

Hyperprolactinemia-Associated Breast Uptake of Radioiodine Following ^{131}I Postablation Scan in Differentiated Thyroid Cancer

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Scanning with whole-body ^{131}I scintigraphy after surgery has been a valuable diagnostic modality in the surveillance of patients with differentiated thyroid cancer. Radioiodine uptake is rarely observed in non-lactating breast tissue, which mimics thyroid cancer metastasis. We now report a case of a 45-year-old female thyroid cancer patient who underwent radioiodine therapy, and in whom breast uptake of radioiodine was observed on a post-therapy whole body scan. Her serum prolactin level was elevated to 328 ng/mL at the time of the radioiodine uptake, and the hyperprolactinemia was induced by her antipsychotic medications. Six months after she discontinued that medication, her serum prolactin level was normalized to 12.6 ng/mL and breast uptake of iodine was no longer present in a follow-up whole body scan. (*Endocrinol Metab* 26:345-347, 2011)

Key Words: Antipsychotic agents, Differentiated thyroid cancer, Hyperprolactinemia

INTRODUCTION

Radioiodine is used in the diagnosis and treatment of differentiated thyroid cancer. But radioiodine uptake can also be observed in non-thyroidal tissue [1]. It is rarely taken up by the non-lactating breast [2-4], mimicking thyroid cancer metastasis. Herein we report a case of ^{131}I breast uptake in a thyroid cancer patient who had hyperprolactinemia due to antipsychotics.

CASE REPORT

A 45-year-old female had a total thyroidectomy for papillary thyroid carcinoma (stage pT3NxMx). The tumor was $1.2 \times 1.1 \times 1.9$ cm in size, located in the left lobe, and had extrathyroidal extensions to sternothyroid muscles. The surgical resection margin was free of carcinoma. As she lost weight (12 kg during the 5 months after surgery), she took several tests, including positron emission tomography-computed tomography (PET-CT). There was no evidence of

tumor recurrence or metastasis on PET-CT (Fig. 1). Following administration of recombinant human thyroid stimulating hormone (TSH), the patient underwent remnant ablation receiving a fixed dose of radioiodine (^{131}I ; 150 mCi) 6 months after surgery. Subsequently, a whole body scan revealed diffuse uptake of the radioiodine into the thyroid remnant, regional lymph node and both breasts (Fig. 2A).

To examine her mammary gland uptake, she underwent mammography and breast sonography. But there was no abnormal finding.

She was a pre-menopausal woman, her last delivery was 12 years ago. On review, she felt breast enlargement and galactorrhea 10 days before radioiodine ablation therapy. She also had menstrual irregularity. She had been treated for panic disorder for 2 years. Two months before a whole body scan, she changed her medications to Escitalopram (Lexapro 5 mg/day), Clonazepam (Rivotril 0.25 mg/day) and Amisulpride (Solian 50 mg/day) for her mood changes. Her serum prolactin level was 328 ng/mL. Because the patient refused, a pituitary fossa image could not be taken. Instead of the image, she wanted to change her medication again.

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She had discontinued antipsychotic medications since November 2010. Three months after her medication change, her prolactin level decreased to 12.6 ng/mL. There was no more galactorrhea. After 6 months, there was no longer radioiodine uptake in either breast on a follow up whole body scan (Fig. 2B).

DISCUSSION

The sodium/iodide symporter (NIS) mediates the iodine accumulation of the thyroid gland [5,6]. NIS is expressed in extrathyroidal tissue, including mammary gland, salivary gland, gastric mucosa,

ciliary body, choroid plexus [7], and more than 80% of breast cancer tissue [8].

Iodine accumulation in the lactating breast has been recognized for more than 50 years. NIS in mammary gland protein (mgNIS) is expressed on the basolateral membrane of alveolar cells in the mammary gland and is markedly induced during lactation in order to provide an adequate supply of iodine to the newborn [9,10].

But in non-lactating breast, mgNIS can be stimulated. There are many stimulators of NIS expression including elevated serum TSH. Among them, prolactin and oxytocin play a role in the induction of NIS expression in mammary gland [11]. These observations are based on animal models or cell lines [5,11], but never confirmed in humans *in vivo*. Hyperprolactinemia associated uptake of radioiodine into breast was reported in other cases, suggesting a cause and effect relationship between a high level of endogenous prolactin and breast radioiodine uptake [3,4,12]. In a previous study, of 302 patients who had thyroid cancer and who underwent ^{131}I whole body scans, breast uptake was observed in 4 cases. One of them had been treated with the anti-dopaminergic drug, sulpiride [12]. The prevalence of drug-induced hyperprolactinemia is underestimated due to the frequent lack of externally visible symptoms, and the reluctance to report it due to the embarrassing nature of the symptoms. So, a careful physical history taking and examination should be done, and the awareness of the clinician is particularly important.

In this case, the patient had used amisulpride (escitalopram). It has been hypothesized that amisulpride may have a selectively higher occupancy of D_2/D_3 receptors at the pituitary level, and increases



Fig. 1. Positron emission tomography-computed tomography performed 5 months after total thyroidectomy. There was no evidence of tumor recurrence or metastasis.

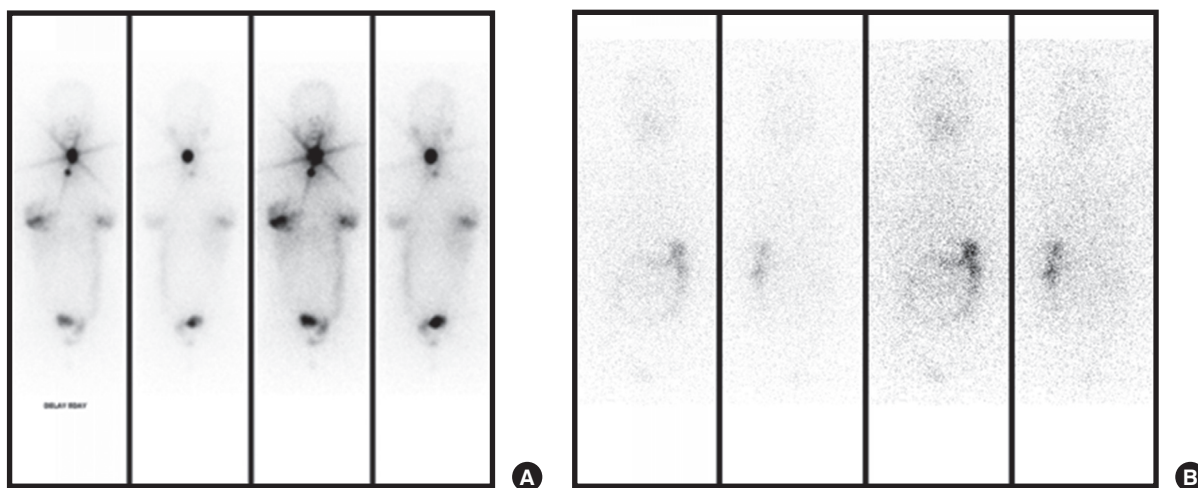


Fig. 2. ^{131}I whole body scan. A. ^{131}I whole body scan performed 72 hours after an radioiodine ablation (RIA) (150 mCi). There were multiple sites of iodine uptake in functioning thyroid tissue or regional lymph nodes in the thyroid area. Diffuse mild breast uptake was observed in scanned images. B. ^{131}I whole body scan performed 6 months after the RIA (150 mCi). There was no longer iodine uptake in either breast.

prolactin levels. Aminosulpiride-induced hyperprolactinemia has been reported after both acute and chronic treatment [13]. Citalopram (SNRI) did not increase prolactin significantly in some studies, but in another study of healthy subjects, 40% elevation was seen after 10 days of treatment [13].

Despite her medical history, her breast uptake of radioiodine could be distinguished from thyroid cancer metastasis by its imaging characteristics [4,14]. For example, it can be seen on a posterior or lateral projection of the chest, or by observing a shift in the site of maximum concentration of radioiodine when the breast position is manually altered. However, breast uptake may be misinterpreted as metastases from differentiated thyroid cancer if it presents with an atypical pattern and is clinically unexpected. So, physicians should rule out cancer metastasis, if the radioiodine uptake is irregular or unilateral, if there is coexisting elevated thyroglobulin levels, or if there are no clinical correlations with breast uptake and other causes [4].

We had to distinguish radioiodine breast uptake from a breast tumor. A high prevalence of mgNIS expression in human breast cancers (more than 80% of them) has been reported [10,15]. mgNIS is upregulated with high frequency during malignant transformation of breast tumors, meaning that it has potential diagnostic and therapeutic value [10]. In our case, the thyroglobulin antigen level was low and thyroglobulin antibody was negative. Also, breast sonography and a PET-CT scan revealed negative results. We also could exclude the possibility of metastasis or a primary breast cancer.

This case is meaningful for several reasons. First, we provide direct evidence that endogenous hyperprolactinemia can induce significant uptake of radioiodine by breast tissue, even in non-lactating mammary gland. Second, because we used recombinant human TSH for remnant ablation, and the patient was in a TSH suppression state before rhTSH administration, we were able to exclude a possible effect of TRH and hypothyroidism induced hyperprolactinemia. Third, the patient underwent PET-CT before WBS. Hence, we could also exclude the possibility of thyroid cancer metastasis or combined breast cancer.

The prevalence of drug-induced hyperprolactinemia is underestimated due to the frequent lack of externally visible symptoms, and the reluctance to report it due to the embarrassing nature of the symptoms. So, a careful physical history taking and examination should be done, and the awareness of the clinician is particularly important.

SUMMARY

We now present a case and literature review about hyperprolacti-

nemia-associated breast uptake of radioiodine, following ¹³¹I postablation scan in a differentiated thyroid cancer patient who had hyperprolactinemia due to antipsychotics.

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