989, a 23-year-old female was diagnosed with thyroid cancer. At that time, she received a total thyroidectomy and modified neck dissection, which revealed a well-differentiated thyroid papillary carcinoma, follicular variant, with capsule and muscle invasion and cervical lymph node metastases. Two months later, she received 3.7 GBq (100 mCi) radioiodine (^{131}I) therapy. The post-therapy ^{131}I whole-body scan (RxWBS) demonstrated diffuse lung uptake, more severe on the right lower lung field (Figure 1). During the

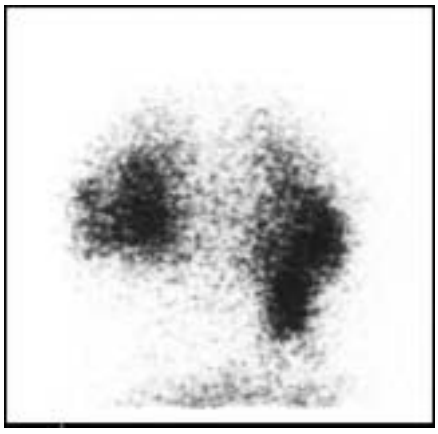

Figure 1. Diffuse lung uptake bilaterally identified by ^{131}I scan

Received 11/18/2005; revised 12/5/2005; accepted 12/9/2005.
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period of 1990~1991, she underwent another two ^{131}I treatments due to the persistence of the disease, with dosages of 3.7 and 5.6 GBq, respectively. She delivered a male baby in December 1993 and a female baby in January 1996, respectively. During the pregnancies, Giemsa-banded chromosomes studies obtained from cultured amniotic fluid were performed. Thereafter, the patient was busy raising her children and missed her follow-up visits for the next four years.

In 1999, upon returning to the hospital, the patient was in a state of suppressed serum TSH (on thyroxin therapy, TSH < 0.1 μU/mL; thyroglobulin (Tg) 1 ng/mL), and ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) was performed using an old-fashioned PET scanner built in 1992 (PC 4096-15 WB, Scanditronix, Uppsala, Sweden) with negative results for metastases (Figure 2). After withdrawal of thyroxin (serum levels: TSH > 60 μU/mL, Tg 59 ng/mL), she received 7.4 GBq of ^{131}I treatment. The RxWBS demonstrated progression of the disease as persistent, disseminated metastases in the lungs and two focal lesions in the superior mediastinum and right supraclavicular region (Figure 3). After treatment, she did not return to the hospital for six years.

In 2005, she was recalled for a reevaluation. Her general appearance was good, with no adverse symptoms or signs. According to the patient, she had been taking thyroxin regularly and living in a healthy state, and her children are in good condition both physically and mentally. Serial blood tests revealed normal cell counts (CBC), normal serum biochemical data, and suppressed serum TSH (< 0.1 μU/mL) with slight elevation of the serum Tg level (3.8 ng/mL). The lung function test revealed a minimally obstructive lung. FDG-PET study performed using a new scanner installed in 2002 (ECAT ACCEL, Siemens, Illinois, USA) was essentially normal, except for mildly increased glucose metabolism in the thymus, which was thought to be a normal variation (Figure 4). Two injections of 0.9 mg thyrotropin alpha (recombinant human TSH; rhTSH: Thyrogen, Genzyme, Cambridge, MA, USA) were given intramuscularly 24 h apart, and subsequent ^{131}I therapy with a relatively smaller dose (1.1 GBq) was given 24 h after the second injection. A slight increase in the serum Tg level (5.5 ng/mL) after the aforementioned TSH stimulation (serum level 184 μU/mL) was noted. The RxWBS showed mildly increased uptake (faint visualization) in the right lower lung field, (Figure 5A) corresponding to the finding of a reticular pattern of the lung marked over the right lower lung field on the chest radiograph (Figure 5B). Compared with the previous study in 1999 shown in Figure 3, the current study showed almost

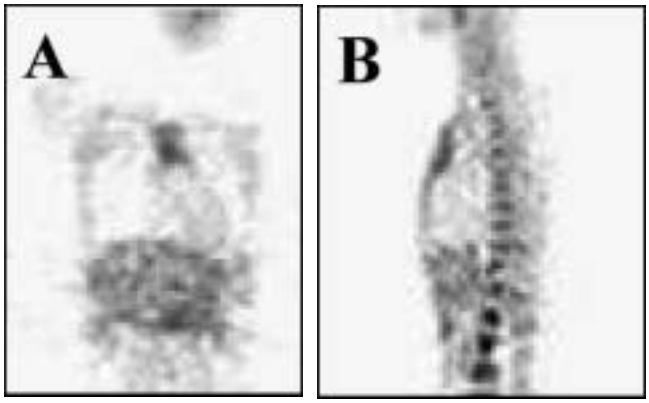

Figure 2. Except for thymic uptake of FDG, which is normal variation, no abnormal uptake demonstrable in the lungs or elsewhere. (A) Coronal section, (B) sagittal section. These images were obtained using an old-fashioned scanner.

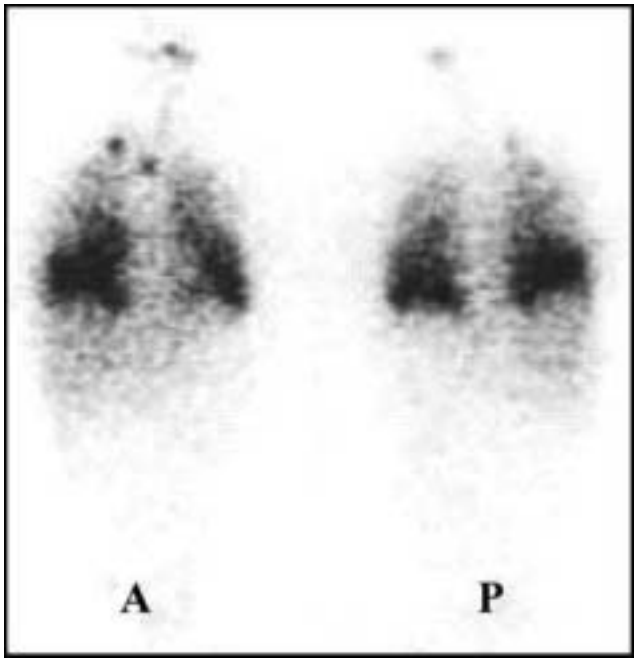

Figure 3. Persistent diffuse lung uptake noted. Additional metastatic lesions in the superior mediastinum and right supraclavicular region are demonstrated.

complete resolution of the metastatic lesions.

Discussion

A total thyroidectomy, resection of as much thyroid tissue as possible, and regional compartmental dissection are the main initial steps for dealing with invasive DTC [4]. Subsequent ^{131}I therapy, which is specifically taken up into both normal and malignant tissues is able to eliminate remnant tissues, microscopic residual cancer, and metastatic foci, and along with long-term thyroid hormone suppressive and supplement therapy, may prolong survival and improve the quality of life [2]. Long-term follow-up should mainly monitor serial measurements of serum Tg levels using a highly sensitive and specific assay in conjunction with ^{131}I WBS for localization. An undetectable serum Tg and a negative WBS usually indicate remission or cure of the disease [5,6]. Use of a recently developed and FDA-approved (in 1998) diagnostic study of rhTSH for surveillance of residual/recurrent or metastatic DTC has been found to be as sensitive and specific as that done after thyroid hormone withdrawal [6,7].

Distant metastasis of DTC, mainly lung or bone metastasis, is uncommon, and a wide range in prevalence has been reported. The incidence of lung metastases at the time of diagnosis is about 3.4% (52/1,516 cases) and that of diffuse lung metastasis is even lower (0.4%) [8,9]. Patients with micronodular metastases of the lung, detected by ^{131}I scan presenting with diffuse lung uptake but not by radiographs

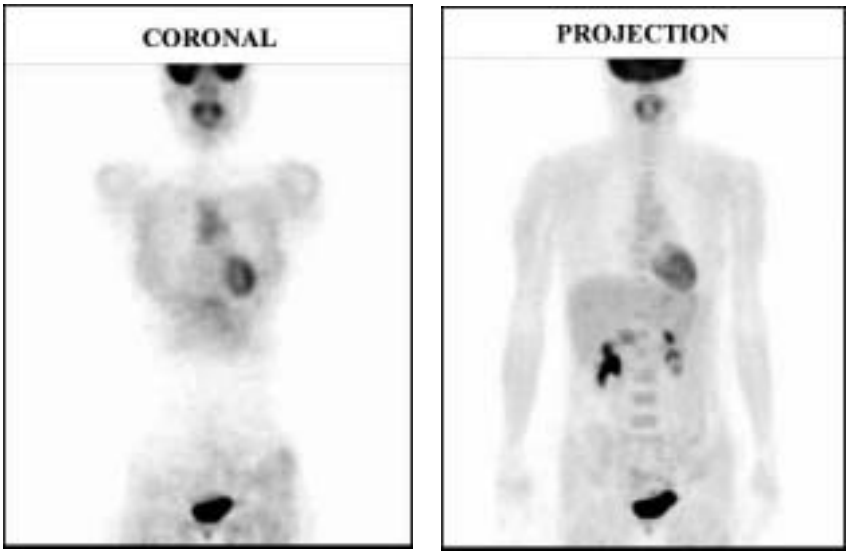

Figure 4. Negative FDG-PET as shown on a projection view (right) and coronal section (left). Note that the thymic uptake can still be visualized.

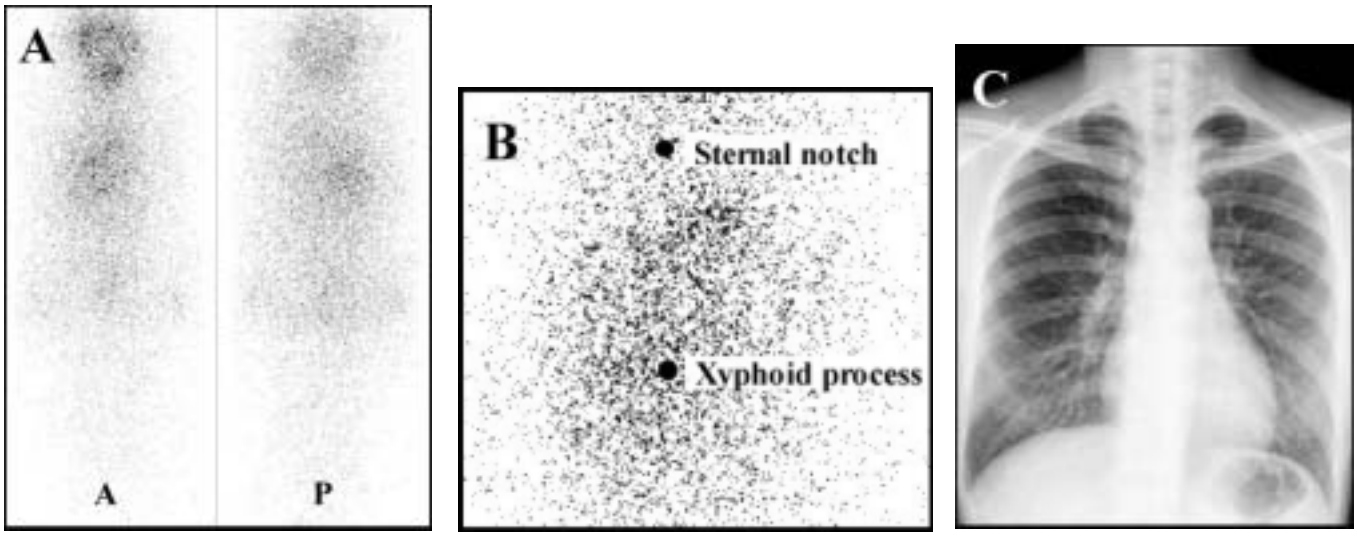

Figure 5. ^{131}I scan: (A) whole-body image, (B) focal view showed faintly increased uptake in the right lower lung field. (C) Chest X-ray revealed reticular lung marking in the corresponding lower right lung field.

had the highest long-term survival rate compared to those with macronodular pulmonary metastases seen on radiographs. The therapeutic outcome is favorable in younger, less-distend, and early-diagnosed patients after large doses of sequential ^{131}I treatment [10-13].

Chronic complications of ^{131}I therapy are rare, but include pulmonary fibrosis which may result from the use of larger doses for diffuse pulmonary metastases [13]. Although transient damage of the ovaries may occur, permanent functional failure usually does not occur. Fetuses conceived subsequent to ^{131}I therapy have no significant increased risk for congenital abnormalities. The risk of developing a secondary malignancy is low.

FDG-PET, a type of metabolic imaging, is a relatively new modality with a high sensitivity for malignant tumor management. ^{131}I uptake into well-differentiated cells and FDG into less-differentiated cells (flip-flop phenomenon) of DTC was first addressed by Feine et al. in 1996 [14]. It is especially useful for patients with abnormally elevated serum Tg but negative ^{131}I WBS, representing dedifferentiation of cancer cells or inadequate resolution and sensitivity of ^{131}I WBS for detecting small foci. The complementary roles of these two modalities in addition to CT scan for DTC are well documented. However, FDG-PET has limited value for diffuse types of metastasis, which is thought to be due to the size of tiny nodules being so small as to be under the detection limits of PET scanning or to an insufficient amount of cumulative activity in nodules, which cannot be delineated by tomographic imaging [15,16].

The establishment of the diagnostic/treatment guideline, the invention and production of rhTSH and the introduction of metabolic imaging modality in the past decade, this patient is able to receive more accurate diagnosis and complete follow-up. We had administered consecutive radioiodine therapies to this patient, which resulted in the improvement of her disease without any complication.

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甲狀腺癌併有散播性肺轉移

許重輝

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16年前 (1989)，一個23歲的年輕女性被發現患有局部侵犯性甲狀腺乳突癌併有頸部淋巴結轉移、肌肉侵犯及兩側肺部散播性轉移。手術後兩年內她共接受13 GBq (350 mCi) 之碘-131治療，於術後第四年及第六年各生下一個至今健康的小孩。十年後 (1999)，她再接受7.4GBq之碘-131治療，治療後之全身掃描發現散播性肺轉移仍存在，但是FDG-PET檢查正常。今年 (2005) 她再度接受FDG-PET檢查、碘-131治療及治療後掃描，這次使用注射合成之人類TSH (rHTSH)替代停服甲狀腺素，結果發現肺轉移幾乎已被消除。有肺部散播性轉移之年輕甲狀腺癌病患，經過大劑量之碘-131治療，預後很好，大部份可治癒，並不排除病患懷孕生子。散播性肺轉移不易被常規胸部X 光造影及FDG-PET發現。

關鍵詞：甲狀腺癌，散播性肺轉移，FDG-PET

核子醫誌2005;18:247-252

94年11月18日受理 94年12月5日修改 94年12月9日接受刊載
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