## **Original article**

## Nabothian cyst associated with high false-positive incidence of iodine-131 uptake in whole-body scans after treatment for differentiated thyroid cancer

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**Objective** This study aimed to analyze the focal uptake of iodine-131 (<sup>131</sup>I) in the upper pelvis superior to the urinary bladder on whole-body images of patients who underwent this treatment after thyroidectomy for differentiated thyroid cancer.

*Methods* Between June 2012 and March 2013, 205 patients (72 men and 133 women, with an average age of 47.9±11.7 years) who underwent <sup>131</sup>I radioactive treatment after thyroid cancer surgery were analyzed retrospectively. Pathological findings confirmed papillary thyroid carcinoma. A whole-body scan was acquired 5 days after 100–120 mCi sodium iodide was administered orally to the patients. Single-photon emission computed tomography/computed tomography (SPECT/CT) scanning was carried out to locate the lesion; this showed abnormal intense activity in the upper pelvis superior to the urinary bladder, which was further evaluated by ultrasonography.

**Results** Using <sup>131</sup>I-SPECT scanning, five (3.76%) female patients were shown to have abnormal focal radioactivity in the lower abdomen. Subsequent SPECT/CT examination showed that the radioactivity was located in the cervix in four of the five patients and in the sigmoid colon in one patient. Transvaginal ultrasonography was performed

## Introduction

Differentiated thyroid cancer (DTC), which includes papillary and follicular cancers, is the most common type of thyroid cancer, accounting for 85% of all thyroid cancers. Radioiodine therapy is often adopted after thyroid carcinoma resection [because of the characteristic of iodine-131 (<sup>131</sup>I) uptake in DTC] to decrease the recurrence rate and risk of metastasis [1].

<sup>131</sup>I whole-body scanning (<sup>131</sup>I-WBS) after <sup>131</sup>I treatment in patients with DTC can provide information regarding metastasis and prognosis and help make decisions related to clinical treatment. With its high sensitivity and specificity, <sup>131</sup>I single-photon emission computed tomography/computed tomography (SPECT/CT) can improve the accuracy of diagnoses and reduce the false-positive rate.

We have previously reported a case of increased iodine uptake in cervical nabothian cysts [2]. Since then, our attention has focused on <sup>131</sup>I-WBS after <sup>131</sup>I therapy in our department; this has indicated that the rate of increased focal iodine activity in the middle of the lower abdomen of patients with DTC is higher than that in the former four patients, which revealed several echo-free regions in the cervix. These findings are consistent with the diagnosis of a nabothian cyst. Three of these patients were administered a second course of radioiodine therapy. Radioactive uptake was still visible at the same sites on whole-body imaging.

**Conclusion** Nabothian cyst should be considered in cases in which abnormal uptake in the upper pelvis superior to the urinary bladder is detected on <sup>131</sup>I whole-body scans after differentiated thyroid cancer resection. *Nucl Med Commun* 34:1204–1207 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Keywords: <sup>131</sup>I whole-body imaging, false-positive finding, nabothian cyst, papillary thyroid cancer, radioiodine therapy

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considered previously. In the current study, patients with papillary thyroid cancer, who had undergone thyroidectomy, radioablation, and WBS with <sup>131</sup>I, were analyzed to explore the possible reason for this higher than expected rate of focal iodine activity.

## Materials and methods Clinical data

Between June 2012 and March 2013, 205 papillary thyroid cancer patients (72 men and 133 women, average age  $47.9 \pm 11.7$  years), with or without lymph invasion, underwent thyroidectomy and <sup>131</sup>I treatment at our department. These cases were analyzed retrospectively. Diagnoses were confirmed pathologically. All patients provided informed consent for participation in the study.

All patients were required to terminate levothyroxine sodium medication (Merck KGaA, Darmstadt, Germany) 3–4 weeks before <sup>131</sup>I treatment. Thyroid function tests (estimation of levels of free triiodothyronine, free thyroxine, thyroid stimulating hormone, thyroglobulin, thyroglobulin antibodies) were carried out before radiotherapy.

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This examination revealed that serum thyroid stimulating hormone levels in all patients were higher than 30 mIU/l (average  $67.76 \pm 17.15 \text{ mIU/l}$ ). The serum concentration of thyroglobulin ranged from 0 to 478 mg/l, with a mean value of  $39.24 \pm 10.66 \text{ mg/l}$ . The second <sup>131</sup>I therapy was usually performed 5–6 months after the first treatment.

# Iodine-131 single-photon emission computed tomography/computed tomography imaging

A whole-body scan was acquired 5 days after 100–120 mCi sodium iodide was administered orally. Patients whose scans showed strip funicular or multidotted concentration in the lower mid-abdomen were subsequently excluded. Patients showing intense radioactivity in the upper pelvis underwent CT scanning to define the sites of radioactivity.

Whole-body <sup>131</sup>I-SPECT scanning was performed using a high-energy collimator (energy peak, 360 keV; window width, 25%; matrix,  $128 \times 128$ ; scan speed, 6 cm/min); CT scanning parameters were as follows: electric current, 130 mA; axial slice thickness, 4 mm. Transvaginal ultrasonography was performed to determine the nature of increased uptake in the cervix.

#### Results

False-positive <sup>131</sup>I uptake in DTC patients could either be because of physiological or pathological traces. In our study, physiological uptake could be seen in the parotid gland, nasopharynx, residual thyroid, stomach, liver, bowel, and urinary bladder on the images of the 205 patients. In addition to a few visible neck metastatic lymph nodes in lymph node invasion patients, increased radioactivity could be seen in the middle of the lower abdomen in five female patients. Subsequent SPECT/ CT images of these five patients indicated that the abnormal activity was located in the cervix of the uterus in four of the patients (Fig. 1) and in the sigmoid colon in one patient. Transvaginal ultrasonography was performed in these four patients to aid diagnosis. This revealed several echo-free regions in the cervix, with diameters between 4.7 and 12 mm (Fig. 2). These findings are consistent with the diagnosis of a nabothian cyst. It is worth mentioning that three of these patients underwent a second course of <sup>131</sup>I treatment; the second set of whole-body images of these patients still showed high radioactivity in the upper pelvis superior to the urinary bladder.

## Discussion

<sup>131</sup>I-WBS is currently considered to be the best method for visualization of residual thyroid tissue or associated DTC metastases [3]. It is deemed to be more sensitive than other diagnostic examinations [4] and has a high specificity of greater than 90% [5]. Normal physiological radioiodine uptake is observed in the salivary glands, oropharynx, gastrointestinal and genitourinary tracts, and breast tissue. An abnormal uptake that occurs outside of these physiological accumulation sites is usually considered to be a result of thyroid cancer metastasis; however, several cases of false-positive radioiodine activity have been reported. Some benign lesions too, such as cysts, infections, and inflammations, can cause nonspecific concentration of radioiodine [6–9], which can easily be confused with thyroid cancer metastases, leading to difficulties in diagnosis.

Uterine cervical nabothian cyst is a common gynecological disease in women of reproductive age. It is caused by chronic inflammation of cervix, with interstitial or epithelial squamous metaplasia, which clogs the glandular tuber, leading to cystic dilation of the endocervical glands and enlargement of the cervix. The cyst can develop anywhere in the cervix. Nabothian cysts are generally small and asymptomatic [10], and are often an incidental finding on clinical and pathological examinations of the uterine cervix [11]. Ultrasound examination is of value for the detection and diagnosis of nabothian cysts [12].

The current study reported abnormal radioactivity in the cervix in four of the five patients showing abnormal radioactivity; cervical nabothian cysts were detected on transvaginal ultrasound examination. As the false-positive incidence of cervical nabothian cysts is so high, patients with an abnormal uptake in the middle of the lower abdomen should be counseled about the possibility of the occurrence of a cervical nabothian cyst.

The uptake of <sup>131</sup>I has been reported in many kinds of cysts, including hepatic cysts [13,14], renal cysts [15,16], lacteal cysts [17], thyroglossal duct cysts [18], nasolacrimal sac cysts [19], pleuropericardial cysts [20], benign epithelial cysts [5], ovarian endometrial cysts [21,22], and sebaceous cysts [23]. False-positive findings on <sup>131</sup>I scans can be due to the following reasons [23]: (a) elimination of iodine in body fluids; (b) inflammation or infection; (c) transudates or cysts; and (d) nonthyroid neoplasms. However, the exact mechanism of <sup>131</sup>I accumulation in a cyst remains unclear. One possible explanation is the exchange of chemical materials through passive or active transport between the cyst and its surrounding tissue [23]. Chronic inflammation may be another possible explanation [9,23].

Concentration of radioiodine in the lower abdomen commonly manifests as physiological uptake in the intestines and bladder. It is easy to identify funicular or discrete dotted uptake in the intestine and nonincreased radioactivity in the empty bladder. False-positive <sup>131</sup>I scans due to various bacterial [24] and fungal [25] infections or inflammatory lesions have been reported previously. In our study, the dotted uptake seen in the sigmoid colon of one of the patients might have been associated with infection or inflammation. We suggested enteroscopic examination, but the patient refused. Dotted uptake in the sigmoid colon was difficult to

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Single-photon emission computed tomography (SPECT) whole-body imaging: (a) black arrow shows the upper pelvis superior to the urinary bladder. Subsequent SPECT/computed tomography (CT) images show that the abnormal activity (white arrow) is located in the cervix of the uterus [(b) axial CT; (c) axial fusion; (d) sagittal fusion; (e) coronal fusion]. L, left; R, right.





Transvaginal ultrasonography, performed to further aid diagnosis, revealed several echo-free regions in the cervix, with diameters between 4.7 and 12 mm. This image shows one of the echo-free regions (white arrow) detected on ultrasound examination (diameter, 5 mm).

distinguish from a cervical nabothian cyst, as both revealed increased radioactivity in the upper pelvis superior to the urinary bladder. There is another report of a uterine leiomyoma with <sup>131</sup>I avidity [26], which also occurred in the lower abdomen. However, <sup>131</sup>I-SPECT/CT is superior to <sup>131</sup>I-WBS in terms of diagnosis.

Clinically, distant DTC metastases predominantly involve the lungs, followed by bone. Brain, breast, kidney, muscle, and skin involvement is rare [27]. However, to our knowledge, there are no published reports on cervical and intestinal DTC metastases. Therefore, we regard nabothian cysts as the primary reason for the false-positive, nonspecific accumulation of <sup>131</sup>I in the middle of the lower abdomen.

## Conclusion

<sup>131</sup>I whole-body imaging is useful in the detection of thyroid remnants and metastatic lesions in DTC patients who have undergone thyroidectomy. However, false-positive <sup>131</sup>I accumulation is commonly reported. Because of high false-positive incidence, cervical nabothian cysts should be considered when focal uptake is caused by nonspecific radioiodine accumulation in the middle of the lower abdomen, as seen in <sup>131</sup>I whole-body scans of female patients with DTC. <sup>131</sup>I-SPECT/CT is a promising technique for further clarification of the lesion location.

#### Acknowledgements Conflicts of interest

There are no conflicts of interest.

#### References

- Lee SL. Radioactive iodine therapy. Curr Opin Endocrinol Diabetes Obes 2012; 19:420–428.
- 2 Liu S, Zhan M, Qu Y, Yu Pan, Zhang Y. Increased iodine uptake in the nabothian cyst. *Clin Nucl Med* 2013; 38:157–158.
- 3 Omur O, Ozbek SS, Akgun A, Yazici B, Mutlukoca N, Ozcan Z. False-positive I-131 accumulation in a hepatic hydatid cyst. *Clin Nucl Med* 2007; **32**: 930–932.
- 4 Pacini F. Follow-up of differentiated thyroid cancer. Eur J Nucl Med Mol Imaging 2002; 29:492–496.
- 5 Bural GG, Peel RL, Mountz JM. Benign epithelial cyst mimicking thyroid cancer metastasis: a false-positive finding on post-therapy I-131 scan. *Clin Nucl Med* 2012; **37**:88–90.
- 6 Mitchell G, Pratt BE, Vini L, McCready VR, Harmer CL. False positive I-131 whole-body scans in thyroid cancer. Br J Radiol 2000; 73:627–635.
- 7 McDougall IR. Whole body scintigraphy with radioiodine-131 a comprehensive list of false-positives with some examples. *Clin Nucl Med* 1995; **20**:869–875.
- 8 Bakheet SM, Hmmami MM. False positive radioiodine whole body scan in thyroid cancer patients due to unrelated pathology. *Clin Nucl Med* 1994; 19:325–329.
- 9 Greenler DP, Klein HA. The scope of false-positive iodine-131 images for thyroid carcinoma. *Clin Nucl Med* 1989; 14:111–117.
- 10 Casey PM, Long ME, Marnach ML. Abnormal cervical appearance: What to do, when to worry? *Mayo Clin Proc* 2011; 86:147–151.
- 11 Clement PB, Young RH. Deep nabothian cysts of the uterine cervix. Int J Gynecol Pathol 1989; 8:340–348.

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- 12 Fogel SR, Slasky BS. Sonography of nabothian cysts. *Am J Roentgenol* 1982; **138**:927–930.
- 13 Okuyama C, Ushijima Y, Kikkawa M, Yamagami T, Nakamura T, Kobayashi K, et al. False-positive I-131 accumulation in a liver cyst in a patient with thyroid carcinoma. *Clin Nucl Med* 2001; 26:198–201.
- 14 Gunawardana DH, Pitman AG, Lichtenstein M. Benign hepatic cyst mimicking a functional thyroid carcinoma metastasis on whole body I-131 imaging. *Clin Nucl Med* 2003; 28:527–528.
- 15 Wen C, luanow E, Oates E, Lee SL, Perrone R. Post-therapy iodine-131 localization in unsuspected large renal cyst: possible mechanisms. J Nucl Med 1998; 39:2158-2161.
- 16 Brachman MB, Rothman BJ, Ramanna L, Tanasescu DE, Adelberg H, Waxman AD. False-positive iodine-131 body scan caused by a large renal cyst. *Clin Nucl Med* 1988; 13:416–418.
- 17 Serafini A, Sfakianakis G, Georgiou M, Morris J. Breast cyst simulating metastases on iodine-131 imaging in thyroid carcinoma. *J Nucl Med* 1998; 39:1910–1912.
- 18 Li D, Meng Z, Zhang G, Yu T, Tan J, Dong F. Visualization of thyroglossal duct cyst in differentiated thyroid cancer patient. *Clin Nucl Med* 2010; **35**: 499–504.
- 19 Mulazimoglu M, Koca S, Tamam MO, Uyanik E, Ozpacaci T. False-positive findings in post-treatment iodine-131 whole-body scintigraphy in a nasolacrimal sac cyst, confirmed with SPECT/CT and MRI. *Clin Nucl Med* 2011; **36**:805–807.

- 20 Francese C, Schlumberger M, Travagli JP, Vera P, Caillou B, Parmentier C. lodine 131 uptake in a pleuropericardial cyst: case report of a false-positive radioiodine total body scan result in a patient with a thyroid cancer. *Eur J Nucl Med* 1991; 18:779–780.
- 21 Srivatsa S, Halkar RK. I-131 uptake in an endometriotic ovarian cyst in a patient with papillary thyroid carcinoma. *The Endocrinologist* 2010; 20:228–229.
- 22 Utamakul C, Sritara C, Kositwattanarerk A, Balachandra T, Chotipanich C, Chokesuwattanaskul P. I-131 uptake in bilateral ovarian endometrial cysts. *Clin Nucl Med* 2009; **34**:537–538.
- 23 Bucker-Davis F, Reynolds JC, Skarulis MC, Fraker DL, Alexander HR, Weintraub BD, Robbins J. False-positive iodine-131 whole body scans due to cholecystitis and sebaceous cyst. J Nucl Med 1996; 37:1690–1693.
- 24 Bakheet SM, Hammami MM, Powe J. Radioiodine bronchogram in acute respiratory tract infection. *Clin Nucl Med* 1997; **22**:308–309.
- 25 Echenique R, Kasi L, Haynie TP, Glenn HJ, Samaan NA, Hill CS. Critical evaluation of serum thyroglobulin levels and I-131 scans in post-therapy patients with differentiated thyroid carcinoma: concise communication. *J Nucl Med* 1982; 23:235–240.
- 26 Hirata K, Shiga T, Kubota KC, Okamoto S, Kamibayashi T, Tamaki N. Radioiodine therapy for thyroid cancer depicted uterine leiomyoma. *Clin Nucl Med* 2009; 34:180–181.
- 27 Song HJ, Xue YL, Xu YH, Qiu ZL, Luo QY. Rare metastases of differentiated thyroid carcinoma: pictorial review. *Endocr Relat Cancer* 2011; 18:165–174.