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Daniella F Pinho*

Department of Radiology, University of Texas Southwestern Medical Center, Texas, USA

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***Corresponding author:** Daniella F Pinho, Department of Radiology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd. Dallas, Texas, USA, Tel: 214.648.8218; Fax: 214-645-2762; E-mail: daniella.pinho@utsouthwestern.edu

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Case Report

That's not Metastatic Thyroid Cancer: Patterns of Non-malignant Radioiodine Uptake

Abstract

Radioactive Iodine (RAI) has been an integral part of the identification, surveillance, and treatment of the most common types of metastatic thyroid carcinoma since its first use in 1941. However, false positive uptake of RAI on whole body scintigraphy scans in tissues other than in metastatic disease is frequently observed. This article presents a case series of relatively uncommon situations of RAI uptake which could be mistaken for malignant uptake. Cases were divided into categories based on uptake mechanism: metabolic, physiologic, inflammatory, and contamination.

Introduction

Radioactive iodine (RAI) has played a key role in the identification and treatment of the most common types of thyroid cancer since its inception in 1936, with the first recorded treatment of hyperthyroidism in 1941 [1]. Use of iodine-131 (I 131) for treatment of thyroid cancer was soon to follow with the first demonstrated uptake from thyroid adenocarcinoma by Seidlin in 1943 [2]. In the years that followed, these first experiences allowed RAI to become a critical radiopharmaceutical in the treatment and surveillance of papillary and follicular thyroid carcinoma.

RAI is produced in a nuclear reactor by the neutron bombardment of Tellurium 127 and has a half-life of 8.02 days. Once ingested, nowadays usually in pill form, about 90% of the dosed RAI is rapidly absorbed and secreted into the extracellular iodine pool [3]. Part of this absorbed RAI is renally excreted, but given the usually high TSH expression in thyroid carcinomas and its effect to increase the expression of the sodium-iodine symporter (NIS), much is taken up into by follicular cells into tissue by the NIS receptors. Once trapped in the follicular cell, it rapidly undergoes organification. Organification is defined as oxidation and eventual binding of the RAI to tyrosine residues on thyroglobulin [4,5]. During this process and for substantial time after, RAI undergoes Beta decay and with consequent damage of the surrounding tissue. RAI predominantly decays by Beta emission to xenon-133, with a gamma emission of 364 keV [3]. Importantly, when I-131 decays, 10% of this decay is expressed as gamma rays, which can be detected by standard gamma cameras thereby allowing for surveillance of disease response and localization of potential metastatic lesions.

Whole body scintigraphy is used in patients with differentiated thyroid carcinomas, for assessment after treatment with RAI, and may also be used for localization of metastatic disease in patients with increase in thyroglobulin levels. However, it is by no means a perfect method. Whereas I-131 is a sensitive marker for the detection of thyroid cancer, it is not specific to thyroid tissue. Physiologic uptake is commonly observed in the salivary glands, thymus, and GI tissue. Thyroid tissue, either residual cells in the thyroidectomy bed or in ectopic location will also have increased RAI uptake [6]. This is commonly seen and well understood. However, RAI uptake has been observed in several other circumstances, which can make the surveillance and treatment of metastatic thyroid cancers extremely difficult. Inflammation, contamination, and importantly metabolism are all conditions in which RAI uptake has been observed [7-10]. It becomes difficult and extraordinarily important in the treatment of patients with metastatic thyroid cancers to be able to determine whether the uptake seen on whole body scintigraphy is representative of metastatic disease or not. Therefore, precise interpretation by a trained radiologist or nuclear medicine physician is critical in optimally managing this high-risk disease.

Based on that, we have highlighted a series of cases which illustrate unique examples of thyroid uptake which would appear to represent metastatic thyroid disease, but in fact do not. This was correlated with the mechanism of localization to further aid understanding and clinical recall. By presenting these cases that illustrate rare, but important instances, in which metastatic disease can be mistaken for other types of uptake, our goal is to prevent patient worry, misdiagnosis, and potential unnecessary treatments.

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Materials and Methods

Clinical cases were retrieved in a retrospective manner from the nuclear medicine database and cases were reviewed and selected. From this extensive dataset, cases which illustrated unique examples of non-malignant and/or non-thyroidal uptake on I-131 whole body scintigraphy scans were thoroughly reviewed. Protected patient information was systematically removed from all images. The uptake on these cases were categorized as metabolic, physiologic, inflammation and contamination. After case selection, a review of the literature was performed to elucidate different physiological mechanisms of iodine localization and to correlate imaging findings.

Cases

Case 1: Metabolic uptake of RAI

Hepatic uptake seen on thyroid scintigraphy was originally thought to be secondary to residual metastatic thyroid cells. Later studies were not able to show its correlation with serum thyroglobulin or distant metastatic disease [3]. Currently, RAI uptake in the liver is attributed to the metabolism of thyroglobulin from either residual normal and/or malignant thyroid cells. There is also evidence for normal hepatic uptake based on findings of functional sodium-iodine symporters (NIS) expressed in the intrahepatic bile ducts which is correlated with the administered dose of I-131. The higher the dose, usually the higher the uptake seen in the liver. Patients with hepatic steatosis can have increased RAI uptake related to delayed excretion secondary to the delayed action of deiodinase in the liver cells (Figure 1).

Figure 1: Iodine metabolism in the liver: Whole body thyroid scan of a 48 y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 128.3 mCi of I-131, showing expected activity in the thyroid bed (black arrow). There is diffuse uptake in the liver (red arrow), possibly related to iodine metabolism from a combination of residual normal and malignant thyroid tissue.

Case 2: Physiologic uptake of RAI

The next cases represent physiologic uptake of RAI (Figures 2-5). This will be reviewed through cases showing colon, thymic, breast, and gastric mucosa (in a gastric diverticulum) uptake.

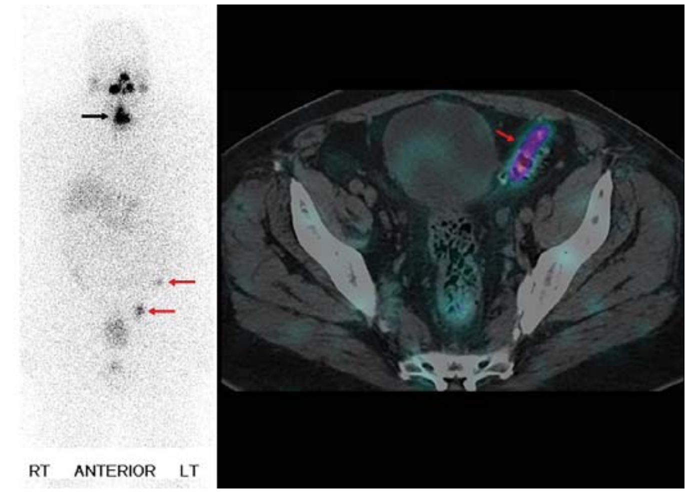

Figure 2: Colon uptake (A) Whole body thyroid scan (anterior view) of a 65 y/o male status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 158.3 mCi of I-131, showing expected activity in the thyroid bed (black arrow) and two foci of radiotracer uptake overlying the left lower quadrant (red arrows). (B) On SPECT-CT images, the foci of I-131 uptake correlates with loops of colon (red arrow).

Case 3: Inflammatory uptake of RAI

Uptake of RAI related to inflammatory tissues is secondary to increased perfusion and vasodilatation. Additionally, enhanced capillary permeability can result in stasis of RAI, with retention in leukocytes in posttraumatic clots or tissues (leukocytes induce iodide organification by myeloperoxidase). Examples of inflammatory disease that can have RAI uptake are illustrated in figures 6 -8.

Case 4: External contamination by RAI

RAI is excreted by all body fluids including sweat, breast milk, urine, vomitus, nasal, tracheobronchial, lacrimal, salivary secretions and feces. Contamination is usually easily recognized by its pattern and location of uptake. Two examples are shown in figures 9,10.

Discussion

I-131 has good sensitivity for the detection of thyroid tissue and is an important lifesaving theranostic agent that can detect and treat thyroid cancer. As detailed above, given that there are other causes of uptake including physiological, metabolic, inflammatory and contamination, RAI is not specific to metastatic thyroid cancer. It is important to recognize the causes and distribution of non-malignant uptake to decrease the number of false positive studies, resulting in a specificity of over 90% as reported on literature [11,12].

The ultimate goal is to improve patient care through more comprehensive radiographic understanding of these

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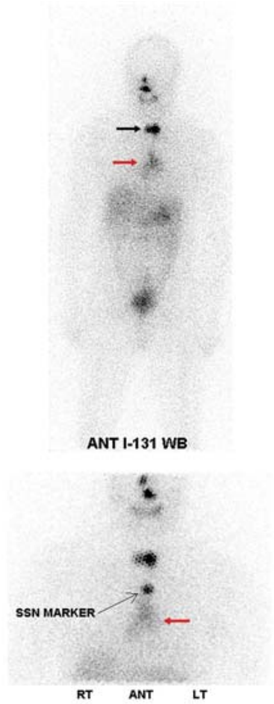

Figure 3: Thymic uptake (A) Whole body thyroid scan (anterior view) of a 35 y/o male status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 120.5 mCi of I-131, showing expected activity in the thyroid bed (black arrow) and accumulation in a triangular distribution in the anterior thorax (red arrow). (B) Spot anterior view of the neck and chest also shows the triangular uptake below the sternal notch marker (SSN) (red arrow), consistent with physiologic thymic uptake.

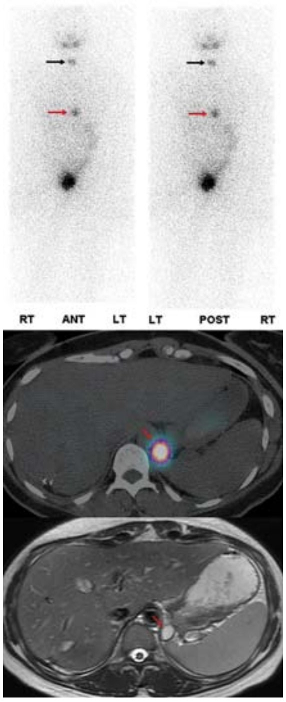

Figure 4: Gastric diverticula / enteric duplication cyst uptake. Whole body anterior (A) and posterior (B) thyroid scan of a 33 y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 127 mCi of I-131, showing expected activity in the thyroid bed (black arrow) and focal tracer accumulation near the midline in the left upper quadrant (red arrow). On further evaluation with SPECT-CT (C), it corresponded to a low attenuation nodule interposed between the left posterior diaphragmatic crura and the medial proximal stomach (red arrow). On MRI (D), a benign cystic lesion was seen in this location (red arrow), representing a either a gastric diverticula or an enteric duplication cyst.

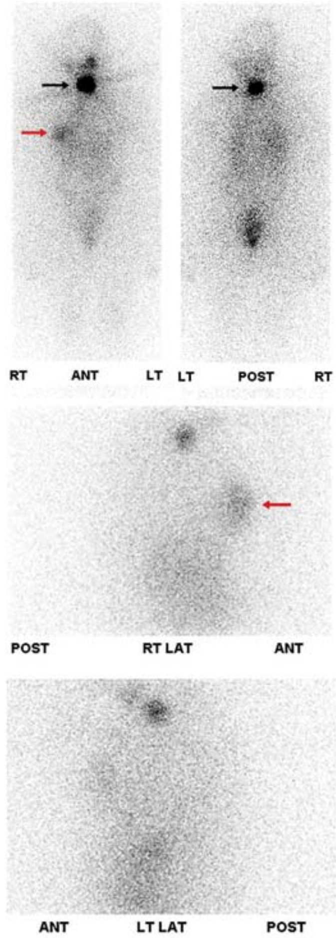

Figure 5: Breast uptake (A) Anterior and (B) posterior whole body thyroid scan of a 61 y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 103.3 mCi of I-131, showing expected activity in the thyroid bed (black arrow) and asymmetric tracer accumulation in the right breast tissue (red arrow), better appreciated on (C) right lateral and (D) left lateral spot views. This patient had a history of left breast cancer status post mastectomy, and the asymmetric uptake is probably related to lack of glandular tissue on the left. Follow up mammography did not show any suspicious findings (not shown).

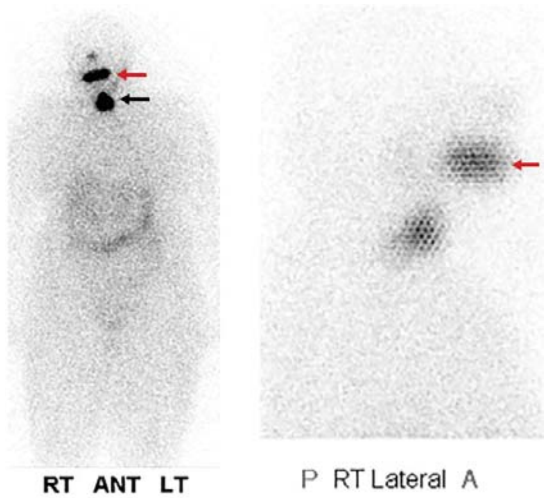

Figure 6: Dental disease (A) Whole body thyroid scan (anterior view) of a 63 y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 99.6 mCi of I-131, showing expected activity in the thyroid bed (black arrow). There is intense uptake in the region of the mouth, related to dental disease (red arrow), also shown in the right lateral view (B). Dental disease was confirmed on physical exam.

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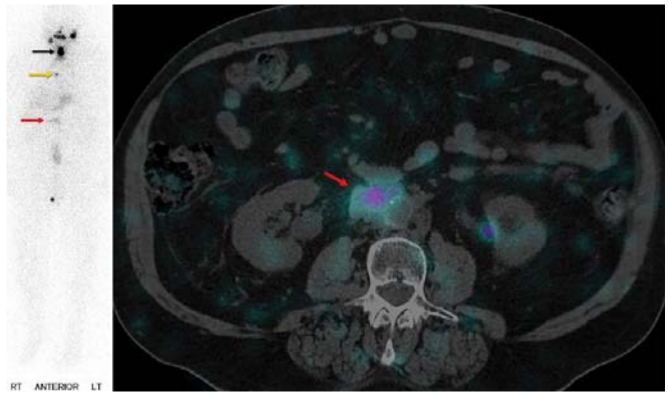

Figure 7: Retroperitoneal fibrosis (A) Whole body thyroid scan of a 74 y/o male status post thyroidectomy for papillary thyroid cancer, 8 days after ablation with 126 mCi of I-131, showing expected activity in the thyroid bed. (black arrow). Focal uptake in the mediastinum correlated to a soft tissue nodule suspicious for metastasis (yellow arrow). Subtle activity in the midabomen (red arrow) is also seen. SPECT-CT images (B) shows that the accumulation in the mid-abdomen correlated to radiotracer accumulation in irregular soft tissue surrounding the inferior vena cava and aorta in the abdomen, corresponding to previously known retroperitoneal fibrosis (red arrow).

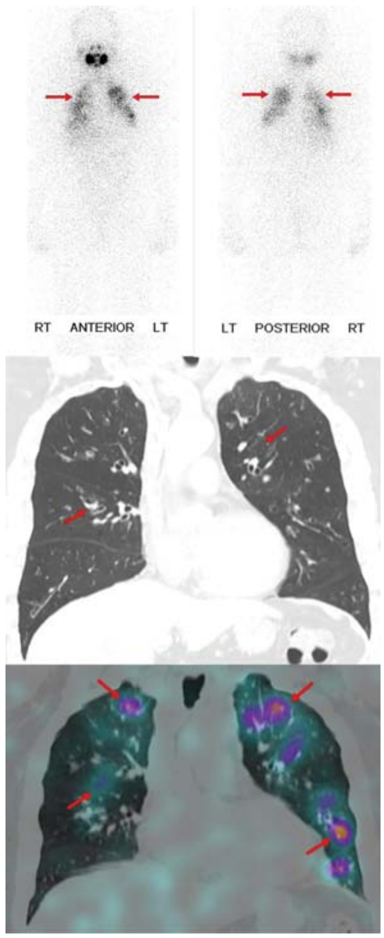

Figure 8: Cystic fibrosis (A) Anterior and (B) posterior whole body thyroid scan of a 38 y/o male status post thyroidectomy for papillary thyroid cancer, 8 days after ablation with 153.7 mCi of I-131 with no significant activity in the thyroid bed. There is heterogeneous diffuse low-level radiotracer uptake throughout the bilateral lungs (red arrows). (C) Coronal chest CT image show bilateral areas of central bronchiectasis, with diffuse airway wall thickening and mucoid impactation (red arrows), consistent with expect changes of cystic fibrosis. (D) coronal SPECT-CT image shows that the uptake seen in the whole body images corresponds to these areas of inflammatory changes in the lungs (red arrows), with no suspicious abnormalities to suggest metastatic disease.

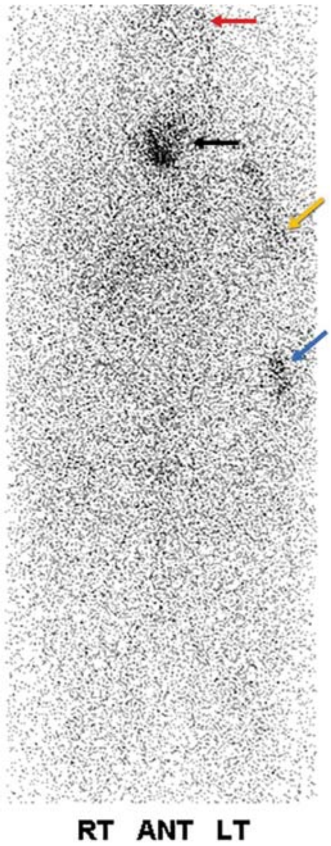

Figure 9: Contamination. Whole body thyroid scan (anterior view) of a 23y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 105 mCi of I-131. There is expected activity in the thyroid bed (black arrow) and multiple areas of superficial uptake on the left scalp (red arrow), left proximal arm / axilla (yellow arrow) and left hand (blue arrow), consistent with contamination.

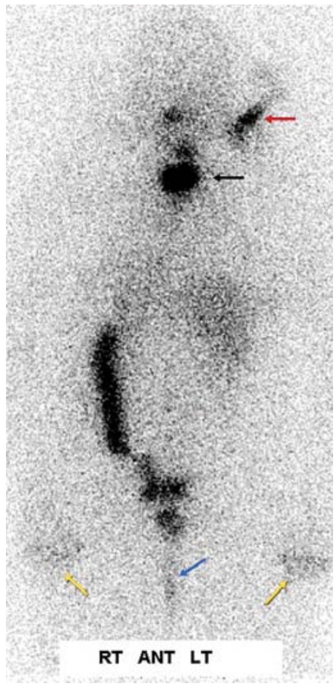

Figure 10: Contamination. Whole body thyroid scan (anterior view) of a 41y/o female status post thyroidectomy for papillary thyroid cancer, 7 days after ablation with 147.6 mCi of I-131. There is expected activity in the thyroid bed (black arrow) and area of uptake lateral to the face on the left, which corresponded to hair uptake (red arrow), bilateral hands (yellow arrow) avnd perineum (blue arrow), consistent with contaminant.

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studies. If doubt remains, SPECT/CT should be used for further delineation of areas of uptake that cannot be explained on the planar images.

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