Disease management of malignant struma ovarii

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Keywords: Malignant struma ovarii - ^{131}I thyroglobulin

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Received:
6 May 2024
Accepted revised:
15 September 2024

Abstract
Ovarian goiter that meets the diagnostic criteria for malignant thyroid tumors or has invasive distant metastasis is called malignant struma ovarii (MSO). The incidence of MSO is very low. The level of serum thyroglobulin (Tg) is helpful to differentiate MSO with highly differentiated pathological type from other ovarian malignancies. But its therapeutic method is currently debated. Herein, we present a case of 54 years old woman, who was admitted to hospital due to frequent abdominal pain for 9 months and with normal serum Tg. Postoperative pathological examination revealed highly differentiated follicular thyroid carcinoma of bilateral ovarian origin, which penetrated bilateral ovarian cortex, involved the serosal surface of left fallopian tube and disseminated to sigmoid mesentery, small intestinal mesentery and pelvic cavity. The disseminated lesions were considered to originate from right ovary. After the total thyroidectomy, iodine-131 (^{131}I) treatment was performed with a dose of 150mCi. The ^{131}I whole-body scintigraphy (WBS) 2 days after treatment showed residual thyroid tissue in the neck and implantation metastasis in mesentery. After 1-year regular follow-up, no significant abnormalities were found in tumor indicators, Tg, thyroid function, neck ultrasound and abdominopelvic enhanced computed tomography (CT). This MSO case with normal Tg and multiple implantation metastasis aimed to discuss its clinical management especially for Tg and ^{131}I and to improve its prognosis.

Hell J Nucl Med 2024; 27(3): 247-250 *Epub ahead of print: 14 December 2024* *Published online: 30 December 2024*

Introduction

Ovarian goiter is a highly differentiated monogerm tumor originating from ovarian germ cells and belongs to a special type of teratoma, most of which are benign tumors. Ovarian goiter that meets the diagnostic criteria for malignant thyroid tumors or has invasive distant metastasis is called malignant struma ovarii (MSO), accounting for about 5% of all ovarian goiter cases [1, 2]. Malignant struma ovarii tends to occur in women aged 40 to 60 years [2] and often involves a single ovary. Patients often seek medical attention as pelvic masses, abdominal pain or menstrual disorders. The level of serum thyroglobulin (Tg) and thyroid hormone often has certain value for preoperative diagnosis of MSO. In clinic, MSO's therapeutic method is currently debated [2, 3], which routinely includes surgery and postoperative adjuvant treatment, such as iodine-131 (^{131}I) therapy, thyroid hormone suppression therapy and chemotherapy. We present a case of MSO with normal Tg and multiple implantation metastasis followed by discussion on its management.

Case presentation

A 54 years old woman was admitted to the department of gynaecology due to frequent abdominal pain for 9 months, with normal level of tumor indicators, Tg, anti-thyroglobulin antibodies (TgAb) and thyroid hormone. The tumor indicators include alpha fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), CA19-9, CA15-3. Doppler ultrasonography (DU), computed tomography (CT) and magnetic resonance imaging (MRI) of the abdominopelvic cavity revealed bilateral adnexal masses, the left mass was about 7.4cm×3.6cm×3.9cm and the right one was about 3.5cm×4.7cm×4.2cm. The patient underwent surgical treatment of laparoscopic total hysterectomy, bilateral salpingo-oophorectomy and pelvic mass removal. Postoperative pathological examination revealed highly differentiated follicular thyroid carcinoma of bilate-

ral ovarian origin, which penetrated bilateral ovarian cortex, involved the serosal surface of left fallopian tube and disseminated to sigmoid mesentery, small intestinal mesentery and pelvic cavity. The disseminated lesions were considered to originate from right ovary. The result of immunohistochemically showed thyroid transcription factor 1 (TTF-1) (+), paired-box gene 8 (PAX-8) (+), cytokeratin 19 (CK19) (-), Ki-67 (1%), tumor suppressor TP53 (P53) (wild type), GATA binding protein 3 (GATA3) (-) and minichromosome maintenances 2 (MCM2) (+,<5%).

Subsequently, the patient underwent a total thyroidectomy. The postoperative pathological examination revealed: 1) bilateral benign nodular goiter, 2) focal fibrous nodule in left thyroid lobe, 3) adenomatous nodules in right thyroid lobe and isthmus. After discontinuation of levothyroxine for three and a half weeks, the level of thyroid stimulating hormone (TSH), Tg and anti-thyroglobulin antibodies (TgAb) respectively was 64.56mIU/L, 14.38ng/mL and 0.72IU/mL. The level of tumor indicators was normal. Then, ^{131}I treatment was performed with a dose of 150mCi. The ^{131}I whole-body scintigraphy (WBS) 2 days after treatment showed: 1) there was small amounts of residual thyroid tissue in the neck (Figure 1, 2) multiple small nodules could be seen in mesentery in CT and had abnormal ^{131}I concentration in ^{131}I imaging, which were considered as implantation metastasis (Figure 2). After one-year regular follow-up, TgAb was less than 1IU/mL and TSH was less than 0.1 mIU/L, Tg gradually decreased to 0.00ng/mL. No significant abnormalities were found in tumor indicators, thyroid hormone, neck ultrasound and abdominopelvic enhanced CT.

Discussion

In clinic, the most common pathological type of MSO is papillarycarcinoma, followed by follicularcarcinoma [4]. Just like most differentiated thyroid cancers, MSO had a similar metastasis pathway, such as papillary carcinoma tended to lymph node metastasis, while follicular carcinoma was more prone to hematogenous metastasis to bones, brain and lungs and so on. Malignant struma ovarii metastasis occurred in 5%~23% of all cases [4]. The clinical manifestation of MSO was lack of specificity [1], which needed differential diagnosis from thyroid cancer with ovarian metastasis, benign ovarian goiter and ovarian carcinoid tumor.

The risk stratification of MSO was similar to that of differentiated thyroid cancer, which might be helpful for developing appropriate postoperative treatment planning [4]. The effectiveness of ^{131}I therapy for MSO has been reported [5-7]. Lager et al. (2018) [8] suggested MSO patients should undergo ovarian surgery, thyroidectomy and followed by ^{131}I

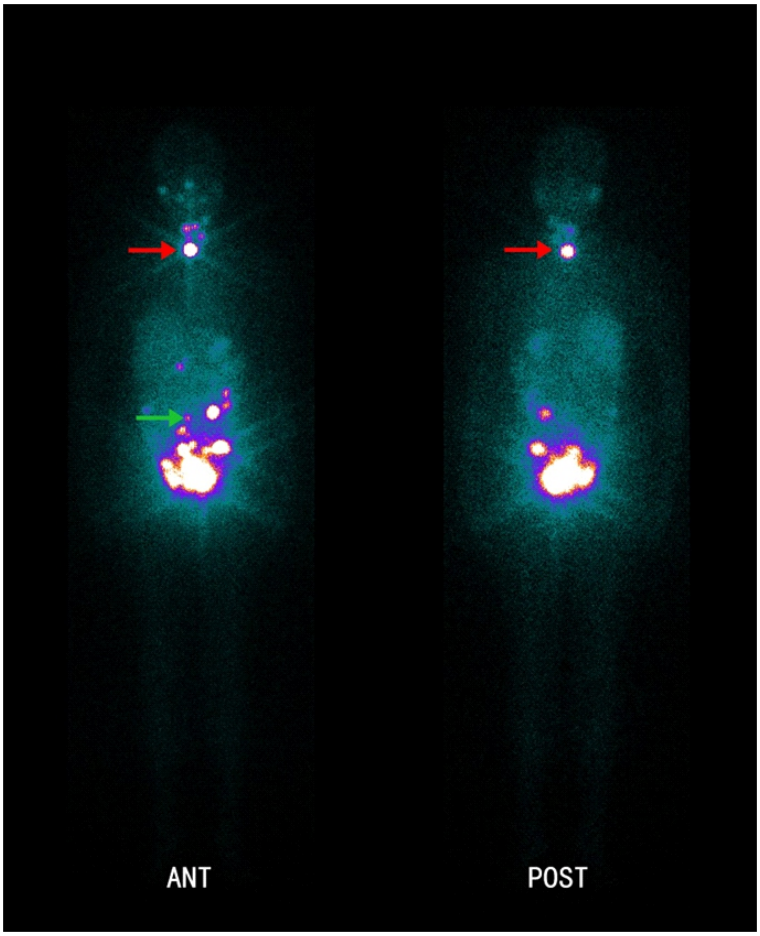

Figure 1. Iodine-131 WBS (ANT and POST). There was residual thyroid tissue in the neck (red arrow) and (ANT) multiply abnormal foci with ^{131}I concentration in abdominopelvic cavity (green arrow).

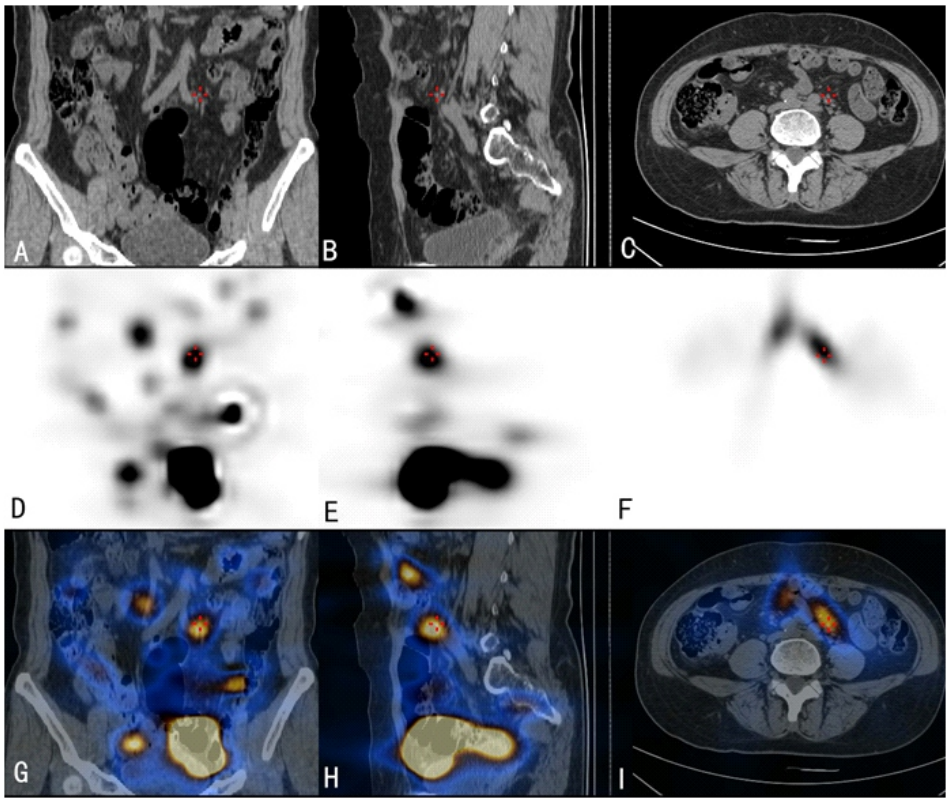

Figure 2. Tomographic images of ^{131}I WBS. The red cross arrows label the implantation metastasis in mesentery, seen as a small nodule in mesentery in CT (A, B and C), abnormal ^{131}I concentration in single photon emission computed tomography (SPECT) images (D, E and F) and corresponding SPECT/CT fusion images (G, H and I).

therapy. Without ^{131}I therapy, it was difficult to evaluate distant metastasis in patients with MSO. The case report of Elshafie et al. (2022) [9] also showed another important role of ^{131}I therapy in disease management, that ovarian surgery and thyroidectomy along with ^{131}I ablation could decrease the chance of recurrence in MSO patients. Based on two postoperative pathologies and immunohistochemistry, this case was confirmed as MSO. Due to dissemination in pelvic cavity, the patient received ^{131}I treatment after thyroid surgery. As we all know, physiological uptake of ^{131}I in abdominopelvic cavity might occur in routine ^{131}I WBS [10], especially in-testinal tract always could be seen. Some pathological uptake also could be seen [10], such as uterine leiomyoma, ovarian teratoma, benign ovarian goiter, serous and mucinous ovarian tumors and so on. The ^{131}I WBS of this patient showed multiple lesions with high ^{131}I concentration in the abdominopelvic cavity, which were generally smaller than 1cm. Combined with postoperative pathologies, the lesions were consistent with implantation metastasis. At 1-year follow-up, the examination showed that the level of Tg decreased rapidly, and no abnormality was found in enhanced CT of abdominopelvic cavity, which further confirmed the efficacy of ^{131}I treatment. Therefore, ^{131}I treatment could fully play a diagnostic role in the routine treatment of MSO after surgery, which might be very important to change the prognosis and long-term follow-up of MSO patients [11].

Thyroglobulin was helpful to differentiate MSO with differentiated pathological type from other ovarian malignancies [9]. Excluding the influence of TgAb, Tg could accurately reflect the tumor burden of MSO patients [11]. During postoperative follow-up, Tg similar with ^{131}I WBS could be used as specific examination for detecting the recurrence and metastasis [12]. But the value of Tg in differentiating benign struma ovarii vs MSO needed further exploration [13, 14]. In addition, the lower level of serum Tg in clinical practice for patients with thyroid cancer was often seen with tumors that might change to be dedifferentiated [14], which might had not the uptake of ^{131}I. The postoperative pathological funding of this patient was highly differentiated follicular carcinoma originating from the ovary, the concentration of ^{131}I in mesentery foci were similar with that of residual thyroid tissue, which meant the implantation foci remained differentiated. At the same time, there was no significant increase in inhibitory Tg levels. Therefore, for this patient Tg might have stronger clinical specificity and be crucial for the prognosis evaluation and long-term follow-up. In clinic, the tumor indicator of CA-125 was a common tumor marker for the surveillance of ovarian cancer and also could be used for the diagnosis of MSO [12]. The level of CA-125 could be higher in other malignancies and benign, pregnancy, endometriosis and menstruation. Due to its low-specificity, the diagnostic value of CA-125 for MSO was limited [15]. Other markers such as PAX8, TTF1 and CK19 and so on also could be used for the auxiliary diagnosis of MSO [13], just like the result of this patient's immunohistochemically. For this case, the CA-125 was normal before surgeries, ^{131}I therapy and during the

follow-up periods and no significant abnormal lesions were found in the follow-up CT. Therefore, in clinic for MSO, serum Tg and low-dose ^{131}I WBS might be more valuable for evaluating the activity of lesions and follow-up. In addition, other examinations such as CT, DU and positron emission tomography/computed tomography (PET/CT) also had high value in the long-term follow-up.

The incidence of MSO is very low [16,17]. To a certain extent, the foci retained the functions of thyroid follicular epithelial cells, such as iodine uptake and secretion of Tg. The overall prognosis was well after comprehensive treatment. The diagnosis and staging of MSO needed to combine with pathological, immunohistochemical, clinical and imaging data. Personalized treatment [3] and follow-up plans needed to be developed based on the specific situation of the patient.

Funding

This study was funded by Health, Science and Technology Project Plan of Hangzhou (no. A20230867).

The authors declare that they have no conflicts of interest

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