Pitfalls of Iodine-131 Whole-Body Scan Mimicking Metastases in Differentiated Thyroid Carcinoma: A Case Series

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Abstract

Thyroid cancer is the most common endocrine malignant tumor and accounts for 1% of all cancers. Management of differentiated thyroid carcinoma is total thyroidectomy, followed by iodine-131 (I-131) radioactive iodine (RAI) therapy for thyroid remnant tissue. I-131 whole-body scan helps in the follow-up evaluation in remnant, residual, and recurrence cases. Principle of uptake of I-131 is through sodium–iodide symporter expression on the cells. Physiological uptake of iodine is usually seen in salivary glands and gastrointestinal tract, and false-positive uptakes are seen in lesions such as mucinous cystadenoma, struma ovarii, hepatic, renal, thymic, and meibomian cysts. Here, we present the review of literature of series of cases observed in our department presenting with false-positive uptake of RAI in vertebral hemangioma, lipoma, sinusitis, teratoma, and uterine leiomyoma.

Keywords: *Diagnostic and therapeutic iodine-131 whole-body scan, differentiated thyroid carcinoma, false-positive uptakes*

Introduction

Differentiated thyroid cancer (DTC) such as papillary and follicular variants constitutes for 90% of all thyroid cancers.[1] Of all newly diagnosed carcinomas thyroid cancer accounts for 3.8% according to National Institute of Health Surveillance and Epidemiology.[2] Since the 1940s, radioactive iodine (RAI) has been component of care in patients with DTC after total thyroidectomy, with the reliance on the fact that iodine trapping, organification, and storage are more prominent in thyroid tissue.[3]

Iodine-131 whole-body scan (I-131 WBS) is a critical tool in the treatment and surveillance of DTC patients.[4] Sodium iodide symporter (NIS) is a plasma membrane glycoprotein and it is the key mechanism of radioiodine uptake at the molecular level which helps in the evaluation of the remnant or recurrence tissue.[5] However, the uptake of iodine is not specific to thyroid cells.

Understanding of radioiodine biodistribution is important while interpreting scintigraphy findings to avoid misconceptions. RAI uptake includes normal functional NIS expression in salivary glands, liver, and gastrointestinal tract. Apart from the physiological cause of uptake retention of RAI in the body may be due to fluids such as saliva, tears, blood, urine mucosal secretions, uptake in inflamed tissue, metallic foreign bodies, and contamination.[5]

Hence, in the evaluation of RAI scintigraphy features, normal or abnormal findings should be correlated with patient's blood values of thyroglobulin, anti-thyroglobulin and thyroid stimulation hormone, histopathological variants of tumor, medical history, anatomical imaging, and physical examination. This evaluation is necessary for understanding the uptake of RAI which in turn helps in guiding the treatment strategy in DTC patients.[5]

Case Reports

Case 1

I-131 WBS in a 39-year-old female patient with papillary carcinoma thyroid in the left lobe and tall cell variant in the right lobe of thyroid. I-131-WBS showed evidence of RAI avid residue and lymph node. Biochemical profile: serum thyroglobulin (S.TG): 102.2 ng/mL, serum anti-thyroglobulin (S. anti-TG): 0.4 IU/L, and thyroid-stimulating hormone (TSH)

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>50.5 mIU/L. Posthigh dose therapy scan (PHDTS) with 100 mCi revealed pretherapy scan documented lesions with another two foci of abnormal RAI avid lesions in the bilateral adnexal region [Figure 1a] corresponding to heterogeneous soft-tissue attenuation with fatty component and calcifications measuring 2.2 cm × 2.7 cm on the right side and 2.5 cm × 3.0 cm on the left side on computerized tomography (CT) images - bilateral teratoma [Figure 1b and c].

Case 2

I-131 WBS in a 33-year-old female patient with follicular carcinoma thyroid with capsule infiltration. I-131 WBS showed radioactive avid tissue in thyroid bed residue, biochemical profile: S.TG: 2.4 ng/mL, S. anti-TG: 17.7 IU/L, and TSH: 64.2 mIU/L. PHDTS with 100 mCi showed pretherapy scan documented lesions along with another focus of radiotracer concentration in the pelvic region [Figure 2a], corresponding to peripherally calcified heterogeneous lesion in the uterus on CT images - with features more in favor of uterine leiomyoma [Figure 2b and c].

Case 3

I-131 WBS in a 50-year-old female patient with multifocal papillary carcinoma thyroid (pT2N1a) with skeletal metastasis. Biochemical profile: S.TG: 76 ng/mL, S. anti-TG: 0.01 IU/mL, and serum TSH (S. TSH): 42.2 mIU/mL. I-131-WBS showed no evidence of RAI in thyroid bed region. PHDTS with 200 mCi revealed multiple foci of RAI avid lesions in soft-tissue thickening in oropharynx bilateral II, III, and IV lymph nodes, in bilateral lungs, left hemipelvis region, and right distal femur region [Figure 3a]. Focal increased radiotracer uptake in the right periorbital region which corresponds to soft-tissue thickening in the right maxillary sinus - Sinusitis on CT images [Figure 3b and c].

Case 4

I-131 WBS in a 43-year-old female patient with multicentric variant of papillary carcinoma thyroid (pT2mN1a) showed evidence of RAI avid thyroid residue and lymph node in the neck region. Biochemical profile: S.TG 8.09 ng/mL, S. anti-TG 18.48 IU/L, TSH 95.05 mIU/L, and PHDTS with 100 mCi showed radioiodine avid focus in left thorax posterior aspect along with pretherapy documented lesions [Figure 4a]. On clinical examination, there is subcutaneous swelling with features more consistent with lipoma, histopathological examination (HPE) after excision turned out to be lipoma [Figure 4c]. Postexcision diagnostic follow-up scan shows no RAI focus in previously documented site in left hemithorax region [Figure 4b].

Case 5

I-131 WBS in a 59-year-old male patient with follicular carcinoma thyroid with skeletal metastasis. Biochemical profile: S.TG: 986 ng/mL, S. anti-TG: 0.9 IU/mL, and S. TSH: 42.2 mIU/mL. I-131 WBS showed focus of RAI avid residue, and multiple foci in bilateral lungs, liver, and lytic lesions involving the right scapula, left 3rd rib, D3, D4, and D7 vertebrae [Figure 5a]. RAI focus at D7 vertebra corresponds to vertebral hemangioma on attenuation-corrected CT images [Figure 5b and c].

Discussion

The sensitivity of diagnostic and posttherapeutic RAI WBS is 60% and 75%, respectively, in DTC.[6] The uptake of

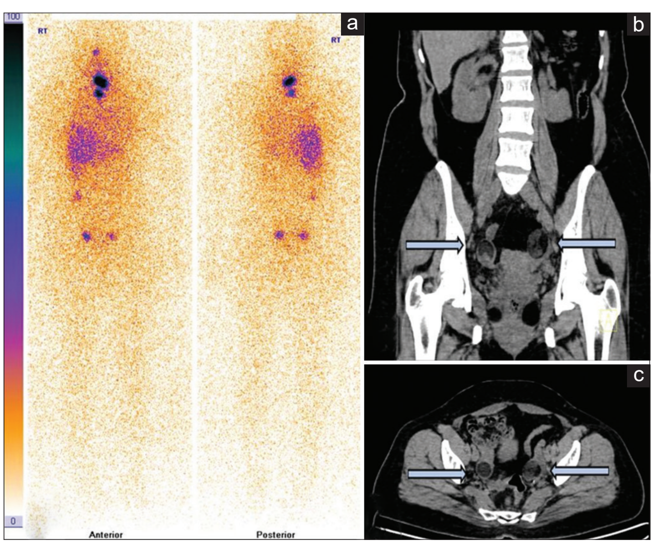

Figure 1: (a) Post high dose therapy scan with anterior and posterior views showing RAI avid lesions in bilateral adnexal regions. (b and c) Coronal and Axial sections CT images showing heterogeneous soft tissue attenuation with fatty component and calcifications measuring approx. 2.2 cm × 2.7 cm on right side and 2.5 cm × 3.0 cm on left side, suggestive of bilateral teratoma as depicted by arrows

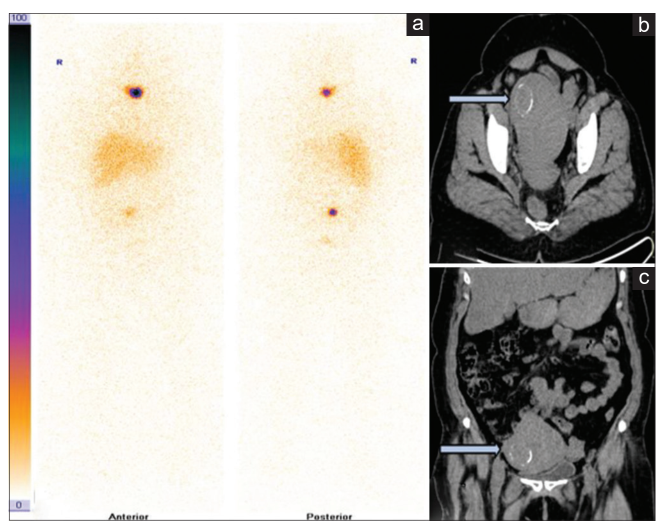

Figure 2: (a) Post high dose therapy scan with anterior and posterior views showing RAI avid focus in thyroid bed region and another focus in the pelvic region. (b and c) Axial and coronal sections CT images showing peripherally calcified heterogeneous lesion in uterus favoring uterine leiomyoma as depicted by arrows

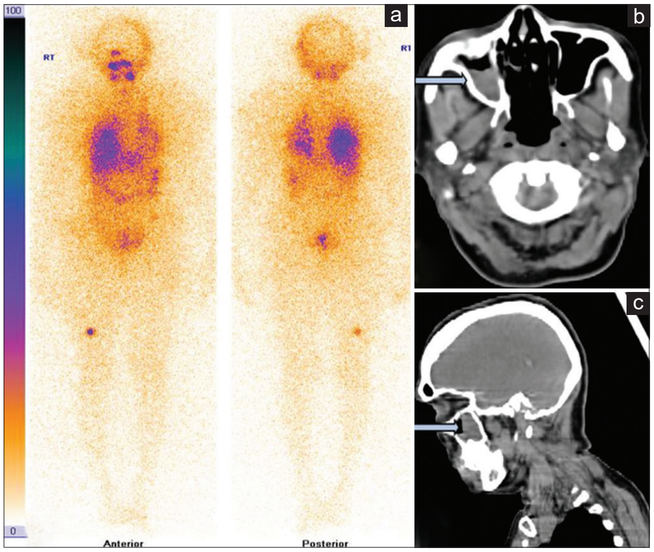

Figure 3: (a) Post high dose therapy scan with anterior and posterior views showing multiple foci of RAI avidity in bilateral lungs and right femur region with focal increased RAI avidity in right periorbital region. (b and c) Axial and sagittal sections CT images showing mucosal thickening in Right maxillary sinus corresponding to sinusitis as depicted by arrows

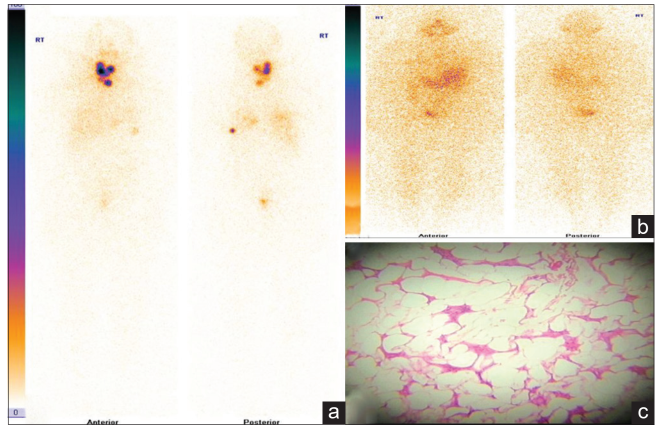

Figure 4: (a) Post high dose therapy scan with anterior and posterior views showing evidence of RAI avid foci in left hemithorax posterior aspect. (b) Post excision and post high dose therapy scan anterior and posterior views showing no evidence of RAI avid foci in the previously documented site in left hemithorax. (c) Histopathological examination slides 4X showing lobules of mature adipocytes with intervening small capillaries - Suggestive of Lipoma

iodine in thyroid follicular cells is mainly depended on the expression of NIS symporter in the basolateral membrane of cells. With similar physical and chemical properties, the RAI is organified and oxidized by thyroid follicular cells with effective half-life of 7.3 days. Despite the high sensitivity and specificity, the RAI WBS is often associated with pitfalls by false-positive uptake.[7]

The physiological causes of uptake are divided into thyroidal, nonthyroidal tissue uptakes, and contamination by physiological secretion of body fluids, whereas pathological causes of RAI uptake include infection, inflammation, trauma, and benign and malignant lesions.

Physiological RAI uptake causes such as ectopic thyroid tissue can be seen either as a result of abnormal migration of thyroid tissue with the most common site being the base of the tongue or along the tract of thyroglossal cyst. Other rare sites of thyroid uptake are seen in the mediastinum, intrathoracic, and distant subdiaphragmatic locations or in organs such as the lung, heart, adrenal glands, gall bladder, duodenum, ovary, pancreas, and intestine.[8]

Expression of NIS symporters in epithelial cells, and retention of excreted secretion is the cause of extra thyroid tissue uptake of iodine. Salivary, lacrimal glands, choroid, ciliary body of the eye, skin, placenta, lactating mammary glands, thymus, prostate, ovary, adrenal, lung, and heart are the sites of nonthyroidal tissue uptakes in the body.[5]

Contamination of radio-iodinated body fluids is one of the commonly acquired findings in RAI WBS. Contamination on hair, skin, clothes, tracheostomy sites, salivary secretions, urine, vomitus, and feces can be easily misinterpreted as metastases. In one of our cases, we noticed a non-homogenous uptake noted in the scalp region on diagnostic RAI WBS. To rule out metastases, we first correlated the patient TG values which is 0.8 ng/mL, CT was done and looked for anatomical lesions, but found to have no significant abnormality. The possible cause for such diffuse uptake in the skull is due to perspiration of RAI through sweat and it is often called as helmet sign. Proper preparation of patients, image acquisition in cleaned couch, lateral, and oblique views usually help in identifying this false-positive uptake, and single photon-emitted CT fused with CT increases the specificity of the diagnosis. Bakheet *et al*. in their case report of RAI uptake in the head and neck mentioned that the overall estimated frequency of external contamination that is mimicking skeletal metastasis in I-131 WBS accounts for 0.5% with a prevalence of 0.3%.[3]

Among the pathological causes, various cystic structures, including bronchogenic, thymic, breast, hepatic, renal, ovarian, epithelial, and sebaceous cysts along the sinuses, are known to show false-positive findings on radioiodine WBS. Wu *et al*., in a recent review of false-positive RAI uptakes, suggested a possible mechanism of entry of radioiodine into cysts to be through passive diffusion or active transporter by the slow exchange of water and chemical elements between the cysts and surroundings.[2,3,7]

Here, we report one case with false-positive uptake in sinus, when clinically evaluated patient had recent history of upper respiratory tract infection before RAI administration. The possible mechanism of uptake, in this case, could be due to inflammatory-mediated hyperemia and increased vascular permeability and retention of organified I-131 by leukocytes during bacterial activity.[9]

There are diverse benign tumors with different histopathological natures such as Warthin's tumor,

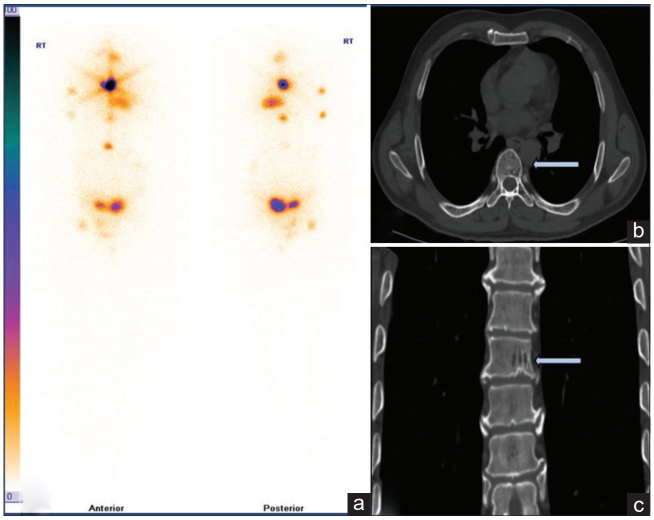

Figure 5: (a) Iodine 131 whole body scan anterior and posterior views showing evidence of RAI avid thyroid bed residue with lung, liver and bone metastases. (b) Axial section CT image showing polka dot appearance (arrow) and (c) Coronal section CT image showing corduroy sign (arrow) in D7 vertebra - suggestive of hemangioma

breast fibroadenoma, and benign conditions such as teratoma. that cause radioiodine uptake mainly due to the expression of NIS. Other benign conditions such as hepatic hemangioma and vertebral hemangioma show false-positive uptake due to intravascular blood pooling and transcapillary escape of iodine with interstitial retention. Here, we present a case series with benign false-positive uptakes in vertebral hemangioma, uterine fibroid, ovarian teratoma, and lipoma.

There are few case reports documenting false-positive uptake in hemangioma. Singh *et al*., in a recent case report, documented vertebral hemangioma with RAI uptake mimicking as vertebral metastases. In one of our cases, vertebral hemangioma showed false-positive RAI uptake. Vertebral hemangiomas are benign vascular tumors with an overall incidence of 10%–15%, most commonly occurring at the dorsal spine. They are often asymptomatic and symptoms develop only due to pressure effects or due to vertebral body destruction. In our case, we performed a CT scan of the dorsal spine to differentiate metastases versus benign pathology and found characteristic polka dot appearance in the axial section and corduroy sign in the sagittal section confirming it to be a benign hemangioma. The possible cause of this uptake in our case could be due to intravascular blood pooling and transcapillary escape of iodine with interstitial retention as documented in the literature.[4]

In our case series, we have two cases with benign tumors one is uterine leiomyoma and the other one is ovarian teratoma that showed RAI uptake. Expression of sodium–iodide symporter, interactions between surrounding tissues that induce aquaporin expressions, or increase in the cell membrane permeability with osmolality changes could be the possible cause of RAI uptake in these cases. This hypothesis for the mechanism of uptake was suggested by Teo *et al*., in a case report, with false-positive uptake in uterine fibroid. We performed additional CT images of the pelvis in these cases and found anatomical evidence of soft-tissue density mass lesion with peripheral calcifications in the uterus, suggesting uterine fibroid in one case and hypodense cystic lesions with areas of soft-tissue component in bilateral adnexa suggesting ovarian teratoma in other cases.[10]

In one of our patients, RAI WBS showed focal increased uptake in the left hemithorax region with low S.TG values of 8.0 ng/mL and anti-TG values of 18.4 mIU/mL, suggesting low possibility for skeletal metastases. This warranted additional clinical examination and imageological investigation to rule out metastases. On clinical examination, a soft, solitary painless mobile swelling, with characteristic slippage sign was elicited raising the possibility of lipoma. However, the patient underwent an excisional biopsy of lipoma and the postoperative HPE report confirmed it to be lipoma. Postexcision follow-up diagnostic RAI WBS revealed no avidity of RAI in previously documented site of lipoma. Similar unusual presentation of RAI uptake in subcutaneous lipoma was documented by Shen G *et al.* in 2016.[11]

Apart from benign conditions, malignant tumors such as adenocarcinoma, squamous cell carcinoma, and small cell carcinoma of the lung also cause false-positive RAI uptake. Expression of the functional NIS protein along with tumoral inflammatory changes and malignant transformation at cellular and subcellular levels are the major causes of iodine affinity resulting in false-positive RAI uptake.

Conclusion

In brief, we conclude that apart from the normal physiological RAI uptake in I-131 diagnostic and therapeutic WBS, there are many false-positive uptakes which affects appropriate decision-making in the management of DTC. Our case series highlights the need for vigilance regarding the causes and mechanisms of false-positive uptakes to improve the quality of reporting without misinterpretation. This results in overall benefit to the patient in terms of risk assessment, high-dose planning, and follow-up strategy, which in turn decreases the burden on patients economically and prevents unnecessary radiation exposure with repeated therapeutic doses and additional surgeries.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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