

Breast Uptake of Radioiodine in Non-breastfeeding Women

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Abstract: We show 2 cases of breast uptake of radioiodine in non-breastfeeding women. A 40-year-old female patient with papillary thyroid carcinoma referred to nuclear medicine department for radioiodine ablation. Post radioiodine whole body scan revealed bilateral uptake at the upper thoracic region. Single photon emission computed tomography/computed tomography (SPECT/CT) confirmed symmetrical mammary gland uptake at both breasts. The patient had a pituitary microadenoma and hyperprolactinemia but she had suspended the treatment looking for pregnancy. We also show another case of a 41-year-old female patient with papillary thyroid carcinoma and extrathyroidal disease, without history of breast cancer, mastitis, hyperprolactinemia, or galactorrhea, also showing symmetrical mammary gland uptake at body scan. These cases exemplify that radioiodine uptake is not specific for thyroid tissue. It can also be seen in healthy non-thyroidal tissue, including breast, or in benign and malignant non-thyroidal tumors, which could be mistaken for thyroid cancer. Despite breast uptake of radioiodine is a common finding in postpartum or lactating women, it is important to correctly evaluate the breast radioiodine uptake and differentiate it from lung or axillary metastatic foci of thyroid cancer. In breast the radioiodine uptake is dependent of the expression of NIS (Sodium iodide symporter). The functional NIS expression in breast is the most important mechanism of breast uptake. SPECT/CT is useful in the differentiation of benign breast uptake with lung metastases or axillary metastases of thyroid cancer.

Keywords: Nuclear Medicine, Radioiodine, Breast Uptake, Non-breastfeeding

1. Content

Case #1

A 40-year-old female patient diagnosed for papillary thyroid carcinoma was referred to nuclear medicine department for radioiodine ablation. She had undergone total thyroidectomy surgery 2 years ago. The postoperative pathological examination revealed 2 cm dominant nodule in the right lobe, lymph vascular invasion and thyroid capsule compromised by tumor (Stage T4N0M0). The patient undergone radioiodine for remnant ablation and received 30 mCi. 3 years later, whole body scan following radioiodine treatment was done. It showed focal radioiodine uptake at thyroidal region without any metastatic foci. It also showed focal radioiodine uptake projected on the upper left jaw, which is not observed in the late images, which, according to patient symptoms corresponded to local subcutaneous inflammatory process.

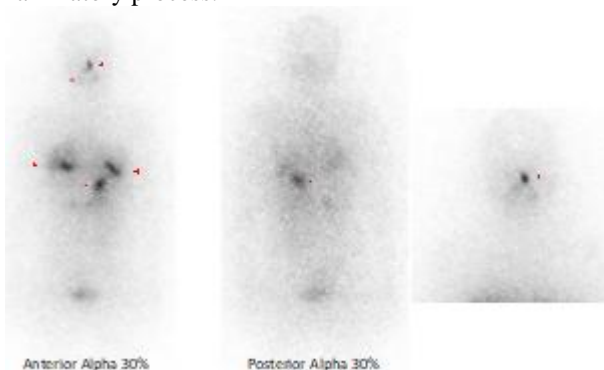


Figure 1: Post-radioiodine whole body scan. Post-radioiodine whole body scan with 10 mCi I-131, planar images, showing uptake at neck on the upper left jaw related to inflammatory process (asterisk). It also shows uptake in thyroidal region (arrowhead) and at both sides of the upper

thoracic region (arrows). Physiologic gallbladder is shown (Point).

It also showed atypical focal radioiodine uptake at both sides of upper thoracic region. Additional single photon emission computed tomography/computed tomography (SPECT/CT) acquisition was performed to localize the radioiodine uptake at upper chest. It confirmed that symmetrical radioiodine uptake corresponded to breast parenchyma at both sides. The patient did not have any history of breast cancer or mastitis.

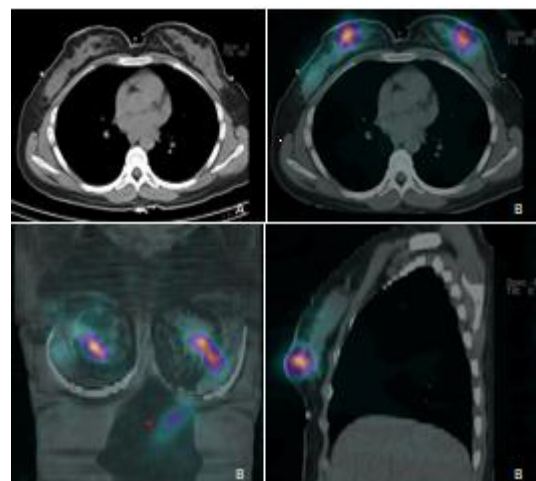


Figure 2: Single photon emission performed after radioiodine whole body scan. CT (A) doesn't show gross mammary abnormalities. PET CT (B) confirmed breast parenchyma uptake in thoracic region. Note gallbladder physiologic uptake (arrow).

6 years ago, the patient was found to have a pituitary microadenoma in the workup of infertility, prior to the

detection of thyroid cancer. The patient was managed with Cabergoline and successful pregnancy was obtained. The Cabergoline was suspended once the patient was pregnant. The patient had breast-fed until 1 year ago and had resumed hyperprolactinemia treatment only a month and a half ago.

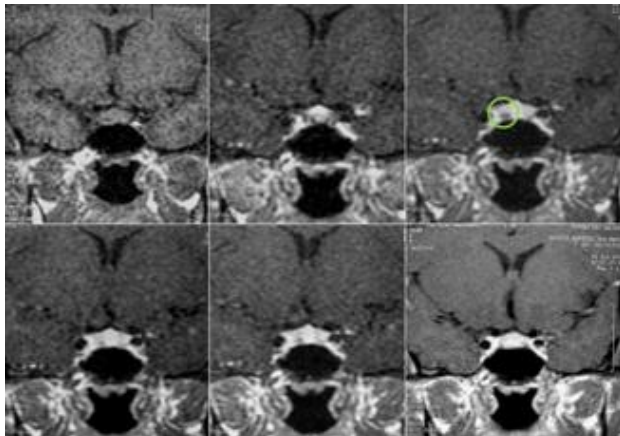


Figure 3: Dynamic contrast enhanced MRI showing contrast between enhancing normal gland and pituitary adenoma (green circle). Pituitary adenoma does not initially enhance in left hypophysis gland.

Case # 2

A 40-year-old female patient diagnosed for papillary thyroid carcinoma 7 months ago. She had undergone total thyroidectomy surgery. Pathology revealed 1.4 cm nodule in the right lobe and extrathyroidal invasion without lymph vascular compromise. Mediastinal lymphadenectomy confirmed compromise of 2 mediastinal nodes with papillary carcinoma (Stage T3N1M0). Patient undergone radioiodine remnant ablation and received 80 mCi. She was referred to nuclear medicine department for radioiodine scan. Whole body scan was done (Figure 4). It showed focal radioiodine uptake at thyroidal region without any metastatic foci. Atypical foci of radioiodine accumulation at both sides of upper thoracic region were noted. Additional single photon emission computed tomography/computed tomography (SPECT/CT) acquisition was performed to localize the radioiodine uptake at upper chest (Figure 5 and figure 6). It confirmed that radioiodine uptake on the chest correspond to breast parenchyma at both sides. The patient did not have any history of breast cancer, mastitis, hyperprolactinemia, or galactorrhea.

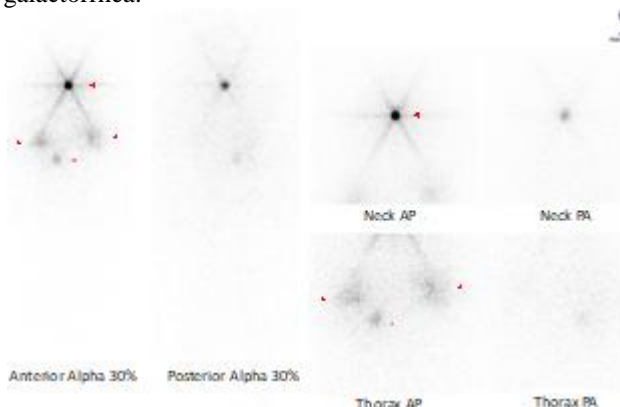


Figure 4: Post-radioiodine whole body scan with 12 mCi I-131 showing uptake at left neck in thyroidal region and at both sides of the upper thoracic region. Physiologic gallbladder uptake is shown.

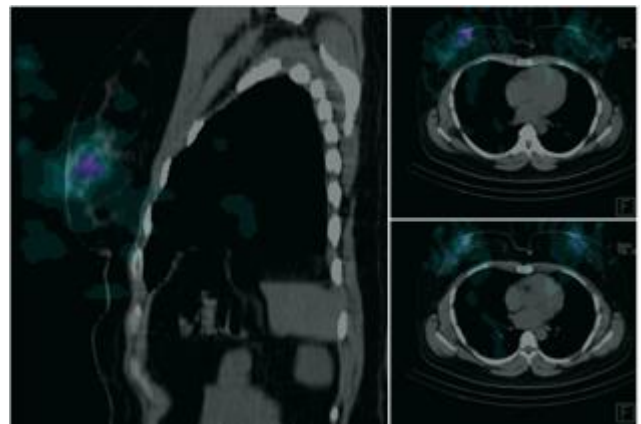


Figure 5: Single photon emission CT performed after radioiodine whole body scan. PET CT confirms bilateral breast parenchyma uptake in upper thoracic region.

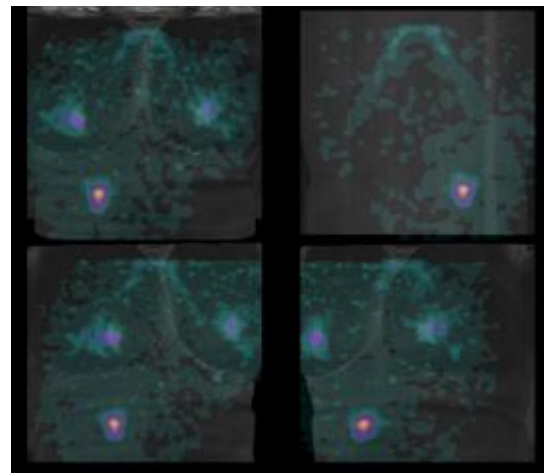


Figure 6: Volumetric reformation of single photon emission CT showing bilateral focal breast parenchyma uptake in aureole area that correspond to thoracic region radioiodine uptake

2. Discussion

Radioiodine has been used for more than five decades for diagnosis and treatment of patients with differentiated thyroid cancer. Precise interpretation of radioiodine whole body scintigraphy can result in avoidance of exposure to high-dose radioiodine and lead patients to optimal management of thyroid disease.

The priority in radioiodine whole body scintigraphy is detection of thyroid cancer; the goal is to differentiate malignant uptakes from physiological or benign uptakes.

Unexpected radioiodine uptake is a frequent finding in radioiodine whole body scintigraphy. There are mechanisms by which unexpected iodine uptake can be explained, some of them, the most frequent, can be explained from the NIS (Sodium/iodide Symporter).

The sodium/iodide symporter (NIS) is an integral plasma membrane glycoprotein that mediates active Iodide transport into the thyroid follicular cells, the first step in thyroid hormone biosynthesis. The transport of iodide across the cell membrane is driven by the electrochemical gradient of sodium (the intracellular concentration of sodium is

approximately 12 mM and extracellular concentration 140 mM). It transports 2 Sodium molecules and one iodine molecule, dependent on the sodium gradient maintained by Sodium/potassium ATPase[1, 2] (Figure 7).

The mechanisms that explain unexpected radioiodine uptake (Table 1) are: 1. functional NIS expression (In thymus, breast, salivary glands and gastrointestinal tract) 2. Pathological NIS expression (Benign and malignant tumors), 4. Physiologic tissue uptake and metabolism of radio iodinated thyroid hormone, 5. Retention of radioiodine in body fluids (saliva, tears, blood, urine, exudate, transudate, gastric and mucosal secretions, etc.) associated with or without structural changes, 6. Retention and uptake of radioiodine in inflamed tissue, 7. Contamination by physiologic secretions, and 8. Idiopathic.

Table 1: Mechanisms of unexpected radioiodine uptake

Functional NIS expression	Thymus, breast, salivary glands and gastrointestinal tract
Pathological NIS expression	Benign and malignant tumors
Physiologic tissue uptake and metabolism of radio iodinated thyroid hormone	Thyroid tissue
Retention of radioiodine in body fluids	Saliva, tears, blood, urine, exudate, transudate, gastric and mucosal secretions
Retention and uptake of radioiodine in inflamed tissue	
Contamination by physiologic secretions	
Idiopathic	

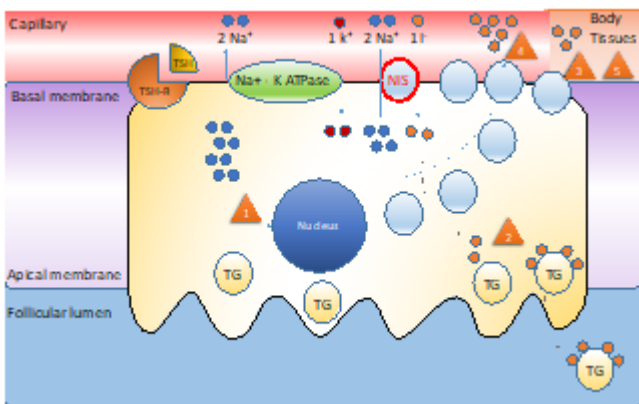


Figure 7: Conventions: TSH: Thyroid stimulating hormone, TSH-R: Thyroid stimulating hormone receptor, TG: thyroglobulin, Na⁺/K⁺ ATPase: Sodium –Potassium ATPase, NIS: Sodium iodide symporter, I⁻: Iodide, Na⁺: Sodium, K⁺: Potassium

The tools that exist to differentiate benign from malignant uptakes are varied, and include biochemical studies, such as TSH and thyroglobulin, medical history, physical examination findings, scintigraphy, CT and SPECT/CT, however the interpretations can be ambiguous.

In a comprehensive manner, the physiologic radioiodine uptake could be due Ectopic thyroid tissue or Non-thyroidal tissue. Ectopic thyroid tissue represents a failure of migration of the thyroid gland. Ectopic thyroid tissue retains its ability to take up iodine and produce thyroglobulin, so it

is easily detected in scintigraphy, being a common false positive of postsurgical uptake at cervical level.

Physiological uptake of radioiodine can also be observed in non-thyroidal tissues. The two main causes of uptake include: functional NIS expression and the retention of excreted iodine. Physiologic radioiodine uptake can be found in head and neck, chest, abdomen, pelvis and bone marrow (Table 2).

Table 2: Anatomical physiologic radioiodine uptake

Choroid plexus	Liver
Lacrimal sac	Biliary tract
Nasopharynx	Gall bladder
Salivary gland	Kidney
Oral cavity	Renal pelvis
Esophagus	Ureter
Remnant thyroid	Urinary bladder
Breast	Large bowel

In breast, the main cause of radioiodine uptake is the expression of NIS. Iodine uptake in lactating breast is a usual finding. The marked induction of NIS on the basolateral membrane of alveolar cells in mammary glands during lactation is the main cause of radioiodine uptake.

The mammary uptake can be classified in four main patterns: Full, focal, crescent and irregular [3]. The full pattern represents marked intense uptake over the breast area that may be homogeneous, the focal pattern is more concentrated centrally in the subareolar region, the crescent pattern is more intense peripherally than central and the irregular pattern is not uniform in shape and size.

Those patterns were initially described in lactating women, however, about 6% of all female patients present with breast uptake unrelated to lactation and the patterns are similar to those observed during breast feeding [4]. It is reported that breast uptake can mimic lung metastasis in 30% of patients [4].

In thyroid cancer, radioiodine is transported into the cancer cells via NIS in differentiated thyroid cells. In undifferentiated thyroid cancers the cells lost their ability to express NIS.

Breast has a high affinity for radioiodine, fact supported by the observation that iodinated contrast material suppress thyroid but not breast radioiodine uptake, which could be related to the larger mass of the breast or to the fact that turnover of iodine in the breast is faster [5].

Prolactin levels are close related with radioiodine breast uptake. In patients with radioiodine breast uptake, galactorrhea can be found in 48% of cases and mild to moderate elevation of prolactin (up to 2.5 times upper normal level) can be found in 24% of cases [4].

A number of physiological states, pathological states and drugs can cause prolactin elevation (Table 3). Physiological states include pregnancy, breast-feeding, stress, exercise, and sleep [6]. Common diseases are related to prolactin levels variations; Long term or inadequately treated primary

hypothyroidism [7, 8] and patients with renal insufficiency may have moderate hyperprolactinemia [8].

Tumoral and non-tumoral intracranial diseases can cause prolactin disorders. A non-prolactin-secreting pituitary tumor, granulomatous infiltration or parasellar mass can cause hyperprolactinemia due disruption or compression of the pituitary stalk related to suppression of the dopamine inhibition.

Fewer than 10% of patients with idiopathic hyperprolactinemia ultimately are found to harbor a microadenoma [9] and spontaneous normalization of prolactin levels occurs in approximately 30% of patients with idiopathic hyperprolactinemia [10]. Of note the treatment with bromocriptine, did not consistently affect the pattern or intensity of breast uptake [4].

Table 3: Etiology of hyperprolactinemia. Adapted from Melmed et al [12]

Physiological	Coitus, exercise, lactation, pregnancy, sleep, stress
Pathological	
Hypothalamic-pituitary stalk damage	Granulomas, infiltrations, Irradiation, Rathke's cyst, trauma: pituitary stalk section, suprasellar surgery, tumors: craniopharyngioma, germinoma, hypothalamic metastases.
Pituitary	Acromegaly, idiopathic, lymphocytic hypophysitis or parasellar mass, macroadenoma (compressive), macroprolactinemia, plurihormonal adenoma, prolactinoma, surgery, trauma.
Systemic disorders	Chest—neurogenic chest wall trauma, surgery, herpes zoster, Chronic renal failure, cirrhosis, cranial radiation, epileptic seizures, polycystic ovarian disease, pseudocyesis.
Pharmacological	Anesthetics, anticonvulsants, antidepressants, antihistamines (H ₂), antihypertensives, cholinergic agonist, drug-induced hypersecretion, catecholamine depletory, dopamine receptor blockers, Dopamine synthesis inhibitor, Estrogens: oral contraceptives; oral contraceptive withdrawal, neuroleptics/antipsychotics, neuropeptides, opiates and opiate antagonists.

Breast uptake should be suspected in all female patients with radioiodine uptake in the chest area, even in the absence of a history of breastfeeding. However, there are suggested cautions in interpretation of radioiodine uptake in the breast in whole body scans because of the possibility of a masked primary lung tumor, breast cancer or thyroidal lung metastases. These alarm signs are:

- Absence of history of breastfeeding.
- Irregular or unilateral uptake.
- Coexisting lung or other metastases.
- Coexisting elevated thyroglobulin levels without other scan findings.

It is important to correctly evaluate the breast radioiodine uptake and differentiate it from lung or axillary metastatic foci of thyroid cancer. Instead of the planar images, SPECT/CT is useful to localize uptake in breasts due to its cross-sectional nature.

Nuclear medicine physician should be more cautious, particularly in the presence of asymmetrical upper chest

uptake in a male patient. Breast uptake of radioiodine is an uncommon finding in male patients without hyperprolactinemia or breast pathology and this finding increases the concern of cancer. Conventional planar scintigraphy should be supported by additional SPECT or SPECT/CT scanning in such situations when available [11].

3. Conclusion

Radioiodine uptake is not specific for thyroid tissue. It can be seen in healthy tissue, including breast or in benign and malignant non-thyroidal tumors. Although breast uptake of radioiodine is a common finding in postpartum or lactating women, it is important to correctly evaluate the breast radioiodine uptake and differentiate it from lung or axillary metastatic foci of thyroid cancer. In breast the main cause of radioiodine uptake is dependent of NIS expression which can be present in different tissues. SPECT/CT is useful in the differentiation of benign breast uptake with lung metastases or axillary metastases of thyroid cancer.

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