Nucl Med Mol Imaging (2015) 49:52–56
DOI 10.1007/s13139-014-0295-z

CASE REPORT

Usefulness of ^{131}I-SPECT/CT and ^{18}F-FDG PET/CT in Evaluating Successful ^{131}I and Retinoic Acid Combined Therapy in a Patient with Metastatic Struma Ovarii

Hyo Jung Seo · Young Hoon Ryu · Inki Lee · Hye Sook Min · Keon Wook Kang · Dong Soo Lee · Dae-hee Lee · June-Key Chung

Received: 1 May 2014 / Revised: 22 August 2014 / Accepted: 24 August 2014 / Published online: 25 September 2014

Abstract Metastatic struma ovarii is an extremely rare disease, and the treatment of choice has not been established. Here, we introduce the case of a 36-year-old female pregnant patient with metastatic struma ovarii. Initial treatment was an exploratory laparotomy to remove multiple peritoneal masses. After delivery, a total thyroidectomy was done for the further ^{131}I-therapy. ^{131}I-SPECT/CT and ^{18}F-FDG PET/CT showed multiple hepatic metastases and extensive peritoneal seeding nodules. Multiple ^{131}I and retinoic acid combination therapies were performed, resulting in marked improvement. ^{131}I-SPECT/CT and ^{18}F-FDG PET/CT were quite useful for evaluating the biologic characteristics of the metastases.

H. J. Seo · D. S. Lee
Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology, Seoul, Korea

H. J. Seo · I. Lee · K. W. Kang · D. S. Lee · J.-K. Chung (✉)
Department of Nuclear Medicine, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehangno, Jongro-gu, Seoul 110-744, Korea
e-mail: jkchung@snu.ac.kr

H. J. Seo
Department of Nuclear Medicine, Anyang SAM Hospital, Gyeonggi-do, Korea

Y. H. Ryu
Department of Nuclear Medicine, Yonsei University College of Medicine, Seoul, Korea

H. S. Min
Department of Pathology, Seoul National University Hospital, Seoul, Korea

D.-h. Lee
Departiment of Oncology, GSAM Hosptial, Gyeonggi-do, Korea

Introduction

Struma means goiter, and struma ovarii is defined as an ovarian tumor with thyroid tissue comprising more than 50 % of the overall mass [1, 2]. Most commonly, it is a part of a teratoma; among them, malignant transformation occurs rarely. In fact, struma ovarii accounts for only 2 % of all teratomas, and malignant struma ovarii has been reported in less than 5–37 % of all cases of struma ovarii [3]. Until now, the the characteristics of malignant struma ovarii have not been evaluated well because of its rarity.

Post-surgical ^{131}I and retinoic acid combination therapy has been recommended for differentiated thyroid cancer including metastases and refractory-papillary thyroid cancer [4–6]. ^{131}I-SPECT/CT can easily be used to localize ^{131}I-avid metastases and evaluate the therapy response to radioiodine [7, 8]. Meanwhile, whole-body ^{18}F-FDG PET/CT has been widely implemented in various cancers using the increased glucose metabolism. However, the metabolic characteristics of malignant struma ovarii have not been evaluated.

Here, we report a patient with malignant struma ovarii in whom ^{131}I and retinoic acid combination therapy using ^{131}I-SPECT/CT and ^{18}F-FDG PET/CT was implemented. These modalities and therapy were very effective for the treatment and follow-up.

Case Report

A 36-year-old pregnant woman complained of multiple pelvic masses. She was admitted to the outside hospital and had an exploratory laparotomy to remove multiple peritoneal masses. She had been previously healthy and had no significant illness. There was no history of smoking or alcohol consumption. After delivery, a total thyroidectomy was

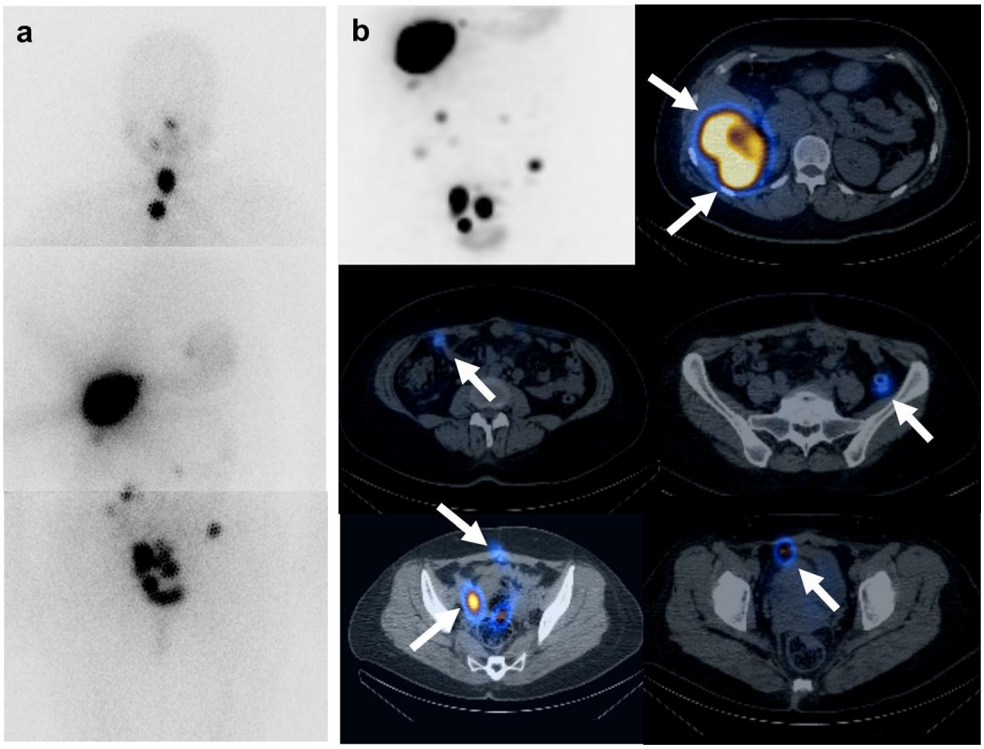

Fig. 1 The first post-therapy ^{131}I whole-body scan and ^{131}I-SPECT/CT. **a** Post-therapy ^{131}I whole-body images (30 mCi) show remnant thyroid glands. Intense iodine-avid lesions in the right lobe of the liver and multiple peritoneal seedings are well visualized. **b** Post-therapy ^{131}I-SPECT/CT of the abdominopelvic cavity was obtained. The maximized intensity projection image is located in the left upper row. More prominent uptake in the multiple hepatic and peritoneal seedings is shown because of the longer acquisition time and three-dimensional modality. On the fusion axial image of ^{131}I-SPECT/CT, hepatic metastases show iodine-avid uptake. Second and third row images show multiple peritoneal seedings with avid iodine uptake regardless of the small size (*white arrow*)

done for the further ^{131}I-therapy in the outside hospital, and there was no thyroid cancer. The patient underwent five radioiodine therapies. After the first ^{131}I ablation therapy (30 mCi), ^{131}I-SPECT/CT showed increased radioiodine uptake in huge hepatic metastases and multiple peritoneal seeding lesions (Fig. 1). The serum Tg level after TSH stimulation was 28,890 ng/ml. ^{18}F-FDG PET/CT was performed 1 month later, which showed huge hepatic metastases with increased FDG uptake and several FDG-avid peritoneal seeding lesions (Fig. 2). The distribution of FDG uptake was different from that of radioiodine uptake.

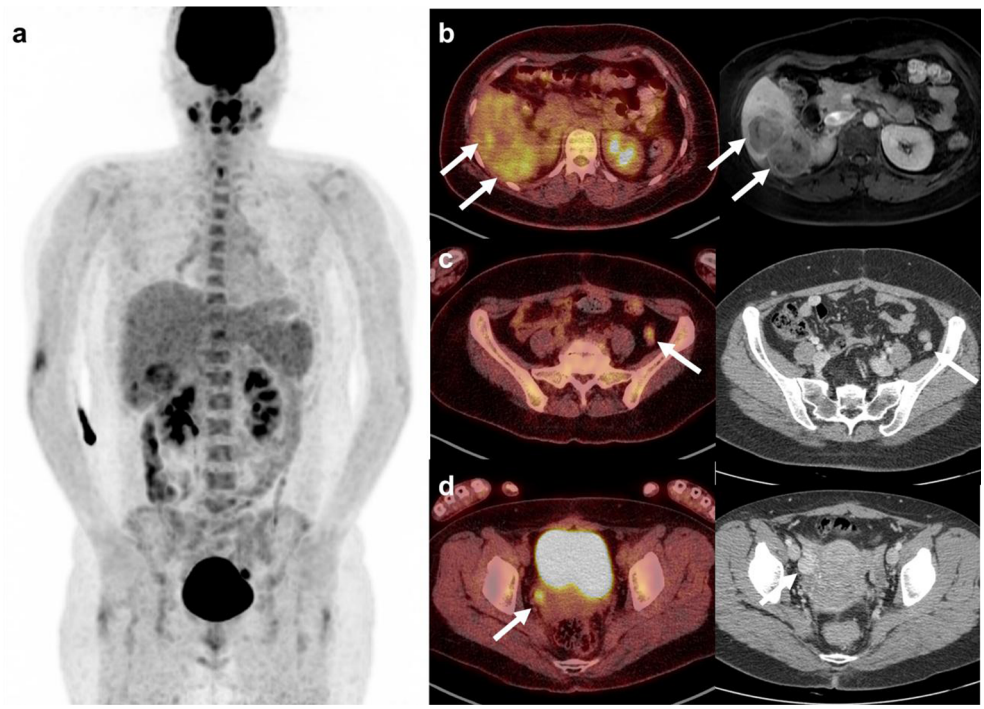

Fig. 2 ^{18}F-FDG PET/CT after the first ^{131}I therapy. **a** Maximized intensity projection image shows hepatic metastasis in the right lobe of the liver and several seeding nodules with variable FDG uptake. **b** Fusion axial image shows a different glucose metabolism. The S5 lesion shows mild FDG uptake, but the S6 lesion shows intense FDG uptake. Multiple heptatic metastases were well correlated with MRI. **c** A small peritoneal seeding in the left iliac fossa shows increased uptake on the fusion PET/CT image and good enhancement on contrast-enhanced CT. **d** Intense uptake in the peritoneal seeding in the right pelvic side wall is visualized on the fusion PET/CT image. A round lesion with good enhancement is noted on contrast-enhanced CT

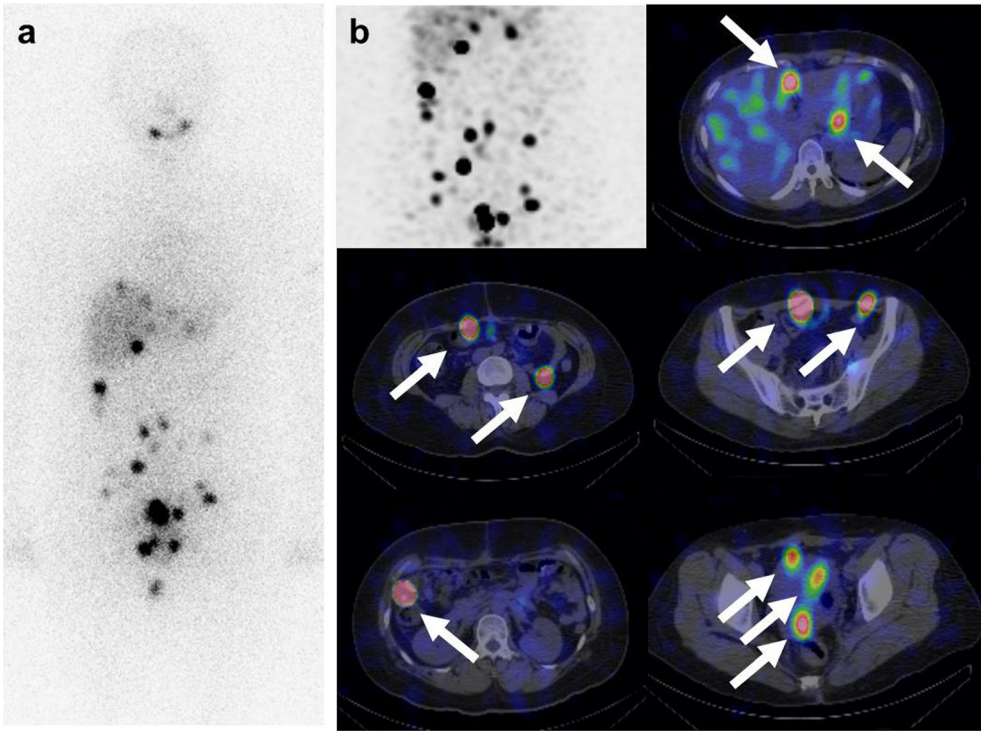

Fig. 3 The second post-therapy ^{131}I whole-body scan and ^{131}I-SPECT/CT combined with retinoic acid. **a** After the removal of hepatic metastases, post- ^{131}I therapy a whole-body scan (200 mCi) was performed. More prominent uptake in the multiple peritoneal seedings is visualized in the perihepatic and abdominopelvic cavity. **b** ^{131}I-SPECT/CT shows intense iodine uptake in the multiple peritoneal seeding nodules. A maximized intensity projection image of the abdominopelvic cavity is demonstrated in the left upper row. Fusion axial images of ^{131}I-SPECT/CT reveal the location of peritoneal seedings in the perihepatic area, perigastric area, right and lower quadrant pelvic cavity, rectovaginal pouch, etc.

To improve the therapeutic effect of radioiodine, we combined it with retinoic acid. Before the second ^{131}I therapy (200 mCi), the huge hepatic metastases in the right lobe of the liver were removed. The sizes of the masses were 6.3 × 5.3 × 5.0 cm and 6.0 × 4.7 × 4.0 cm. The masses were pathologically proven to be metastatic follicular carcinoma with poor differentiation. On the post-therapy ^{131}I-SPECT/CT, innumerable peritoneal seedings with avid iodine uptake were visualized in the perihepatic and subhepatic areas and pelvic cavity (Fig. 3). The serum Tg level after TSH stimulation was 165.3 ng/ml. However, PET/CT performed 2 weeks later showed only minimal uptake in several peritoneal seeding nodules. Therefore, the ^{131}I whole-body scan and ^{131}I-SPECT/CT were useful to evaluate the remnant peritoneal seedings.

A third ^{131}I therapy combined with retinoic acid (200 mCi) was performed. The radioiodine whole-body scan shows a further decrease in the number and uptake amount of seeding nodules. The serum Tg level declined to 68.6 ng/ml after TSH stimulation. A fourth ^{131}I therapy (200 mCi) was performed.

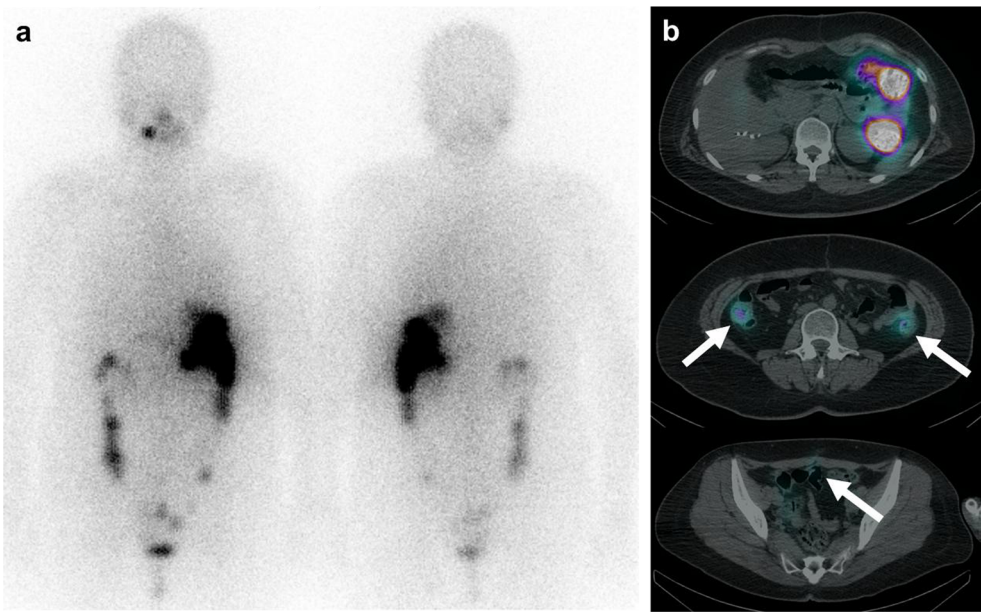

Fig. 4 The fifth post-therapy ^{131}I whole-body scan and ^{131}I-SPECT/CT. **a** Post-therapy ^{131}I whole-body scan (200 mCi) reveals physiologic stomach and bowel uptake. Suspicious uptake is visualized in the pelvic cavity. **b** Fusion axial images of ^{131}I-SPECT/CT show matched physiologic bowel uptake in the upper row and faint uptake in the previous seeding lesions in the pelvic cavity in the middle and lower row (*white arrow*). There was no significant lesion with avid iodine uptake. The patient showed a markedly improved state

Table 1 Levels of TSH, stimulated Tg, non-stimulated Tg and TgAb according to the ^{131}I therapies and follow-up

Date	TSH	Tg	Tg-Ab	^{131}I therapy	Dose	Retinoic acid
9 April 2014	<0.05	2.83	51			
17 January 2014	<0.05	2.75	40			
23 September 2013	<0.05	3.75	36			
22 June 2013	72.43	42.3	<20	5th	7.4GBq	Yes
20 May 2013	<0.05	5.2	23			
16 February 2013	35.65	39.17	40	4th	7.4GBq	Yes
28 December 2012	0.06	0.16	<20			
25 October 2012	39.62	68.55	<20	3rd	7.4GBq	Yes
27 June 2012	76.64	165.3	<20	2nd	7.4GBq	Yes
9 May 2012	0.43	12.13	<20			
15 February 2012	0.38	7,410	-			
18 January 2012	87.05	28,890	30	1st	1.11GBq	No
15 November 2011	–	1,717	<25			
29 September 2011	0.8	1437	116			
18 May 2011	1.53	816.9	26			
22 March 2011	1.29	936.7	29			
24 March 2010	0.36	352	<25			

Faint uptake in a few peritoneal seeding lesions is visualized on the ^{131}I-SPECT/CT. A further decrease in the stimulated Tg is observed (39.2 ng/ml). A fifth post-therapy ^{131}I-SPECT/CT showed no significant uptake in the abdominopelvic cavity. The serum Tg level did not change significantly (42.3 ng/ml). There was only physiologic bowel uptake (Fig. 4). During the 4-year follow-up, the patient had five ^{131}I therapies, four times with retinoid acid. The size and metabolic intensity of the metastatic lesions had decreased. Right now, the serum Tg level without TSH stimulation is 2.83 ng/ml. The serum Tg level according to ^{131}I therapy is summarized in Table 1.

Discussion

Malignant struma ovarii is a very rare disease [9–12]. The clinical course of extraovarian spread and the gold standard therapy have not been fully established. Here we report the disease characteristics using ^{131}I-SPECT/CT and ^{18}F-FDG PET/CT and the successful clinical outcome of a patient with malignant struma ovarii after ^{131}I therapy and the use of retinoic acid.

The typical treatments of malignant struma ovarii are radioiodine therapy following surgical resection. The surgery for malignant struma ovarii varies from unilateral oophorectomy to total abdominal hysterectomy and bilateral salpingo-oophorectomy with omentectomy. Malignant struma ovarii has similar morphological features as well-differentiated thyroid carcinoma. Therefore, the therapy and follow-up should be based on well-differentiated thyroid cancer. Radioiodine therapy is a well-known treatment for well-differentiated thyroid cancer; it reduces the recurrence and mortality rate at 20 years after ^{131}I therapy compared to the untreated group [13], and it is the treatment of choice for malignant struma ovarii [2]. One important point is that total thyroidectomy should be performed before radioiodine treatment [1, 14] because of high avidity of radioiodine to normal thyroid compared to metastatic lesions.

In this study, the patient had multiple large hepatic metastases and peritoneal seedings. The metastatic lesions showed high radioiodine uptake and variable FDG uptake. This might represent the metabolic heterogeneity of metastases from thyroid cancer. ^{131}I therapy combined with retinoic acid showed good treatment response in this patient. Previously, we reported that a high response rate of this combination therapy is expected in young patients. Therefore, the successful treatment with ^{131}I therapy could be combined with the benefits of retinoic acid in this case. After the removal of hepatic metastases, the ^{131}I whole-body scan and ^{131}I-SPECT/CT images showed higher iodine-avid uptake in the multiple peritoneal seedings. This might be because of the redistribution of radioiodine and also the redifferentiation from the retinoic acid treatment. This patient experienced no significant side effects from the retinoic acid and had a good clinical course. Compared to previous reports [1, 15], this patient demonstrated extensive metastatic lesions. This patient improved markedly after ^{131}I and retinoic acid combination therapy.

^{131}I-SPECT/CT and ^{18}F-FDG PET/CT were helpful for evaluating and comparing the characteristics of malignant struma ovarii. Metastases with high FDG uptake were

removed by surgery, and metastases with high iodine uptake improved markedly with repeated ^{131}I combined with retinoic acid therapy. Therefore, we recommend using dual modalities for the treatment of malignant struma ovarii.

Conflict of Interest Hyo Jung Seo, Young Hoon Ryu, Inki Lee, Hye Sook Min, Keon Wook Kang, Dong Soo Lee, Dae-hee Lee and June-Key Chung declare that they have no conflict of interest.

Ethical Standard The patient gave informed consent prior to inclusion in the study.

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