Incidental Findings of Intense Radioiodine Uptake in Struma Ovarii and Bilateral Nonlactating Breasts Simultaneously on Postablation ^{131}I SPECT/CT for Papillary Thyroid Cancer

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Abstract A 52-year-old woman diagnosed with papillary thyroid carcinoma was referred for ^{131}I therapy following total thyroidectomy. She was given 4,810 MBq (130 mCi) of ^{131}I following 4 weeks of thyroid hormone withdrawal. A posttherapy scan showed intense, focal activity in the pelvis and intense, diffuse activity on both sides of the chest, which was localized to the right ovary and both breasts on SPECT/CT examination. She had bilateral nipple pain and a history of antidopaminergic drugs as combination medication for her rheumatoid arthritis and prokinetics during radioiodine therapy. On a ^{123}I whole-body scan 9 months later after stopping the drugs, bilateral breast uptake was not visible; however, right ovarian focal uptake was still visualized. Bilateral salpingo-oophorectomy was performed, and revealed struma ovarii with substantial internal necrosis due to radioiodine therapy. This case is interesting as two rare entities, ^{131}I therapy-related struma ovarii and drug-related breast uptake, were simultaneously visualized.

Keywords Struma ovarii · Bilateral breast uptake · Papillary thyroid cancer · SPECT/CT · Post-radioiodine whole-body scan

Introduction

Radioiodine ablation with a whole-body scan is a well known therapeutic regimen for differentiated thyroid cancer. Abnormal radiotracer accumulation following ^{131}I or ^{123}I administration may suggest the need for further evaluation and therapy. With the advent of single photon emission tomography/computed tomography (SPECT/CT), more precise anatomic localization is possible. Benign uncommon findings have been reported in some patients including ovarian masses and nonlactating breasts. We report here a case with two incidental rare sites of radioiodine uptake in a struma ovarii and nonlactating breasts related to antidopaminergic drugs.

Case Report

A 52-year-old woman diagnosed with papillary thyroid cancer was referred for ^{131}I therapy following total thyroidectomy. Postoperative pathologic examination revealed bilateral papillary carcinoma with capsular invasion and central lymph node metastases (stage pT1bN1aMx). She was given 4,810 MBq (130 mCi) of ^{131}I following 4 weeks of conventional levothyroxine withdrawal. Whole-body imaging on day 7 after radioiodine administration showed focal uptake in the thyroglossal duct remnant (Fig. 1a). There was also very intense focal uptake with the star artifact in the right pelvic cavity and on both sides of the chest (Fig. 1a). Subsequent SPECT/CT confirmed lesions in the right ovary and bilateral breasts (Fig. 1b, c).

On the day of admission for radioiodine therapy, the patient's serum stimulated thyroglobulin was 0.84 ng/mL (normal range 2.0–70 ng/mL), antithyroglobulin was 28.40 U/mL (normal range <60 U/mL), and thyroid stimulating hormone

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Fig. 1 **a** Whole-body imaging on day 7 after radioiodine administration shows focal uptake in the thyroglossal duct remnant. There is also intense focal uptake with the star artifact in the right pelvic cavity and on both sides of the chest. **b, c** Subsequent SPECT/CT images show lesions in the right ovary and bilateral breasts

was 62.26 $\mu\text{IU/mL}$ (normal range 0.3–5.0 $\mu\text{IU/mL}$). Because her stimulated thyroglobulin was low, metastases were not expected. On ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) performed to rule out metastasis from thyroid cancer, no hypermetabolic lesion was seen in the right ovary, and there was mild diffuse FDG uptake in both breasts (Fig. 2a, b). On the CT scan of PET/CT without contrast enhancement, the ovary was seen as a solid and cystic mass with high attenuation (85 HU) in the solid portion (Fig. 2c). The ovary and the mammary glands were examined by ultrasonography. The transvaginal scan revealed a cystic and solid mass in the right ovary of about 4.8 cm in size (Fig. 2d), and the breast scan revealed no abnormal findings.

The patient had a history of bilateral nipple pain and engorgement when the imaging was performed. The possibility of pregnancy had already been ruled out by transvaginal ultrasonography. With regard to her drug history, she had been taking levosulpiride (Levopride) 25 mg twice daily for 3 years. From her day of admission for radioiodine therapy, domperidone (Motilium) was also prescribed for 1 week to relieve her dyspepsia. When she stopped the two drugs, her nipple pain and engorgement subsided and her menstruation started again following 1 year of amenorrhea.

A ^{123}I whole-body scan and stimulated thyroglobulin testing were performed 9 months after radioiodine ablation; there was no residual uptake in the neck or breasts (Fig. 3a). The stimulated thyroglobulin level was below 0.15 ng/mL (normal range 2.0–70 ng/mL), but ovary uptake was still visualized

(Fig. 3b). We were not able to compare the activities on of both ^{131}I and ^{123}I whole-body scans, as ^{131}I usually shows higher intensity than ^{123}I . The gynecologic surgeon performed bilateral salpingo-oophorectomy. The pelvic mass was a struma ovarii with mostly internal necrosis and showed atrophied follicles along the lining of the cystic wall (Fig. 4).

Discussion

There have been several reports regarding benign struma ovarii. One of these reports concerned a benign functioning struma ovarii with hyperthyroidism, provisionally diagnosed by clinical and radiologic findings and confirmed on total hysterectomy and bilateral salpingo-oophorectomy [1]. There are two reports of nonfunctioning struma ovaries diagnosed incidentally after iodine therapy for which oophorectomy was performed immediately [2, 3]. A very rare case was reported of cystic ovarian metastasis from papillary thyroid cancer that was diagnosed on a post-therapy whole-body scan with increasing thyroglobulin, and also confirmed on pelvic surgery [4]. In contrast to the above cases with immediate surgery after a presumptive diagnosis, one patient was diagnosed with possible benign struma ovarii on postablation scan and ovarian surgery was postponed for 6 months [5].

In our case, the diagnosis was confirmed on a follow-up ^{123}I whole-body scan after initial clinical diagnosis, and surgery was performed 1 year later. As the ovary showed intense iodine accumulation on the ^{123}I whole-body scan, we

Fig. 2 **a, b** ^{18}F -FDG PET/CT images show no hypermetabolic lesion in the right ovary and mild diffuse FDG uptake in both breasts. **c** The CT image of PET/CT without contrast enhancement shows the ovary as a solid and cystic mass with high attenuation (85 HU) in the solid portion. **d** The transvaginal sonographic image shows a cystic and solid mass in the right ovary of about 4.8 cm in size

suspected that there would be a large amount of residual thyroid tissue. However, the gross specimen showed scarce residual gross thyroid tissue inside the ovarian cystic wall, and microscopically atrophied follicles were only visualized along the lining of the wall. The pathologist informally reported this

lesion as similar to a simple cyst, so a correct diagnosis would have been difficult without clinical information. The follicles of pathologic slides seemed more atrophied compared with those from the patient in whom radioiodine therapy was performed 6 months after pelvic surgery. However, there was no

Fig. 3 Follow-up imaging. **a, b** The ^{123}I whole-body scan shows no residual uptake in the neck or breasts. However, the planar and SPECT/CT images still show ovary uptake

Fig 4 **a** On gross examination, the resected ovary shows a multilocular hemorrhagic cyst with no solid area. **b** The ovarian cyst is lined with a simple columnar to cuboidal epithelium with no solid area (H&E, original magnification $\times 40$). **c** The ovarian stroma close to the cyst shows atrophic follicles with small hyperchromatic nuclei containing colloid-like material (H&E, original magnification $\times 200$). **d** On immunohistochemical staining, these follicles show immunoreactivity for thyroglobulin scattered around the cystic wall (thyroglobulin, original magnification $\times 400$)

direct explanation for the tissue changes after iodine treatment [5]. These histopathologic findings confirmed the gross and microscopic changes after radioiodine accumulation in the struma ovarii. Because most of the internal thyroid tissue had disappeared in response to treatment, and although most of the thyroid follicles were of abnormal size or shape, we were not able to demonstrate abnormal nuclei representing malignant transformation which are very rare.

In six previous case reports searched, breast uptake of radioiodine was caused by hyperprolactinemia in all the patients [6–10]. In two of these case reports, each of one patient, the hyperprolactinemia was caused by a pituitary tumor [6, 7], and in one case report of two patients, the hyperprolactinemia was a result of risperidone and cabergoline treatment, respectively [8]. In one case report, also of two patients, the hyperprolactinemia was a result of risperidone treatment and chronic renal failure [9]. Lastly, in one case report, the reason for the hyperprolactinemia was not stated [10]. Hammami and Bakheet discussed the relationship between hyperprolactinemia and breast uptake of radioiodine, and consider that there are four probable causes of hyperprolactinemia: various drugs, breast stimulation, hypothyroidism and prolactinoma [11].

In our patient, the possible cause of breast uptake of radioiodine was drugs or prolactinoma, because breast stimulation and hypothyroidism were excluded by her history and by laboratory findings. Prolactinoma was ruled out by ^{18}F -FDG PET/CT, and the fact that symptoms including breast engorgement and nipple pain disappeared after cessation of the drugs also opposed prolactinoma as the cause of

hyperprolactinemia. This accumulation was therefore probably due to long-standing levosulpiride ingestion for her rheumatoid arthritis and temporary domperidone ingestion for 1 week to suppress dyspepsia during radioiodine therapy. Unfortunately, plasma prolactin was not measured. In a large, multicenter, double-blind, placebo-controlled trial investigating the drug treatment of dyspepsia, 408 patients were treated with oral levosulpiride 25 mg three times daily for 1 month, and 7 % of the female patients receiving levosulpiride had hyperprolactinemia and related symptoms [12]. However, symptoms such as galactorrhea and breast pain have been found to be decreased with the chronic use of levosulpiride [13, 14]. We therefore suspect that domperidone with concomitant levosulpiride on admission for radioiodine therapy may have promoted the breast-related symptoms. In fact, domperidone leads to the elevation of prolactin levels in most patients within 3 days to 2 weeks after initiation of the drug [13]. On discontinuation, galactorrhea ceases within 7 days [13]. As this patient had been taking levosulpiride for 3 years, concomitant use of domperidone could have been the cause of the breast-related symptoms.

We report here a very rare case with two rare findings incidentally demonstrated by ^{131}I whole-body scan. Several cases of benign struma ovarii have been reported, but the pathologic examination in this patient was quite unique due to the effect of radioiodine therapy 1 year before surgery. Nonlactating breasts also rarely accumulate radioiodine, so we need to take a careful history and use other diagnostic tools for further evaluation.

Compliance with Ethical Standards

Conflict of Interest H.-k. Shim, M.R. Kim declare no conflicts of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent The institutional review board of our institution approved this case study, and the requirement to obtain informed consent was waived.

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