Case Report ISSN 2689-1069

Clinical Reviews & Cases

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

Mark D. Chambers, DVM, MD, Mazhar U. Khan, MD, Maureen Chinweze, CNMT, Ella Brenda Scott, CNMT, Steven J Secrest, CNMT, RT, Sing-Yung WU, MD, PHD*

Radiology/ Nuclear Medicine Service, v.a. Medical Center, Long Beach /University of California, Irvine.

***Correspondence:**
Sing-yung Wu, MD, PhD, Professor Emeritus, Department of Radiological Science, UC Irvine College of Medicine.

Received: 24 May 2021; **Accepted:** 20 June 2021

Citation: Chambers MD, KhanMU, Chinweze M, et al. 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. Clin Rev Cases. 2021; 3(1): 1-5.

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 I-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-131was 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.

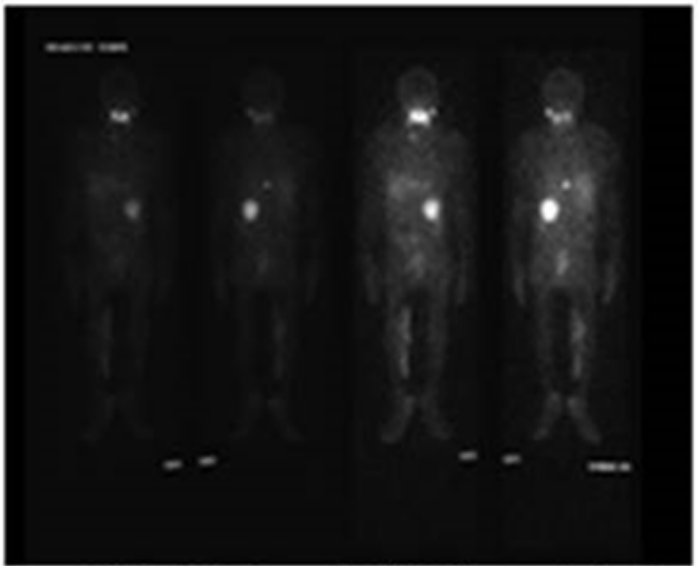

Figure 1: Post-treatment I-131 Total Body Scan on 8/19/2014: illustrates focal activity in the lower spine, at the T10/T11 level, which showed no interval change from a prior post-ablation scan on 7/24/2013.

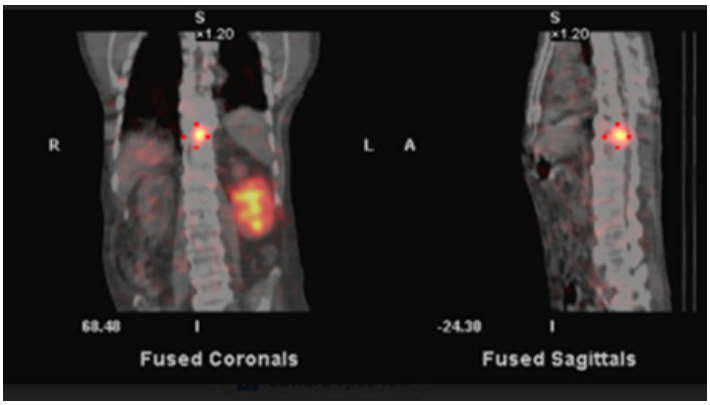

Figure 2: Fused SPECT/CT on 8/19/2014, demonstrated I-131 focal uptake at T10/T11 level.

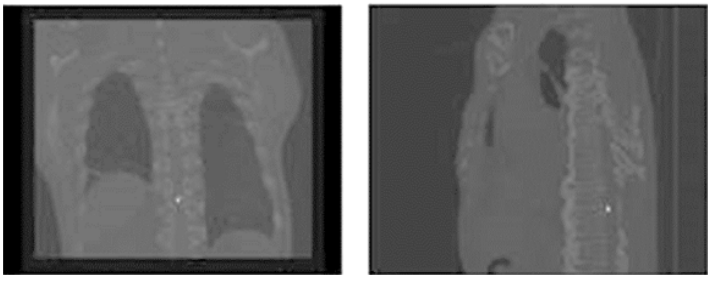

Figure 3: CT of the Chest dated 9/29/2014 demonstrated a metallic density, likely shrapnel posterior to the T10—T11 disc space and focal radioiodine uptake likely relates to inflammatory/benign etiology.

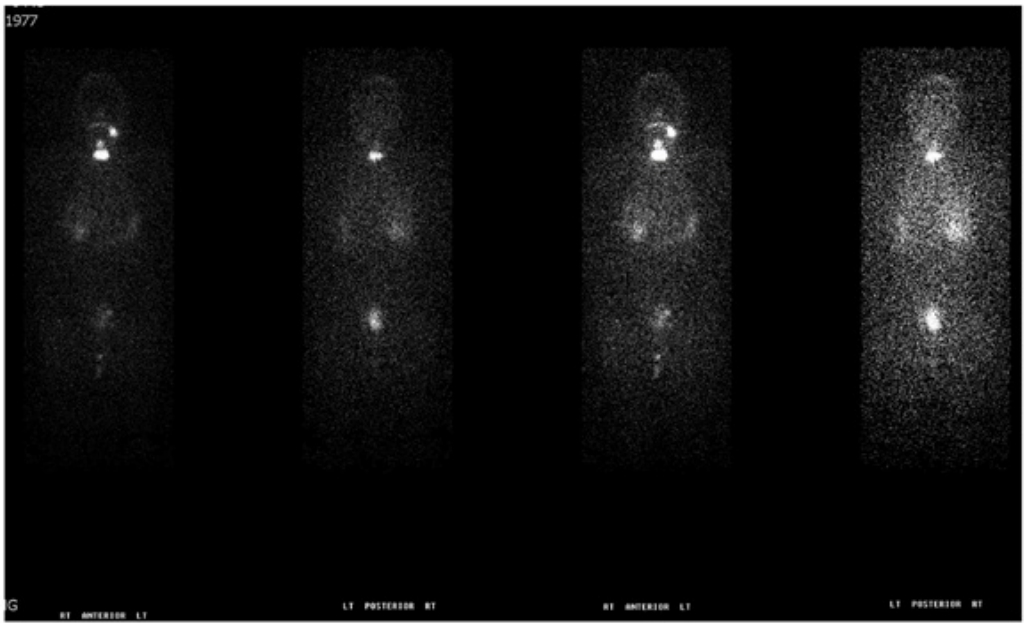

Figure 4: Post-treatment I-131 Total Body Scan on 12/19/2018: illustrates focal activity in the left submandibular area. Residual thyroid activities were seen in mid-cervical and physiological activities were seen in oral cavity, nasopharynx, gastric and hepatic region and urinary tract.

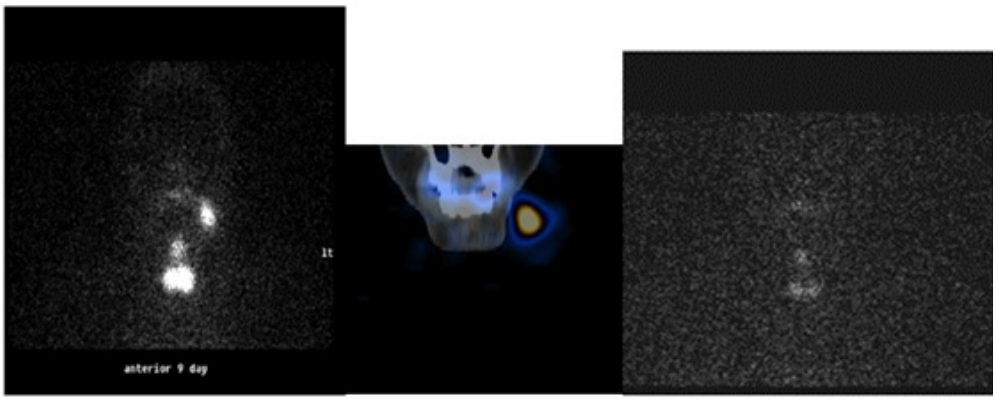

Figure 5: (left) Plantar imaging in anterior projection showing the focal intense activity in the left submandibular region; (middle) Fused SPECT/CT, demonstrated I-131 focal uptake outside of left submandibular gland representing salivary contamination at root of beard; (right) anterior projection of the planar image performed after the beard was shaved off.

Discussion

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 radioiodine 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

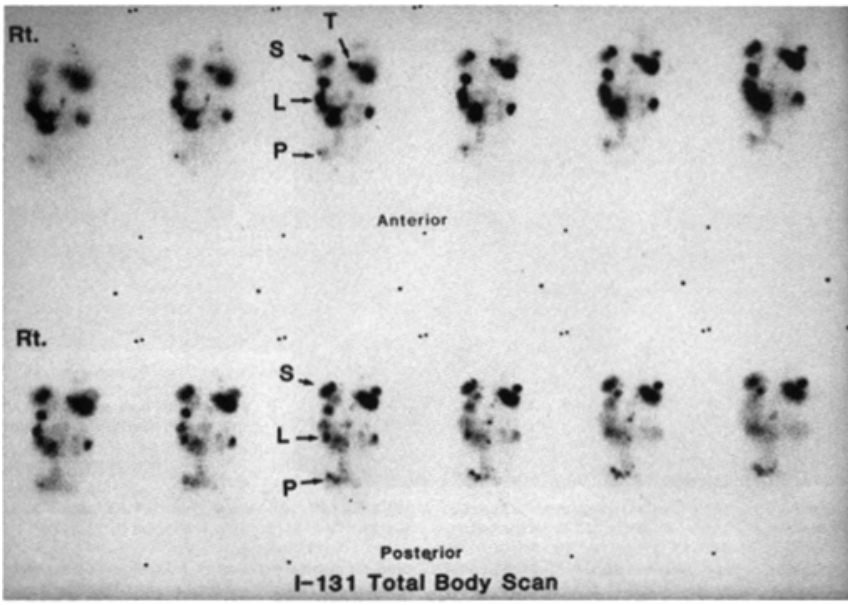

Figure 6: Total-body scan 72 hr. after oral administration of 5 mCi of I-131 reveals disseminated foci throughout body in the patient with metastatic gastric adenocarcinoma; T: the thyroid; S: the right shoulder; L: the liver; P: right pelvic bone lesions.

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

Mechanisms	Anatomical Areas	Clinical Entities	Note
Physiological	Oro-naso-cavities	Naso-lacrimal sac cyst, paratid gland duct, epiphora	Salivary gland/saliva/tear
	Gastro-intestino-esophagus	Achalasia, Zenker's diverticulum, esophageal dilatation, hiatus hernia, gastric valvulus, achalasia, Barrett's esophagus, intrathoracic stomach, Meckel's diverticulum,	Gastric uptake/secretion
	Intestine	Duodenum diverticulum	Passive flow-in of intestinal iodine
	Thymus		NIS and iodine uptake by Hassall's Bodies
	Other thoracic	pleuro-pericardial, bronchogenic cysts	Passive diffusion (or partially active) and retention of iodine
	Breast	Hyperprolactinemia	NIS expression and iodine uptake
	Hepato-biliary tract	Hepato-steatosis, simple hepatic cyst	Metabolism of iodinated protein, Intra-hepatic duct NIS expression, blood pooling
	Urinary tract	Ectopic kidney, urine retention	Route of excretion
		Renal cyst	Unclear (? NIS expression or other transport protein)
	Gestational sac		Uterus NIS expression and iodine transport from mother to fetus.
Contaminations	Scalp, wig, beard, hands, lip, body surface	Handkerchief sign, helmet sign, necklace sign, hot nose sign, hot hand sign	Contamination associated with exercise, vomiting, tobacco chewing, urine incontinence
Inflammation and hyper-vasculation, capillary hyper-permeability	Scalp, surgical scab, Oro-naso-cavities,Gastro-intestino-esophagus Hepato-biliary tract	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	Inflammatory reaction, Mediated by leukocytes iodide organification by means of a myeloperoxidase or by Secretion of mucin containing iodide salts
Benign Tumors		Meningioma, Cavernous angioma, osteoid osteoma, Hepatic/ vertebral hemangioma, uterine myoma,	High vascularity plus capillary permeability
		Warthin's Tumor, Oncocytoma (parotid gland),	Active transport
		Thyroglossal duct cyst, Breast fibroadenoma, Struma Cordis, Struma ovarii, mucinous cystadenoma, teratoma, serous cystadenofibroma	NIS expression
		Neurilemoma, breast fibroadenoma	Unknown
Malignant Tumors		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	NIS expression+ inflammation
		Bronchioloalveolar cell carcinoma	Glandural mucin secretion
		Ovarian tumor, peritoneal seeding of malignancy, cervical carcinoma	unknown

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

1. Wu SY, T Brown, N. Milne, et al. I-131 total body scan - extra thyroidal uptake of radioiodine, Semin Nuc Med. 1986; 16: 82-84.
2. Wu SY, J Kollin, E Coodley, et al. I-131 total body scan: localization of disseminated gastric adenocarcinoma, J Nuc Med. 1984; 25: 1024-1029.
3. Maruoka Y, Abe K, Baba S, et al. Incremental diagnostic value of SPECT/CT with 131I scintigraphy after radioiodine therapy in patients with well-differentiated thyroid carcinoma. Radiology. 2012; 265: 902-909.
4. Zilioli V, Peli A, Panarotto MB, and et al. Differentiated thyroid carcinoma: Incremental diagnostic value of 131I SPECT/CT over planar whole body scan after radioiodine therapy. Endocrine. 2017; 56: 551-559.
5. Oh JR, Ahn BC. False-positive uptake on radioiodine whole-body scintigraphy: physiologic and pathologic variants unrelated to thyroid cancer, Am J Nucl Med Mol Imaging. 2012; 2: 362-385.
6. Shen DH, RT Kloos, E L Mazzaferri, et al. Sodium iodide symporter in health and disease, Thyroid. 2001; 11: 415-425.
7. Klebanoff SJ, Hamon CB, Role of myeloperoxidase-mediated antimicrobial systems in intact leukocytes. J Reticuloendothel Soc. 1972; 12: 170-196.
8. Ranade R, Pawar S, Mahajan A, et al. Unusual False Positive Radioiodine Uptake on 131I Whole Body Scintigraphy in Three Unrelated Organs with Different Pathologies in Patients of Differentiated Thyroid Carcinoma: A Case Series, World J Nucl Med. 2016; 15: 137-141.
9. Triggiani V, Giagulli VA, Iovino M, et al. False positive diagnosis on (131)Iodine whole-body scintigraphy of differentiated thyroid cancers, Endocrine. 2016; 53: 626-635.
10. Chudgar AV, Shah JC, Pictorial review of False-positive results on radioiodine scintigrams of patients with differentiated thyroid cancer, Radiographics. 2017; 37: 298-315.
11. Jia CP, Moadel R, Freeman LM, Focal thoracic uptake uptake mimicking lung metastasis on 131I post-therapy whole-body scan in patients with thyroid carcinoma, Clin Nucl Med. 2014; 39: 360-362.
12. Thientunyakit T, False-positive 131I whole-body scan in well-differentiated thyroid cancer patient with respiratory bronchiolitis, Clin Nucl Med. 2013; 38: 730-734.
13. Wang R, Zhou K, Fan QP, et al. A false-positive I-131 finding of duodenum diverticulum in thyroid cancer evaluated by SPECT/CT: a case report, Medicine (Baltimore). 2018; 97: e9997.
14. Oral A, Yazici B, Eraslan C, et al. Unexpected False-positive I-131 uptake in patients with differentiated thyroid carcinoma, Mol Imaging Radionucl Ther. 2018; 27: 99-106.
15. Nishiyama Y, Yamamoto Y, Takahashi K, et al. False-positive iodine-131 whole-body imaging due to gestational sac. Clin Nucl Med. 1998; 23: 535-536.
16. Wu SY, Chambers MD, Khan MU, et al. A Shrapnel Fragment Deposited 45 Year ago caused a False Positive RAI Uptake in the Spine in a Patient with Papillary Thyroid Carcinoma: A Review of Mechanisms and Literature, Clin in Oncol. 2017; 2: 1328-1329.