



Incidental I-131 Uptake in Ovarian Carcinoma in a Patient with Differentiated Thyroid Carcinoma: A Case Report

Amordekhai Imvan Parlindungan Sihombing, Trias Nugrahadi, Achmad Hussein Sundawa Kartamihardja

Department of Nuclear Medicine and Molecular Theranostics, School of Medicine, Universitas Padjadjaran –
Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

ABSTRACT

Introduction: Radioactive iodine (I-131) therapy is an essential component in the management of differentiated thyroid carcinoma (DTC) following total thyroidectomy. Post-therapy whole-body scintigraphy (PT-WBS) with I-131 aims to detect residual thyroid tissue, recurrence, or metastatic spread. Radiiodine uptake outside the thyroid region may suggest metastases or false-positive findings, thus requiring careful interpretation. **Case:** A 47-year-old woman with *differentiated thyroid carcinoma* (DTC) underwent I-131 therapy. The PT-WBS and single photon emission computed tomography/computed tomography (SPECT/CT) revealed no I-131 uptake in the thyroid bed, but instead showed unexpected I-131 uptake in bilateral ovarian masses. Subsequent histopathological and immunohistochemical evaluation after total hysterectomy with bilateral salpingo-oophorectomy confirmed that the masses were ovarian carcinoma. **Discussion:** Radiiodine uptake in ovarian carcinoma is extremely rare and may be attributed to the expression of the sodium-iodide symporter (NIS) in the ovarian surface epithelium (OSE). Other contributing factors may include increased tumor vascularity, local inflammation, and enhanced capillary permeability that facilitate iodine retention. **Conclusion:** This case highlights the importance of considering non-thyroidal malignancies in the interpretation of PT-WBS findings, particularly when atypical uptake is observed.

Keywords: Case report, differentiated thyroid carcinoma, I-131, ovarian carcinoma, SPECT/CT.

ABSTRAK

Pendahuluan: Terapi iodium radioaktif (I-131) merupakan bagian penting dalam tata laksana kanker tiroid berdiferensiasi pasca-tiroidektomi total. *Whole-body scintigraphy* pasca-terapi (PT-WBS) I-131 bertujuan untuk mendeteksi jaringan tiroid sisa, kekambuhan, atau metastasis. Penangkapan I-131 di luar regio tiroid dapat mengindikasikan adanya metastasis atau tangkapan positif palsu, sehingga memerlukan interpretasi yang cermat. **Kasus:** Wanita usia 47 tahun dengan DTC menjalani terapi I-131. Hasil PT-WBS dan *single photon emission computed tomography/computed tomography* (SPECT/CT) menunjukkan tidak ada penangkapan I-131 di regio tiroid, namun teridentifikasi akumulasi I-131 pada massa di kedua ovarium. Hasil pemeriksaan histopatologi dan imunohistokimia pasca-histerektomi total dan salpingo-ooforektomi bilateral mengonfirmasi bahwa massa tersebut adalah karsinoma ovarium. **Pembahasan:** Penangkapan I-131 sangat jarang pada karsinoma ovarium, mungkin disebabkan oleh ekspresi *sodium-iodide symporter* (NIS) pada epitel permukaan ovarium (OSE). Faktor lain yang dapat berkontribusi meliputi peningkatan vaskularisasi pada tumor, proses inflamasi, dan peningkatan permeabilitas kapiler yang memungkinkan retensi iodium. **Simpulan:** Kasus ini menekankan pentingnya mempertimbangkan keganasan non-tiroid dalam interpretasi hasil PT-WBS, serta perlunya evaluasi histopatologi jika ditemukan tangkapan tidak lazim. **Amordekhai Imvan Parlindungan Sihombing, Trias Nugrahadi, Achmad Hussein Sundawa Kartamihardja. Ambilan I-131 insidental oleh Karsinoma Ovarium pada Pasien Karsinoma Tiroid Berdiferensiasi: Laporan Kasus.**

Kata Kunci: Laporan kasus, kanker tiroid berdiferensiasi, I-131, kanker ovarium, SPECT/CT.

<https://doi.org/10.55175/cdk.v53i05.1919>



Cermin Dunia Kedokteran is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

INTRODUCTION

Differentiated thyroid cancer (DTC), which includes papillary and follicular carcinoma, accounts for more than 90% of all thyroid malignancies.¹ The initial treatment of

DTC typically involves total or near-total thyroidectomy, with or without lymph node dissection. Radioactive iodine (RAI) therapy plays a critical role in the postoperative management of selected patients and is

well established for both therapeutic and diagnostic purposes.²⁻³

Whole-body scintigraphy (WBS) with I-131, especially when performed post-therapy

Alamat Korespondensi amordekhaishihombing@gmail.com

CASE REPORT



(PT-WBS), serves as a sensitive imaging modality for detecting remnant thyroid tissue and metastatic lesions in patients with intermediate- to high-risk DTC.²⁻⁴ Both normal and neoplastic thyroid cells, although to a lesser extent in malignant forms, retain the unique ability to take up and organify iodine. This capability is mediated by the sodium-iodide symporter (NIS), an integral membrane glycoprotein responsible for the active transport of iodide into the cell. Following uptake, iodide is organified and stored by binding to thyroglobulin through enzymatic processes. Importantly, NIS expression is not exclusive to thyroid tissue and can also be found in various extrathyroidal tissues, both normal and malignant.⁵ This report presents a rare case of intense I-131 uptake in an ovarian carcinoma patient who had previously undergone RAI therapy for DTC. We also discuss potential mechanisms underlying this unexpected uptake pattern.

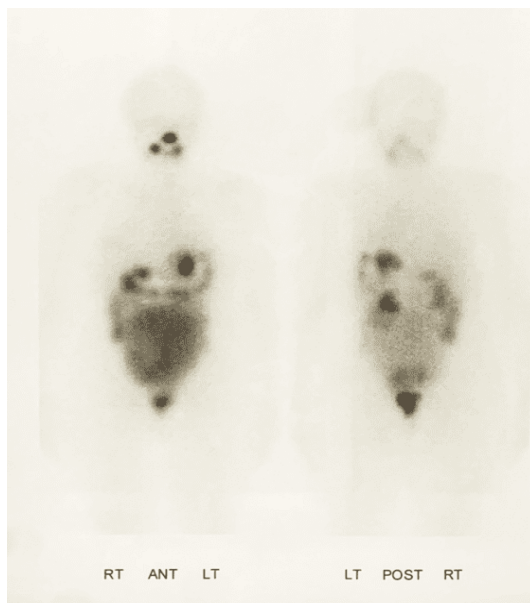
CASE

A 47-year-old woman diagnosed with papillary thyroid carcinoma (PTC) underwent total thyroidectomy. Histopathological examination confirmed classic PTC without evidence of capsular or vascular invasion. The tumor was staged as T2N0M0. The patient was scheduled to receive radioactive iodine (I-131) therapy to ablate any residual

thyroid tissue or microscopic tumor remnants following surgery. Thyroid hormone therapy was withdrawn for four weeks to achieve endogenous TSH stimulation before I-131 administration. Pre-therapy assessments included complete blood count, serum thyroglobulin (Tg), thyroid-stimulating hormone (TSH), anti-thyroglobulin antibody (TgAb), chest radiography, and neck ultrasonography. Laboratory results revealed normal hematological parameters, elevated Tg and TSH levels, and suppressed TgAb titers. Chest radiography showed no pathological

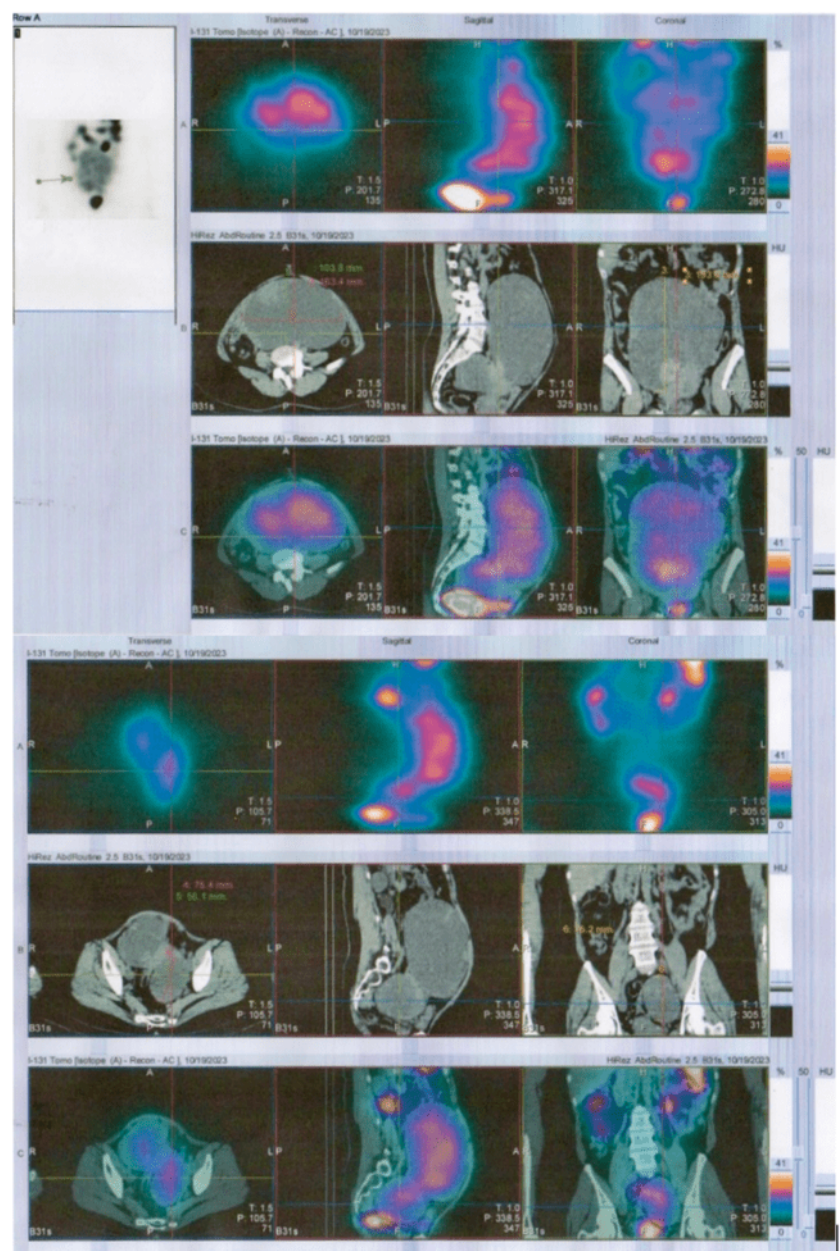
findings. Neck ultrasound identified a solid lesion with internal calcifications in the left thyroid bed, suggestive of remnant thyroid tissue.

The patient received an oral dose of 150 mCi of I-131 and was hospitalized for two days. Post-therapy whole-body scintigraphy (PT-WBS) showed no I-131 uptake in the thyroid bed lesion, consistent with a non-avid postoperative remnant. Unexpectedly, increased I-131 accumulation was observed in bilateral adnexal regions (**Figure 1 and 2**).



*Documentation by Amordekhai Imvan Parlindungan Sihombing.

Figure 1. Planar WBS. There is diffuse I-131 uptake in the abdominal region.



*Documentation by Amordekhai Imvan Parlindungan Sihombing.

Figure 2. SPECT/CT WBS. There are masses in both ovaries that take up I-131.



The patient was referred to the gynecology department for further evaluation. Following comprehensive imaging and clinical assessments, she underwent a total hysterectomy with bilateral salpingo-oophorectomy. Histopathological analysis revealed high-grade ovarian carcinoma. Immunohistochemical staining demonstrated positive expression of Napsin A, and negative results for TTF-1, WT-1, PR, and p53, findings supportive of primary ovarian clear cell carcinoma (OCCC). The patient subsequently received systemic chemotherapy consisting of paclitaxel and carboplatin administered every three weeks.

DISCUSSION

A radioiodine whole-body scan plays an important role in the management of patients with differentiated thyroid cancer (DTC), as DTC cells are more efficient at trapping circulating radioiodine than other tissues.⁶ Uptake of iodine by cancer cells is primarily related to the expression of the sodium-iodide symporter (NIS), which actively transports iodide into these cells. Extrathyroidal tissues such as the stomach, salivary glands, and breast are also known to express NIS and can physiologically take up iodine.⁷

On whole-body scans with diagnostic or therapeutic doses of I-131, focal radioiodine uptake is typically considered to represent metastatic lesions in thyroid cancer patients who have undergone total thyroidectomy, except for known physiological uptake in the salivary glands, stomach, gastrointestinal tract, and urinary system. In addition to these well-known physiological areas, post-therapy WBS (PT-WBS) normally demonstrates thyroid remnants and, when present, foci of metastatic disease. However, radioiodine uptake can also be observed in unexpected locations on planar imaging, PT-WBS, or static images due to benign or inflammatory conditions as well as non-thyroidal tumors.⁸

This case illustrates a rare and diagnostically challenging presentation of I-131 uptake in a primary ovarian malignancy. The uptake was

initially suspected to represent metastatic thyroid carcinoma or struma ovarii. However, histopathological and immunohistochemical evaluation confirmed the diagnosis of ovarian clear cell carcinoma (OCCC).

This unexpected I-131 uptake in the adnexal region may be explained by the functional expression of the sodium-iodide symporter (NIS) in ovarian carcinoma cells, as previously described by Riesco-Eizaguirre, *et al.*, Their study demonstrated that NIS is not only expressed in normal female reproductive epithelium but also frequently overexpressed in epithelial ovarian cancer.⁹ Notably, such expression may facilitate active iodide transport into the tumor, contributing to false-positive findings on post-therapy whole-body scintigraphy in patients undergoing radioactive iodine treatment for DTC.

Other mechanisms underlying I-131 uptake in ovarian carcinoma are also observed in both benign and malignant tumors. Benign tumors, in particular, have been reported to show unexpected RAI uptake. This may be attributed to physiological NIS expression in epithelial tissues, as seen in salivary gland tumors,^{10–13} breast fibroadenomas,¹⁴ and ovarian tumors.^{15–18} Highly vascular tumors, including meningiomas^{19,20} and hemangiomas,^{21–25} may demonstrate RAI pooling and apparent uptake on whole-body scintigraphy.

Pathological accumulation of radioactive iodine (RAI) in non-thyroidal malignancies and their metastases has also been reported in various anatomical sites.²⁶ The underlying mechanisms are similar to those observed in benign tumors, including NIS expression and high vascularity. Additionally, a local inflammatory response within malignant tissues may enhance I-131 accumulation through inflammation-mediated hyperemia, increased vascular permeability, and potentially the retention of organified iodine by activated leukocytes during bactericidal processes.^{27–29}

Our patient with DTC exhibited unexpected I-131 uptake in the adnexal region, later diagnosed as ovarian clear cell carcinoma, which is likely explained by this NIS-mediated iodide transport in non-thyroidal malignancy. This finding aligns with previous reports^{9,15–18} suggesting that radioiodine uptake may occur in ovarian tumors independent of thyroid metastasis. Importantly, this highlights the need to differentiate true metastatic thyroid lesions from incidental uptake due to unrelated primary tumors. Histopathological confirmation remains essential in atypical WBS findings.^{30,31}

The importance of hybrid imaging techniques such as SPECT/CT cannot be overstated. These tools allow for precise anatomical localization and can significantly reduce the risk of misinterpretation associated with planar imaging alone. In fact, some cases of false-positive uptake can only be definitively diagnosed through surgical excision and histological analysis, especially in the pelvic region, where physiological and pathological findings often overlap.^{30,31}

Therefore, clinicians interpreting WBS in female patients, particularly those of reproductive age, should consider functional NIS expression in ovarian tissue when formulating a differential diagnosis when encountering unexpected pelvic uptake. Misinterpretation may result in unwarranted RAI therapy, delay in appropriate oncologic management, or failure to detect second primary malignancies.

CONCLUSION

Iodine-131 uptake in ovarian carcinoma may mimic metastatic thyroid cancer and lead to diagnostic confusion. Beyond NIS expression, factors such as tumor hypervascularity, local inflammatory responses, and passive radiotracer retention can contribute to false-positive findings. This case emphasizes the need for careful integration of clinical, hybrid imaging, and pathological data to ensure accurate interpretation and appropriate management.

REFERENCES

1. Sherman SI. Thyroid carcinoma. *Lancet*. 2003;361(9356):501–11. doi:10.1016/S0140-6736(03)12488-9.
2. Lim H, Devesa SS, Sosa JA, Check D, Kitahara CM. Trends in thyroid cancer incidence and mortality in the United States, 1974–2013. *JAMA*. 2017;317(13):1338–48. doi: 10.1001/jama.2017.2719.



3. Orosco RK, Hussain T, Noel JE, Chang DC, Dosiou C, Mittra E, et al. Radioactive iodine in differentiated thyroid cancer: a national database perspective. *Endocr Relat Cancer*. 2019;26(10):795–802. doi: 10.1530/ERC-19-0292.
4. Seidlin SM, Marinelli LD, Oshry E. Radioactive iodine therapy: effect on functioning metastases of adenocarcinoma of the thyroid. *JAMA*. 1946;132(14):838–47. doi: 10.1001/jama.1946.02870490016004.
5. Ravera S, Reyna-Neyra A, Ferrandino G, Amzel LM, Carrasco N. The sodium/iodide symporter (NIS): molecular physiology and preclinical and clinical applications. *Annu Rev Physiol*. 2017;79:261–89. doi: 10.1146/annurev-physiol-022516-034125.
6. Hyer S, Newbold K, Harmer C. Early and late toxicity of radioiodine therapy: detection and management. *Endocr Pract*. 2010;16(6):1064–70. doi:10.4158/EP10170.RA.
7. Riesco-Eizaguirre G, Santisteban P. A perspective view of sodium iodide symporter research and its clinical implications. *Eur J Endocrinol*. 2006;155(4):495–512. doi: 10.1530/eje.1.02257.
8. Triggiani V, Giagulli VA, Iovino M, Guastamacchia E, Licchelli B, Resta F, et al. False positive diagnosis on ¹³¹I whole-body scintigraphy of differentiated thyroid cancers. *Endocrine*. 2016;53(3):626–35. doi: 10.1007/s12020-015-0750-3.
9. Riesco-Eizaguirre G, Garcia Leoni S, Mendiola M, Estevez-Cabrero MA, Gallego MI, Redondo A, et al. NIS mediates iodide uptake in the female reproductive tract and is a poor prognostic factor in ovarian cancer. *J Clin Endocrinol Metab*. 2014;99(7):E1199–208. doi: 10.1210/jc.2013-4249.
10. Ilgan S, Narin Y, Arslan N, Aksu A, Bayhan H. Warthin's tumor and I-¹³¹ body scan. *Clin Nucl Med*. 1999;24(9):721–2. doi:10.1097/00003072-199909000-00029.
11. Caglar M, Tuncel M, Usubutun A. Increased uptake on I-¹³¹ whole-body scintigraphy in Warthin tumor despite false-negative Tc-^{99m} pertechnetate salivary gland scintigraphy. *Clin Nucl Med*. 2003;28(11):945–6. doi: 10.1097/01.rlu.0000093316.56231.91.
12. Gekeler J, Luers JC, Krohn T, Beutner D. False-positive findings in F-¹⁸ FDG PET and whole-body scans with I-¹³¹ in Warthin tumor of the parotid gland. *Clin Nucl Med*. 2010;35(2):105–6. doi: 10.1097/RLU.0b013e3181c7bf39.
13. Broekhuizen-de Gast HS, van Isselt JW, Roef MJ, Lam MG. Oncocytoma of the parotid gland causing false-positive result on I-¹³¹ whole-body scintigraphy. *Clin Nucl Med*. 2011;36(8):701–3. doi: 10.1097/RLU.0b013e318217a65f.
14. Berger F, Unterholzner S, Diebold J, Knesewitsch P, Hahn K, Spitzweg C. Mammary radioiodine accumulation due to functional sodium iodide symporter expression in a benign fibroadenoma. *Biochem Biophys Res Commun*. 2006;349(4):1258–63. doi: 10.1016/j.bbrc.2006.08.170.
15. Kim EE, Pjura G, Gobuty A, Verani R. ¹³¹I uptake in a benign serous cystadenoma of the ovary. *Eur J Nucl Med*. 1984;9(9):433–5. doi: 10.1007/BF00295581.
16. Qiu ZL, Xu YH, Song HJ, Luo QY. Unusual ¹³¹I uptake in a benign mucinous cystadenoma of the ovary in a patient with papillary thyroid cancer. *Clin Nucl Med*. 2010;35(12):965–6. doi: 10.1097/RLU.0b013e3181f9dee9
17. Flug J, Lameka K, Lee R, Katz DS, Sung WW, Yung E. False-positive I-¹³¹ uptake by an ovarian serous cystadenofibroma. *Clin Nucl Med*. 2012;37(2):178–80. doi: 10.1097/RLU.0b013e31823933d2.
18. Almohamad FA, Ahmad T, Ahmad B, Hussain K, Hadid L, Zein M, et al. False-positive radioiodine accumulation in a huge pelvic mass after thyroidectomy for papillary carcinoma: a case report from Syria. *J Surg Case Rep*. 2018;2018(2):rjy028. doi: 10.1093/jscr/rjy028.
19. Schmidt M, Scheidhauer K, Urbanek V, Luyken C, Friese M, Voth E, et al. Metastasizing follicular thyroid carcinoma with intracranial iodine-¹³¹ uptake in brain edema due to a frontal meningioma. *Nuklearmedizin*. 2000;39(1):38–9. doi: 10.1055/s-0038-1632241.
20. Sinha P, Conrad GR, Holzhauser M. Incidental detection of a falx meningioma on post-therapy radioiodide whole-body imaging. *Clin Nucl Med*. 2002;27(12):916–7. doi: 10.1097/00003072-200212000-00025.
21. Bulzico DA, Vaisman F, Pessoa NC, Corbo R. Cavernous angioma mimicking a differentiated thyroid carcinoma brain metastasis. *Clin Nucl Med*. 2011;36(1):62–3. doi: 10.1097/RLU.0b013e3181feefc2.
22. Mohan V, Jones RC, Drake AJ 3rd, Daly PL, Shakir KM. Littoral cell angioma presenting as metastatic thyroid carcinoma to the spleen. *Thyroid*. 2005;15(2):170–5. doi: 10.1089/thy.2005.15.170.
23. Karyagar S, Uyanik E, Mulazimoglu M, Karyagar SS. Uptake of ¹³¹I on a post-thyroid ablation whole-body scan due to cavernous liver hemangioma, mimicking metastases. *Hell J Nucl Med*. 2009;12(2):177–8. PMID: 19675879.
24. Laguna R, Silva F, Vazquez-Selles J, Orduna E, Flores C. Vertebral hemangioma mimicking a metastatic bone lesion in well-differentiated thyroid carcinoma. *Clin Nucl Med*. 2000;25(8):611–3. doi:10.1097/00003072-200008000-00008.



25. Khan S, Dunn J, Strickland N, Al-Nahhas A. Iodine-123 uptake in vertebral haemangiomas in a patient with papillary thyroid carcinoma. *Nucl Med Rev Cent East Eur.* 2008;11(1):30–3. PMID: 19173186.
26. Wu K, Ozomaro U, Flavell R, Shin JJ, Van Nostrand D. Causes of false-positive radioactive iodine uptake in patients with differentiated thyroid cancer. *Curr Radiol Rep.* 2021;9:6. doi: 10.1007/s40134-021-00381-7.
27. Van den Broek PJ, Buys LF, van Furth R. Interaction of povidone-iodine compounds, phagocytic cells, and microorganisms. *Antimicrob Agents Chemother.* 1982;22(4):593–7. doi: 10.1128/AAC.22.4.593.
28. Wapnir IL, van de Rijn M, Nowels K, Amenta PS, Walton K, Montgomery K, et al. Immunohistochemical profile of the sodium/iodide symporter in thyroid, breast, and other carcinomas using high density tissue microarrays and conventional sections. *J Clin Endocrinol Metab.* 2003;88(4):1880–8. doi: 10.1210/jc.2002-021544.
29. Wapnir IL, Goris M, Yudd A, Dohan O, Adelman D, Nowels K, et al. The Na⁺/I⁻ symporter mediates iodide uptake in breast cancer metastases and can be selectively down-regulated in the thyroid. *Clin Cancer Res.* 2004;10(13):4294–302. doi: 10.1158/1078-0432.CCR-04-0074.
30. Shapiro B, Rufini V, Jarwan A, Geatti O, Perez CT, Gross MD. Artifacts, anatomical and physiological variants, and unrelated diseases that might cause false-positive whole-body ¹³¹I scans in patients with thyroid cancer. *Semin Nucl Med.* 2000;30(2):115–32. doi: 10.1053/nm.2000.5414.
31. Barbaro D, Campenni A, Forleo R, Lapi P. False-positive radioiodine uptake after radioiodine treatment in differentiated thyroid cancer. *Endocrine.* 2023;81(1):30–5. doi: 10.1007/s12020-023-03338-2.