Interesting False Positive Radioiodine Uptake on I-131 Whole Body Scintigraphy with Different Mechanisms in Two Patients Diagnosed Differentiated Thyroid Carcinoma: A Review of Literature

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ABSTRACT

Introduction: Radioiodine total body scan is used to detect recurrent differentiated thyroid cancer in neck and metastatic lesions. We recently encounter cases of false positive in two veteran: one suffered from shrapnel wound 45 years ago in the back; while another veteran had focal contamination underneath his Dutch beard.

Cases Report: The first case was a 69-years-old Vietnam War male veteran with paraplegia and a history of papillary thyroid carcinoma, he was s/p total thyroidectomy 5/2013 (T3, N1). He received 143 mCi following the surgery. Ultrasound examination revealed recurrence, which was treated with left neck dissection and followed with a dose of 254 mCi of I-131 on 8/2014. A post-RAI treatment scan revealed a focal uptake in the posterior component of T10/T11 vertebra, which, in retrospect, was present in the prior post-ablation scan in 7/2013 without any interval change. A chest CT in 9/2014 revealed a sub-centimeter metallic density in the same site; likely shrapnel deposited 45 years ago. Thus, focal radioiodine uptake likely relates to inflammatory/benign etiology. Suppressed Tg was 3.9 in 8/2015, decreased from 5.3 ng/mL in 2/2015.

The second case was a 41-years-old male veteran s/p total thyroidectomy with central neck dissection in 10/2018 and found one positive LN on left. Final path report was papillary thyroid cancer - staging T1a, N1. The patient received 75.9 mCi of I-131 for remnant ablation in 12/2018 and followed with a total body scan, which showed a focal activity subjacent to left submandibular gland. The activity persisted in a repeat scan after the patient claiming had thoroughly washed his Dutch-style beard. The SPECT/CT revealed the focal activity was not in the left submandibular area and might represent a contamination in the adjacent mustache. This was confirmed by a repeat planar image performed after the beard was shaved off.

Discussion: Focal radioiodine uptake is a sensitive marker for detection of recurrence of differentiated thyroid cancer, s/p total thyroidectomy and RAI ablation. However, radioiodine uptake is not specific for thyroid tissue. It can also be seen in healthy tissue, including thymus, breast, liver, and gastrointestinal tract, or in benign diseases, such as cysts and inflammation, or in a variety of benign and malignant non-thyroidal tumors, which could be mistaken for thyroid cancer. These case studies provide examples of potential false-positive uptake of radioiodine in the whole-body scan and illustrate how such unexpected findings can be appropriately evaluated. Chronic trauma may recruit leukocytes that known to induce iodide organification by means of a myeloperoxidase. Therefore, retention of radioiodine in leukocytes of posttraumatic tissues may also explain various reports of false-positive uptake in sites of inflammation. Secretion of mucin containing iodide salts has also been suggested as another possible mechanism of iodine accumulation associated with chronic inflammatory conditions. Since radioiodine, normally concentrates in saliva, in-patient with beard should always watch for hidden contamination.

Conclusion: Wounds caused by shrapnel fragments could be a common problem for veterans returning from overseas. Recognizing that false positive results could occur in RAI total body scan is clinically important.
Keywords
Cancer, Thyroid carcinoma, Radioiodine,

Introduction
The 1-131 total-body scan is specific and sensitive for demonstrating metastatic differentiated thyroid carcinoma [1,2]. Studies of total of 345 patients showed that the 1-131 total-body scan had a sensitivity of 84.4% for detecting metastatic differentiated thyroid carcinoma with a specificity, 98.1% as compared with Tg, 94.3%. In interpreting the 1-131 total-body scan, the normal tracer activity found in gastrointestinal tract, salivary glands, oropharynx, lactating breast, and urinary bladder might hinder interpretation [1,2]. Liver uptake of radioiodine may also occur when there is significant residual functional thyroid tissue present. Presumably, this is because the liver is active in metabolizing thyroid hormones and their analogs. Ectopic thyroid tissue [2] is occasionally found in substernal, sublingual, or intrathoracic regions.

Cases Report
Case 1
A 69-years-old Vietnam War veteran with paraplegia and a history of Papillary Thyroid Carcinoma, he was s/p total thyroidectomy 5/2013 (T3, N1) multifocal with lympho-vascular and capsular invasion. 8/8 lymph nodes being positive and s/p 1-131 remnant ablation (7/2013) two months later with 143 mCi. Suppressed Tg in 1/14 was 5.9 ng/mL. A dose of 254 mCi of I-131 was given in 8/2014 for metastatic PTC after left-sided neck dissection and found 5/8 LN positive in 4/2014. A post-RAI treatment scan with Spect/CT revealed a focal uptake in the posterior component of T10/T11 vertebra (Figures 1 and 2) which, in retrospect, was present in the prior post-ablation scan in 7/2013 without any interval change. A chest CT in 9/2014 (Figure 3) revealed a sub-centimeter metallic density in the same site; likely shrapnel deposited 45 years ago. Thus, focal radioiodine uptake likely relates to inflammatory/benign etiology. Suppressed Tg was 3.9 ng/mL in 8/2015, decreased from 5.3 ng/mL in 2/2015. Recent follow-up Tg varied from 5.0 ng/ml in 1/2020 to 4.3 ng/ml in 7/2020 with negative Tg antibody (< 1.0 IU/ml). Last neck ultrasound examination in 9/2020, which was unchanged from 9/2019, again revealed no definite residual thyroid tissue, soft tissue mass or suspicious lymph node.

Case 2
A 41-years-old male veteran had total thyroidectomy with central neck dissection in 10/2018 and found one positive LN on left. Final pathology report was papillary thyroid cancer - staging T1a, N1. The patient received 75.9 mCi of I-131 for remnant ablation in 12/2018 and followed with a total body scan, which showed a focal activity subjacent to left submandibular gland. The activity persisted in a repeat scan after the patient claiming had thoroughly washed his Dutch-style beard (Figure 4). The SPECT/CT revealed the focal activity was not in the left submandibular gland and might represent a contamination in the adjacent mustache (Figure 5). This was confirmed by a repeat planar image performed after the beard was shaved off.

Figure 1: Post-treatment I-131 Total Body Scan on 8/19/2014: illustrates focal activity in the lower spine, at the T10/T11 level, which showed no interval change from a prior post-ablation scan on 7/24/2013.

Figure 2: Fused SPECT/CT on 8/19/2014, demonstrated I-131 focal uptake at T10/T11 level.

Figure 3: CT of the Chest dated 9/29/2014 demonstrated a metallic density, likely shrapnel posterior to the T10—T11 disc space and focal radioiodine uptake likely relates to inflammatory/benign etiology.
The specificity of RAI whole body scan for detecting residual or recurrent local and metastatic disease is generally reported to be greater than 90% [2]. Incremental diagnostic value of I-131 SPECT/CT was found over planar whole-body scan after radioiodine therapy [3,4]. Recognition of normal and pathologic biodistribution of iodine is imperative for the nuclear medicine physician to avoid interpretation pitfalls and unnecessary repeated therapeutic doses [1,5]. A radiiodine scan showing abnormal uptake outside the thyroid bed must be studied carefully and alternative reasons for the finding must be considered. In the present case, we demonstrate radioactive salivary contamination buried deep inside the beard (Figure 4 and 5).

Since radioiodine normally concentrates in gastric juice and saliva, one may find tracer activity in the esophagus in a variety of conditions, such as esophageal stricture, Zenker’s diverticulum, gastro-esophageal reflux, hiatal hernia, achalasia, Barrett’s esophagus, intrathoracic gastric cyst and postoperative colon interposition (Table 1). The linear esophageal activity generally mandates simple additional images following both eating and drinking as well as using SPECT/CT [3,4]. Other false positive due to urinary contamination, hypervascularity, benign and malignant tumor should be recognized in order to reach a correct diagnosis (Table 1).

We have reported a patient with disseminated gastric adenocarcinoma with remarkable uptake of radioiodine in the presence of a normal thyroid gland and function (Figure 6) [2]. The study to identify NIS (sodium iodide symporter) in tumor tissue was inconclusive partly due to prolonged storage of the tissue [6].

In general, the expression of NIS is a key mechanism of RAI uptake in functioning thyroid tissues. NIS is a glycoprotein
Figure 6: Total-body scan 72 hr. after oral administration of 5 mCi of I-131 reveals disseminated foci throughout body in the patient with metastatic gastric adenocarcinoma; T: the thyroid; S: the right shoulder; L: the liver; P: right pelvic bone lesions.

Table 1: Mechanism-oriented false positive results on radioiodine I-131 whole-body scan.

<table>
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<th>Mechanisms</th>
<th>Anatomical Areas</th>
<th>Clinical Entities</th>
<th>Note</th>
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<tr>
<td>Physiological</td>
<td>Oro-naso-cavities</td>
<td>Naso-lacrimal sac cyst, paratid gland duct, epiphora</td>
<td>Salivary gland/saliva/tear</td>
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<tr>
<td></td>
<td>Gastro-intestino-esophagus</td>
<td>Achalasia, Zenker’s diverticulum, esophageal dilatation, hiatus hernia, gastric valvulus, achalasia, Barrett’s esophagus, intrathoracic stomach, Meckel’s diverticulum,</td>
<td>Gastric uptake/secretion</td>
</tr>
<tr>
<td>Intestine</td>
<td>Duodenum diverticulum</td>
<td></td>
<td>Passive flow-in of intestinal iodine</td>
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<td>Thymus</td>
<td></td>
<td></td>
<td>NIS and iodine uptake by Hassall’s Bodies</td>
</tr>
<tr>
<td>Other thoracic</td>
<td>pleuro-pericardial, bronchogenic cysts</td>
<td></td>
<td>Passive diffusion (or partially active) and retention of iodine</td>
</tr>
<tr>
<td>Breast</td>
<td>Hyperprolactinemia</td>
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<td>NIS expression and iodine uptake</td>
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<td>Hepato-biliary tract</td>
<td>Hepato-steatosis, simple hepatic cyst</td>
<td></td>
<td>Metabolism of iodinated protein, Intra-hepatic duct NIS expression, blood pooling</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>Ectopic kidney, urine retention</td>
<td></td>
<td>Route of excretion</td>
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<tr>
<td>Renal cyst</td>
<td></td>
<td></td>
<td>Unclear (? NIS expression or other transport protein)</td>
</tr>
<tr>
<td>Gestational sac</td>
<td></td>
<td></td>
<td>Uterus NIS expression and iodine transport from mother to fetus.</td>
</tr>
<tr>
<td>Contaminations</td>
<td>Scalp, wig, beard, hands, lip, body surface</td>
<td>Handkerchief sign, helmet sign, necklace sign, hot nose sign, hot hand sign</td>
<td>Contamination associated with exercise, vomiting, tobacco chewing, urine incontinence</td>
</tr>
<tr>
<td>Inflammation and hyper-vasculation, capillary hyper-permeability</td>
<td>Scalp, surgical scab, Oro-naso-cavities,Gastro-intestino-esophagus Hepato-biliary tract</td>
<td>Folliculitis (scalp), Sialo-adenitis, Sinusitis, Dacryo- cystitis, trauma (biopsy acupuncture sites), subdural hematoma, tracheotomy, surgical suture, wound (foreign bodies), trachea-bronchitis, aspergilloma, bronchi-ectasis, tuberculosis, MI, peri-carditis, cholecystitis, sarcoidosis, arthritis</td>
<td>Inflammatory reaction, Mediated by leukocytes iodide organification by means of a myeloperoxidase or by Secretion of mucin containing iodide salts</td>
</tr>
<tr>
<td>Benign Tumors</td>
<td>Meningioma, Cavernous angioma, osteoid osteoma, Hepatic/vertebral hemangioma, uterine myoma,</td>
<td></td>
<td>High vascularity plus capillary permeability</td>
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<td></td>
<td>Warthin’s Tumor, Oncocytoma (parotid gland), Active transport</td>
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<td></td>
<td>Thyroglossal duct cyst, Breast fibroadenoma, Struma Cordis, Struma ovarii, mucinous cystadenoma, teratoma, serous cystadenofibroma</td>
<td>NIS expression</td>
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<tr>
<td></td>
<td>Neurilemoma, breast fibroadenoma</td>
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<td>Unknown</td>
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<tr>
<td>Malignant Tumors</td>
<td>Adenocarcinoma, squamous cell carcinoma, small and large cell carcinoma, metastatic lung CA, malignant struma ovarii, Breast cancer, gastric adeno-carcinoma, metastatic liver CA and bone CA</td>
<td>NIS expression+ inflammation</td>
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<td></td>
<td>Bronchioloalveolar cell carcinoma</td>
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<td>Glandular mucin secretion</td>
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<td></td>
<td>Ovarian tumor, peritoneal seeding of malignancy, cervical carcinoma</td>
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<td>Unknown</td>
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</tbody>
</table>

Table 1: Mechanism-oriented false positive results on radioiodine I-131 whole-body scan.
located in the basolateral plasma membrane of thyroid follicular cells [6]. Iodide in thyroid follicular cells is oxidized and binds with tyrosine residues of Tg to be organified and it is catalyzed by TPO. Iodide anion not organized by TPO undergoes rapid efflux from follicular thyroid cells. Thus, a balance between NIS-mediated iodide uptake and TPO-inhibited efflux determines the intracellular concentration of iodide.

RAI whole body scan is an integral part of detection of NIS expression in patients with diagnosis of differentiated thyroid carcinoma looking for recurrence or metastatic lesion. The scan is also helpful in selecting patients who might benefit from RAI therapy. Thus, precise interpretation of RAI whole body scan can be helpful in the avoidance of unnecessary exposure to high-dose of radioiodine therapy. In the present case, the identification of the false positive RAI scan (Figure 1) from a shrapnel wound was contributory to the avoidance of unnecessary radioiodine exposure.

The present case studies provide another two examples of potential false-positive uptake and illustrate how such unexpected findings can be appropriately evaluated. Chronic trauma may recruit leukocytes that known to induce iodide organification by means of a myeloperoxidase [7]. Therefore, retention of radioiodine in leukocytes of posttraumatic tissues may also explain various reports of false-positive uptake in sites of inflammation. Secretion of mucin containing iodide salts has also been suggested as another possible mechanism of iodine accumulation associated with chronic inflammatory conditions.

The following table summarizes the various mechanisms that can cause false-positive results on radioiodine scan [1,2,5,8-16] can help therapy decision-making and patient management.

### Conclusion

Wounds caused by shrapnel fragments could be a common problem for veterans returning from overseas. Recognizing that false positive results could occur in RAI total body scan is clinically important. In addition, SPECT/CT improved detection and localization of I-131 accumulation in lymph node metastases and distant metastases as well as contamination as shown in the present case (beard), compared with whole-body scintigraphy in assessing lower/upper stage in a significant number of patients with differentiated thyroid carcinoma and it can affect therapy decision-making and patient management.

### References