

Metastatic follicular struma ovarii complicating pregnancy: a case report and review of the literature

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A 35-year-old woman was determined to have an ovarian cyst and underwent a right ovarian cystectomy at 10 weeks of gestation. A histopathological examination revealed follicular carcinoma arising in a teratoma. No evidence of metastasis was found after delivery. She underwent a total thyroidectomy, followed by radioactive iodine (RAI) therapy. However, her serum thyroglobulin level increased to 1,437 ng/ml (normal range: 0-52 ng/ml) after 10 months. Radioiodine scintigraphy and abdominal computed tomography revealed liver metastasis and peritoneal seeding. She underwent debulking surgery of the liver, right salpinx, and peritoneal seeding nodules. A pathological examination showed metastatic follicular carcinoma with focal poorly differentiated features. Adjuvant RAI therapy was restarted, and her serum thyroglobulin levels returned to normal. In conclusion, metastatic lesions were successfully treated with a combination of debulking surgery and RAI therapy. Close medical follow-up monitoring serum thyroglobulin levels is mandatory in such patients. (*Korean J Hepatobiliary Pancreat Surg* 2012;16:123-127)

Key Words: Struma ovarii; Metastatic follicular carcinoma; Liver metastasis; Radioactive iodine therapy

INTRODUCTION

Struma ovarii is a rare monodermal ovarian teratoma composed predominantly of thyroid tissue.¹ Approximately 15% of all ovarian teratomas have a small non-significant focus of thyroid tissue. Metastases of malignant struma ovarii occur in <5% of cases,^{2,3} and frequent metastatic sites are the liver, peritoneum, lungs, and bone. We present a case of metastatic follicular carcinoma of the liver and peritoneum arising from struma ovarii.

CASE

A right ovarian cyst was discovered in a 35-year-old woman during a routine follow-up examination for her second pregnancy. She underwent a right ovarian cystectomy and incidental appendectomy at 10 weeks of gestation. A histopathological examination revealed follicular carcinoma arising in a teratoma with infiltrative

growth and lymphovascular invasion. After delivery in October 2010, she was transferred to our hospital for further evaluation. Because there was no definite abnormal hypermetabolic lesion on positron emission tomography (PET), she was followed with regular thyroid function tests. However, her serum thyroglobulin level increased to 1,437 ng/ml (normal range: 0-52 ng/ml). She underwent an endoscopic total thyroidectomy in January 2012, and the histopathological examination revealed incidental nodular hyperplasia in the thyroid gland. She received radioactive iodine (RAI) therapy.

Nevertheless, serum thyroglobulin levels increased to 28,890 ng/ml after RAI therapy. The patient had no specific findings on physical examination. Laboratory tests, including blood cell counts and serum levels of liver enzymes, electrolytes, and creatinine were within normal limits. I-131 scans revealed increased uptake in the right upper quadrant of the abdomen (Fig. 1A). Abdominal computed tomography (CT) revealed an 8.5×6.3 cm-sized

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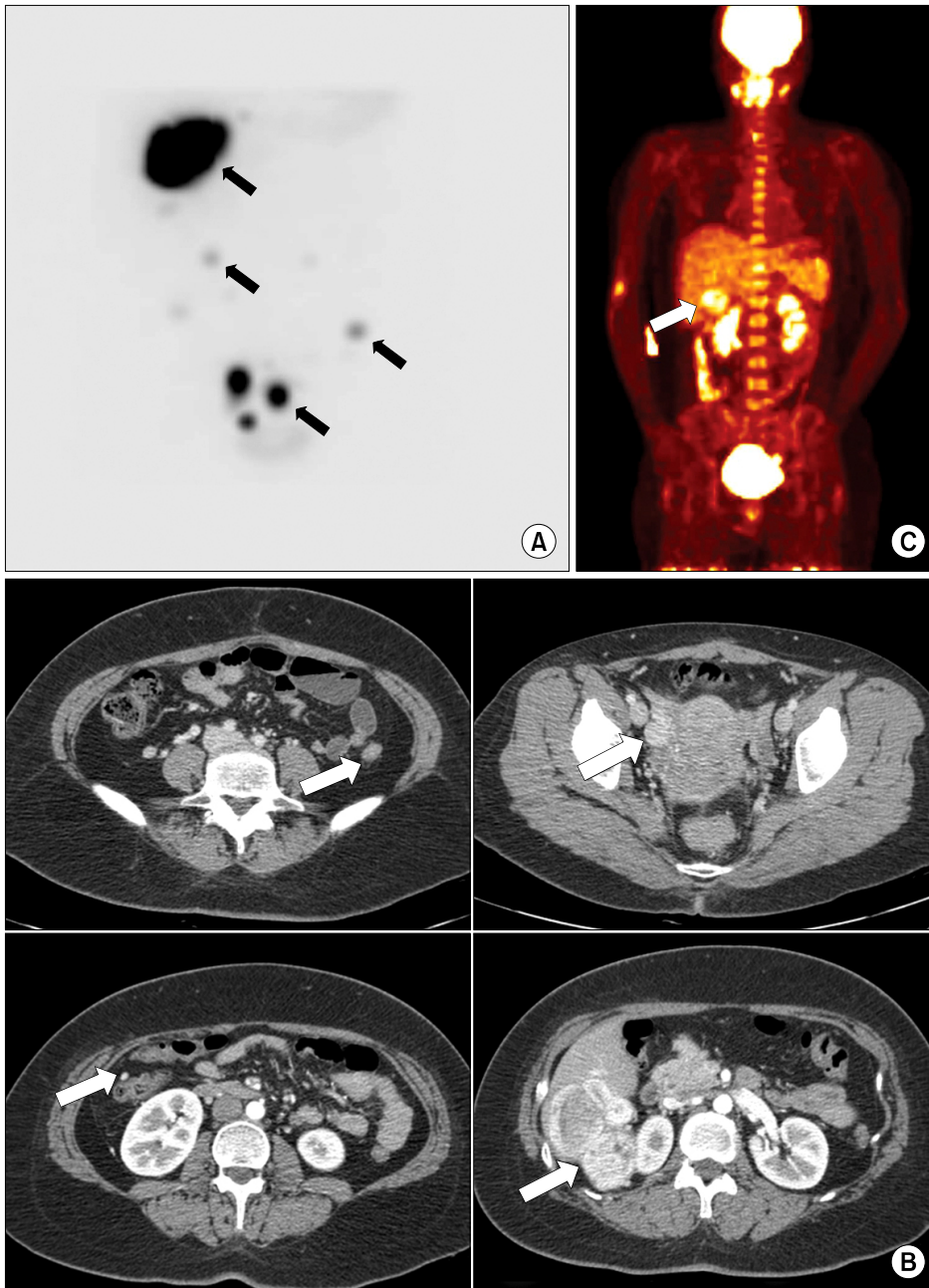


Fig. 1. Imaging studies of the metastatic struma ovarii. (A) An iodine-131 scan after radioactive iodine therapy. This test revealed several nodules in the right upper quadrant of the abdomen (liver, arrow), peritoneum (arrow), and pelvic cavity (arrow). (B) Computed tomography scans showing an enhanced conglomerate nodular mass (arrow) in segment 6 of the liver with several daughter nodules and multiple seeding nodules (arrow). (C) The fluorodeoxyglucose-positron emission tomography (¹⁸F-DG-PET) scans showing increased uptake in the exophytic liver mass (arrow) and lymph nodes in neck level II.

metastatic mass in the segment 6 of the liver and variable-sized seeding nodules in both the paracolic gutter and the pelvic cavity (Fig. 1B), but no systemic metastatic lesions were observed on PET scans (Fig. 1C). In the operative field, the liver had an exophytic mass and a demarcation line along segment 6, and the pelvic cavity showed multiple seeding nodules in the right salpinx and ovary. Variably sized seeding nodules were discovered in the right diaphragm, small bowel mesentery, and pelvic cavity. We resected the metastatic lesions in segment 6 of the liver and the right salpinx with the infundi-

bulopelvic ligament. The peritoneal seeding nodules were grossly resected. The patient started a soft diet on postoperative day 3, and the percutaneous drainage tube was removed on postoperative day 5.

The histopathological examination reported that the liver mass and the nodules in the right salpinx and right diaphragm were compatible with metastatic follicular carcinoma (Fig. 2). In particular, the pathologist mentioned that the metastatic lesion of the liver focally showed a poorly differentiated area.

She has been subsequently treated with RAI therapy

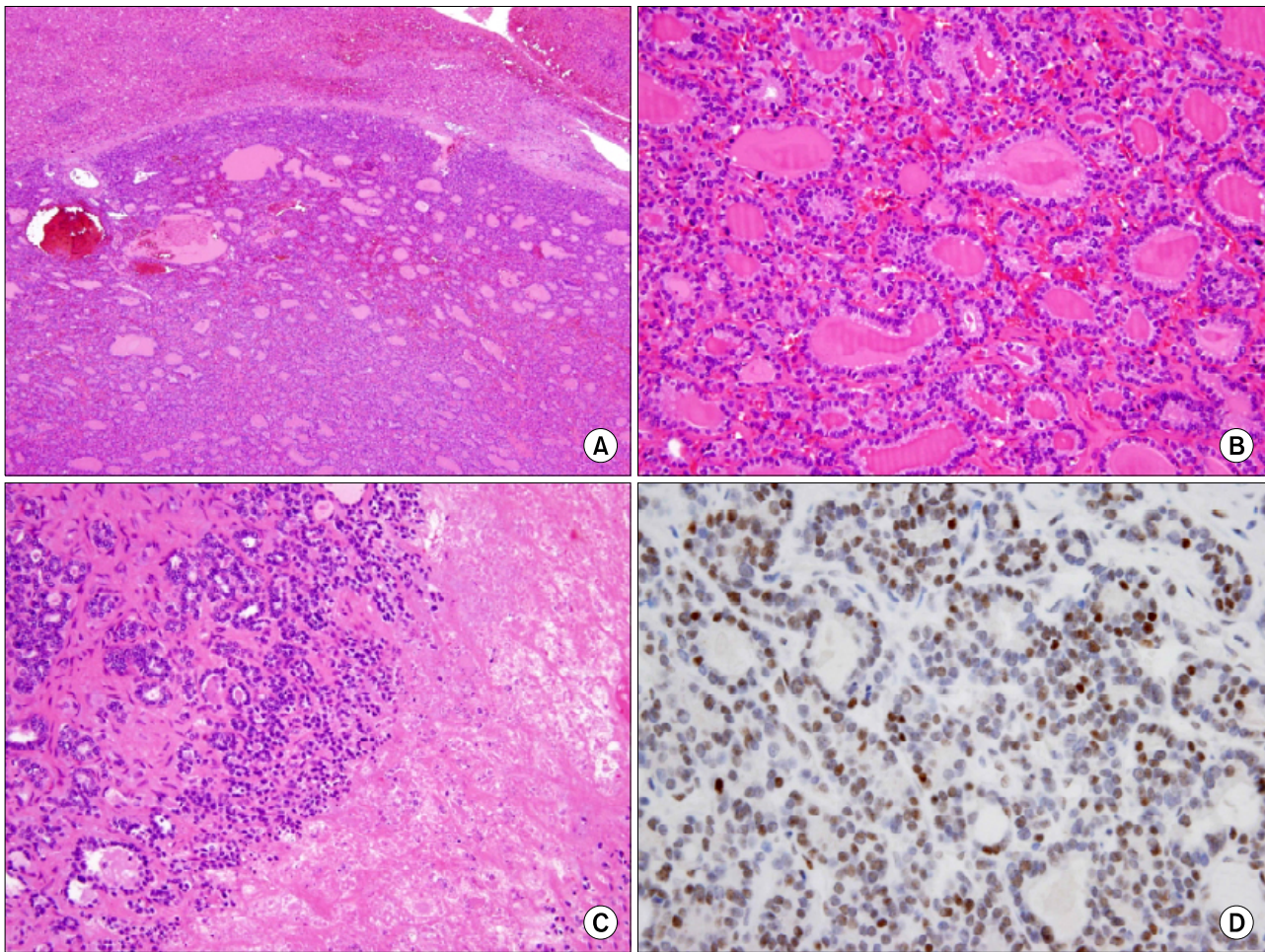


Fig. 2. Pathological examination of the metastatic follicular struma ovarii. (A) A metastatic follicular carcinoma in the liver at the bottom. (B) High-power magnification of the metastatic lesion in the liver shows many follicular masses. (C, D) Multifocal necrosis (C) and positive P53 staining (D) represent the possibility of malignant transformation.

and recent serum thyroglobulin levels were 12 ng/ml.

DISCUSSION

Von Kalden first described struma ovarii in 1895, which is an ovarian teratoma that contains >50% mature thyroid tissue. This tumor usually occurs in the fifth and sixth decades of life. Most patients are asymptomatic and have pelvic masses (45%) on screening tests, such as ultrasonography or CT. Patients present with acute pelvic pain (40%), menstrual irregularities (9%), and hyperthyroidism (5-8%).^{1,4} A preoperative diagnosis of struma ovarii is impossible, but patients with hyperthyroidism can be diagnosed by measuring serum thyroid-stimulating hormone, and thyroxine, and conducting thyroglobulin I-123 scintigraphy. In contrast, Garg et al.³ raised the pos-

sibility of a link between pregnancy and struma ovarii, as in the present case.

No consensus of opinion exists for treating a thyroid-type carcinoma arising in struma ovarii. Primary surgical resection is essential for successful treatment, and various procedures have been reported in the literature (Table 1). A total abdominal hysterectomy and bilateral salpingo-oophorectomy with omentectomy are suitable for postmenopausal women or premenopausal women who have completed childbearing. Conservative surgeries such as unilateral oophorectomy or cystectomy are appropriate to preserve fertility.

Some investigators have demonstrated that RAI therapy reduces recurrence after a total thyroidectomy in cases of metastatic struma ovarii with increased serum thyroglobulin levels. Thyroidectomy is useful for excluding pri-

Table 1. Literature review of malignant follicular struma ovarii cases

Reference	No. of cases	Initial surgery (no. of cases)	Thyroidectomy and RAI	Other therapies	Recurrence sites	Outcome of follow-up
International cases						
Dardik et al. (1999) ¹⁰	2	TAH/BSO	Yes	RTx	Peritoneum, paraaortic nodes	NED
Bolat et al. (2005) ¹¹	1	USO	No	No	Contralateral ovary	NED
Cherng et al. (2005) ¹²	1	USO	Yes	No	Pelvis and liver	NI
Makni et al. (2005) ¹³	1	USO	Yes	CTx	Liver	DOD
Janszen et al. (2008) ⁶	3	TAH/BSO (1), BSO (1), USO (1)	Yes	No	Liver	NED
Roth et al. (2008) ⁸	4	USO (1), TAH/BSO (3)	No	No	No	NED
Yücesoy et al. (2010) ¹⁵	1	TAH/BSO	No	No	No	NED
Marcy et al. (2010) ¹	1	USO	Yes	CTx	Peritoneum, liver, lung, adrenal, bone	DOD
Domestic cases						
Kwon et al. (2002) ¹⁴	6	USO (3), Cystectomy (3)	No	No	No	NI
Kim et al. (2012) ¹⁶	1	TAH/BSO	No	No	No	NED
Baek et al. (2004) ¹⁷	1	TAH/BSO	No	CTx	No	NED
Lee et al. (present case)	1	Cystectomy	Yes	No	Liver, peritoneum, ovary	NED
Summary	23	USO, 9 (39.1%); AH/BSO 11 (47.8%); BSO, 4 (17.4%); Cystectomy, 4 (17.4%)	Yes 9 (39.1%) No 14 (60.9%)	RTx, 2 (8.6%); CTx, 3 (13.1%); No, 17 (73.9%)	Liver, 6 (26.1%); Peritoneum, 4 (17.4%); Ovary, 2 (8.6%); Paraaortic nodes, 2 (8.6%); Pelvic cavity, 1 (4.3%); Adrenal gland, 1 (4.3%); No metastasis, 13 (56.5%)	NED, 14 (60.9%); DOD, 2 (8.6%); NI, 7 (30.4%)

TAH/BSO, total abdominal hysterectomy/bilateral salpingo-oophorectomy; RTx, radiotherapy; NED, no evidence of disease; USO, unilateral salpingo-oophorectomy; NI, not indicated; CTx, chemotherapy; DOD, died of disease

mary thyroid cancers with subsequent ovarian metastases and for evaluating the effectiveness of RAI therapy.^{5,6} Adverse effects of RAI therapy treatment are transient amenorrhea and premature menopause. Studies of pregnancy outcomes after RAI therapy reveal no harmful effects; however, miscarriage may occur when conception occurs within 6 months of the last RAI therapy.⁶ Other adjuvant treatments after total thyroidectomy such as chemotherapy and thyroid suppression are effective for treating metastatic struma ovarii.⁷

Serum thyroglobulin levels can be used as a marker of metastatic disease. Patients with normal thyroglobulin levels need close medical observation with regular thyroglobulin measurements. In contrast, patients with increased serum thyroglobulin levels require a total thyroidectomy followed by RAI therapy. In addition, radioiodine imaging can be used as a tool for detecting meta-

static lesions.^{3,6} In this case report, the patient underwent RAI therapy after total thyroidectomy, but serum thyroglobulin levels increased, indicating that RAI therapy may have been ineffective for treating her disease, or that the tumour growth was too fast to respond to RAI therapy. Fortunately, her serum thyroglobulin level returned to the normal range after the second debulking operation. Therefore, regular serum thyroglobulin measurements might be one of the surveillance tools for cases such as this.

Most cases of struma ovarii are benign, but malignant changes have been reported in 5-15% of cases.^{2,4} Extravarian spread is rare even in malignant struma ovarii and occurs in <5% of patients.^{2,3} Papillary carcinoma (21%) and follicular carcinoma (54%) are the most frequent types of carcinomas among thyroid-type carcinomas of struma ovarii.¹ A typical follicular carcinoma is more likely to metastasize to the lungs, liver, and central nervous

system, whereas a papillary carcinoma tends to involve the abdominal cavity and lymph nodes.⁸ Poor prognostic factors are initial extraovarian spread, adhesion to adjacent organs, size >5 cm, and >50% proliferating thyroid tissue.⁹ Our patient developed peritoneal dissemination and huge liver metastases 2 years after the ovarian cystectomy. Moreover, the last pathological examination showed that the metastatic follicular carcinoma of the liver had the potential for transformation to poorly differentiated carcinoma compared to that in the initial pathological examination. Therefore, this patient required close medical observation with regular thyroglobulin measurements.

In conclusion, we present a rare case of metastatic follicular carcinoma to the liver and peritoneum initially arising in struma ovarii of a young woman. These metastatic lesions were successfully treated with debulking surgery and RAI therapy after a total thyroidectomy. However, because she had several poor prognostic factors, close medical follow-up by serum thyroglobulin monitoring was mandatory.

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