Struma ovarii maligna

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Submitted: 2012-06-14 Accepted: 2012-09-03 Published online: 2013-05-05

Key words: **malignant struma ovarii; bone metastasis; radioiodine therapy**

Neuroendocrinol Lett 2013; **34**(2):97–101 **PMID:** 23645304 NEL340213C01

Abstract

INTRODUCTION: Malignant struma ovarii is a rare ovarian neoplasm composed predominantly of mature thyroid tissue.
CASE REPORT: A right ovarian tumor was discovered at ultrasound examination in a 20-year-old woman. Complete right ovariectomy was done – histopathological examination revealed papillary thyroid carcinoma arising in struma ovarii (malignant struma ovarii). Patient underwent subsequent total thyroidectomy – the thyroid was found to be without any pathological lesions. After operations the patient received ablative radioiodine treatment (200 mCi ^{131}I). An ^{131}I posttherapeutic whole-body radioiodine scintigraphy was performed and showed uptake in bone metastases. L-thyroxine TSH suppresive doses followed radioiodine ablation and thyroglobulin level is monitored. Next doses of radioiodine has been scheduled.
DISCUSSION: Authors suggest that the management of malignant struma ovarii should be the same as differentiated thyroid cancer, so after surgical excision of ovarian neoplasm, we recommend thyroidectomy, radiotherapy with ^{131}I and levothyroxine suppressive therapy. Long-term follow-up for the detection of metastases or tumor recurrence by serial serum thyroglobulin measurements and ^{131}I scan may be required in patients with this rare tumor.

CASE REPORT

INTRODUCTION

Teratomas are tumors derived from germ cells, which constitute approximately 15–20% of ovarian tumors (Salman *et al.* 2010; Makani *et al.* 2004). They are composed of tissues originating from two or three germ layers (ectoderm, endoderm, mesoderm).

Approximately 5–15% of teratomas contain thyroid tissue – if teratoma is composed in more than 50% of thyroid tissue – struma ovarii can be recognized (Devaney *et al.* 1993). Struma ovarii is a rare neoplasm – constitutes less than 5% of all ovarian teratomas (Salman *et al.* 2010). Five to ten percent of them are malignant ones (Devaney *et al.* 1993; Roth & Talerman *2*007; Kostoglou-Anthanassiou *et al.*2002), containing most often papillary carcinoma – in 44%, or less frequent follicular carcinoma – in 30% (Makani *et al.* 2004). Struma ovarii was first described in 1889 – then thyroid follicular cells were found as a part of ovarian tumor (Boettlin 1889). Malignant struma ovarii was described first by Wetteland in 1956 (Wetteland 1956).

Here we present a case of malignant struma ovarii diagnosed in 20-year-old patient.

CASE REPORT

In 20-year-old patient suffering from lower abdominal pain, gynecological ultrasound was performed which revealed partly cystic partly solid right ovarian tumor measuring 10×6 cm. The concentration of CA 125 was within a normal range. Patient underwent surgical treatment – tumor enucleation with wedge resection of the right ovary was performed. Histopathological result was: papillary thyroid cancer. Immunohistochemical study: THY+, TTF+, CK7+, CK19+, CHR–, INH–.

Therefore patient was referred to the endocrinology clinic. The diagnostic tests showed euthyreosis: TSH – 1.76 μIU/ml, fT4 18.51 pmol/l, fT3 5.83 pmol/l. The concentration of thyroglobulin – tumor marker characteristic for differentiated thyroid cancer – was elevated – Tg 228.09 ng/ml, in the absence of interfering factors. Ultrasound of the thyroid gland showed homogeneous echogenic structure with no deviations. Gynecological ultrasound revealed a right ovary 3.8×1.2 cm, without focal lesions, the left ovary 2.7×1.6 cm with the structure of higher echogenicity sized 1.15 cm. The hormonal studies in the field of sex hormones did not reveal any deviations. Because the patient reported pain in the left hip joint, X-ray of the left ilium was performed. The presence of osteolitic lesion in the central part of the left iliac crest with dimensions of 6.6×3.8 cm was found. To verify changes in the ovary and the ilium MRI of the pelvis was performed. Solid, well-demarcated lesion in the left ilium with maximum dimensions: length 55 mm, thickness 26 mm, height 60 mm was shown. Destruction of the cortical layer of the internal part of the left ileum with simultaneous infilitration of the diploe by the tumor mass was noted but with no any other infiltration of the surrounding tissues nor iliolumbar muscle (Figure 1). Within the right ovary presence of the fluid space with maximum dimensions of 16×11 mm, in the left ovary similar changes with maximum dimensions of 12×11 mm – probably the Graafian vesicles were found. According to the results of the diagnostics, the need for radical surgery and subsequent treatment with iodine-131 radioisotope was decided.

Due to the young age of the patient and her desire to have children it was decided to perform right salpingo-oophorectomy and to save ovary and fallopian tube on the left side. No neoplastic tissue was found in the subsequent pathological examination. Then total thyroidectomy, as a preparation for radioiodine therapy was done. Removed thyroid gland histopathologically did not present any lesions which confirmed the earlier correct result of the thyroid ultrasound examination. L-thyroxine replacement therapy at a dose providing to TSH suppression was introduced.

Isotopic treatment at the Clinic of Endocrinology, Metabolism and Internal Medicine was carried out 3 months later. Three weeks before the planned therapy L-thyroxine supplementation was discontinued in order to obtain optimum conditions for the radioiodine treatment. The performed studies revealed: TSH 47.12 iU/ml and significantly elevated levels of thyroglobulin – 496.38 ng/ml in the absence of interfering factors. Neck ultrasonography revealed the remnants of the thyroid gland – in the right lobe projection 8×4×4 mm, 4×4×4 mm in the left lobe projection. The presence of a dominant follicle size of 20 mm in the left ovary with no pathology in the project of the right adnexa was observed in the gynecological ultrasound examination. The patient received 200 mCi of the radioiodine ^{131}I. In the following posttherapeutic scintigraphy revealed pathological tracer accumulation in projection of the

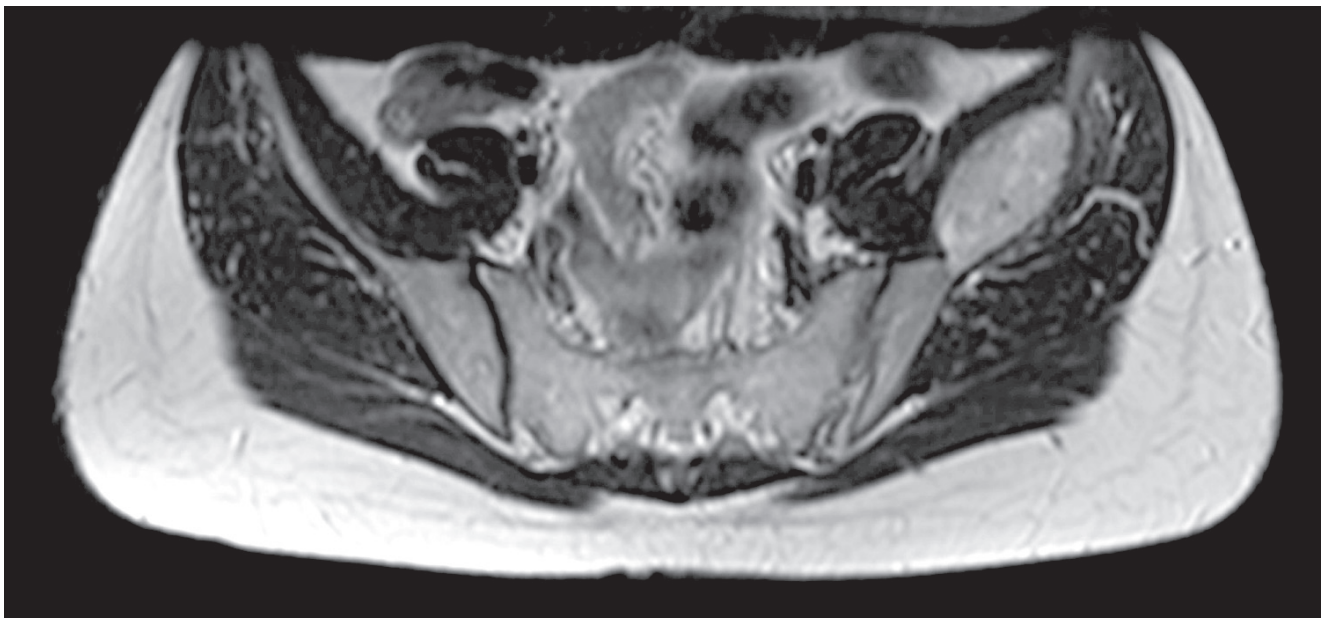

Fig. 1. MRI of the pelvis.

left hip joint – a spot of known metastatic focus. Other foci of pathological tracer accumulation was not visualized. Bone scintigraphy revealed a focus of pathological tracer accumulation in the confines of the front left hip, left hip joint and the lower part of the left ilium (Figure 2). After isotopic treatment TSH suppressive dose of L-thyroxine was introduced again.

In control examinations performed after approximately 6 months after treatment improvement in both biochemical, as well as imaging studies were observed. Tg concentration was 43.17 ng/ml for TSH 0.005 μU/ml – at a dose of 150 μg/day of L-thyroxine. No thyroid tissue remnants were visualised in the neck ultrasonography. No pathological tracer accumulation was shown in the bone scintigraphy (Figure 3) – compared with the previous study scintigraphic remission of the lesion in the left ilium was found. Computed tomography revealed the presence of osteolytic spot (48×58×10 mm) in the left ilium. Gynecological ultrasound examination was performed again – it visualized lesion of increased echogenicity with dimensions 1.4 ×0.6 cm in the left ovary, there was no pathology found in the projection of right adnexa. In the hormonal studies growth of gonadotropins – FSH 107 mIU/ml, LH 72.86 mIU/mL was noted, probably due to the damage of the left ovary by radioiodine therapy. The patient received estrogen/progestin therapy.

The patient was treated twice more with radioiodine (dose of 150 mCi ^{131}I each time). Significant improvement was obtained, expressed in fall of serum Tg – during the last treatment at TSH serum 48 μU/ml, Tg concentration was 48.04 ng/ml. The lesion in the hip bone is stable in imaging studies. The isotopic treatment is planned to be continued.

DISCUSSION

Struma ovarii is a rare ovarian neoplasm. It represents 0.2–1.3% of all ovarian tumors (Kostoglou-Anthanassiou *et al.* 2002). It occurs at any age, but most often is diagnosed in 5th–6th decade of life (Devaney *et al.* 1993; Makani *et al.* 2004), at an older age compared to our patient. In most cases the tumor is unilateral, more often occupying the left than the right ovary (Kostoglou-Anthanassiou *et al.* 2002), unlike in our case.

There is no characteristic signs and symptoms of struma ovarii. Clinical symptoms that may manifest due to the presence of a struma ovarii are: lower abdominal pain, palpable abdominal mass, ascites, abnormal vaginal bleeding (Yoo *et al.* 2008). There are few cases of pseudo-Meigs syndrome reported in both benign and malignant struma ovarii (Jiang *et al.* 2010). Despite the significant content of thyroid tissue in the tumor, symptoms of hyperthyroidism are observed only in approximately 5–8% of cases (Makani *et al.* 2004, Dardik *et al.*1999; Kano *et al.* 2000). There are only several reports of elevated serum CA 125 (cancer antigen 125) (Altaras *et al.* 1986). Most patients are diagnosed after operation of ovarian tomour incidentally found during routine ultrasound examination.

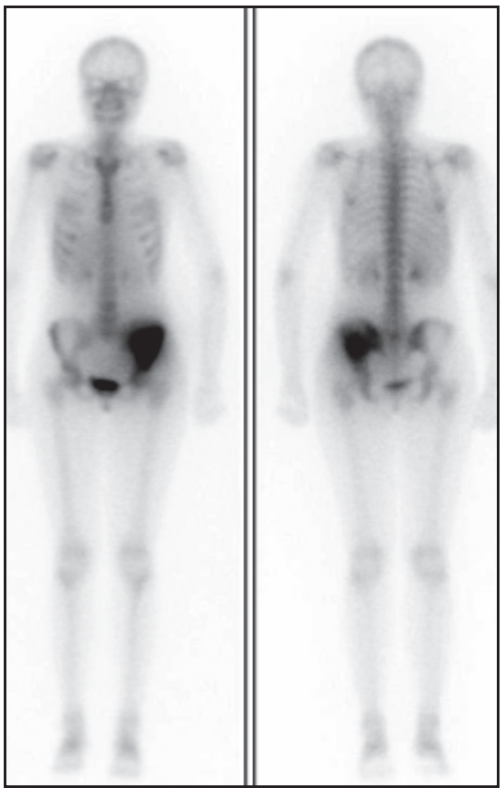

Fig. 2. Bone scan performed after first radioiodine therapy.

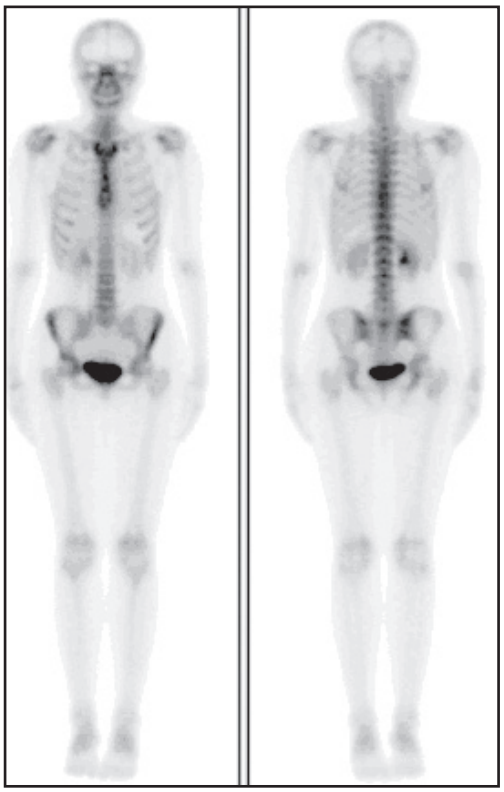

Fig. 3. Bone scan performed 6 months after radioiodine therapy

About 5–10% of struma ovarii are malignant (Kostoglou-Anthanassiou *et al.* 2002). The guidelines for diagnosis of primary thyroid carcinoma are mostly used for the diagnosis of thyroid-type carcinoma arising in struma ovarii (the criteria for malignancy is similar to that seen in thyroid gland) (Devaney *et al.* 1993). Papillary carcinoma is the most common thyroid-type carcinoma occurring in struma ovarii. Papillary carcinoma shows malignant nuclear features designated as ground-glass overlapping nuclei, intranuclear inclusions and nuclear grooves (Devaney *et al.* 1993; Zhang *et al.* 2010). Follicular carcinoma is the second most common type of carcinoma arising in struma ovarii. The diagnosis of follicular carcinoma is more difficult. Capsular neoplastic invasion which covers the whole of its thickness (but rarely the presence of capsula in the ovarian lesions is found), infiltration of blood vessels or surrounding tissues or the presence of metastases (Roth & Talerman *2*007; Zhang & Axiotis 2010) must be demonstrated. The presence of metastasis always implies the diagnosis of malignant struma ovarii. Cytokeratin 19, HBME-1 and galectin-3 are immunohistochemical markers helpful in differentiating between malignant and benign lesions (Cheung *et al.* 2001). Malignant struma ovarii must be distinguished from thyroid cancer metastases to the ovary, which are extremely rare (Logani *et al.* 2001; Young *et al.* 1994). In our case, no neoplastic changes in the removed thyroid gland were found.

Metastases are uncommon and they are seen in 5–23% patients with malignant struma ovarii (Makani *et al.* 2004; Dardik *et al.* 1997; DeSimone *et al.* 2003). They can spread via lymphatic vessels to nearby lymph nodes, through continuity to the omentum or direct spread to the peritoneal cavity or through blood vessels to the bones, lungs or brain. Metastases in the presence of follicular carcinoma usually are seen to the lungs, liver and central nervous system, whereas in the case of papillary cancer metastases are frequently observed in the peritoneal cavity and regional lymph nodes (Roth *et al.* 2008). Bone metastases are rare – in the available literature only a few cases are reported (Yamashita *et al.* 2010).

Treatment of malignant struma ovarii is still under discussion. The unquestionable fact is surgical excision of the tumor. The standard treatment is total hysterectomy, bilateral salpingo-oophorectomy, omentectomy with lymphadenectomy. For younger patients who wish to preserve fertility , conservative surgery such as unilateral oophorectomy is appropriate, if there are no extraovarian changes (Yassa *et al.* 2008; Hatami *et al.* 2008).

The management after initial treatment is still controversial. Some authors have advocated the management of malignant struma ovarii as other germ cell tumours (Ayhan *et al.* 1993), while others suggest that the management should be the same as for differentiated thyroid carcinoma (Dardik *et al.* 1997; Mattuci *et al.*2007). After treatment of primary tumor subsequent proceedings should include total thyroidectomy and complementary radioiodine therapy (DeSimone *et al.* 2003; Mattuci *et al.* 2007; Willemse *et al.* 1987; Yassa *et al.* 2008). This gives the possibility to control the stage of the disease, based on a study of thyroglobulin, which is a useful and sensitive marker of tumor recurrence (Rose *et al.* 1998), and authorizes the execution of diagnostic iodine whole body scintigraphy. In case when strumectomy was not done, both thyroglobulin and iodine scintigraphy become less useful in follow-up and assessing the stage of the disease (Balci & Kabasakal *2*005).

It is difficult to assess prognosis in malignant struma ovarii. Literature data indicates that the 10 and 25 years survival are 89% and 84% respectively (Robboy *et al.* 2009), and metastases are rare (DeSimone *et al.* 2003). Devaney *et al.* (1993) studied 54 cases of struma ovarii (13 cases of malignant struma ovarii) – none of the patients had clinical evidence of reccurent disease and none received adjuvant therapy. DeSimone *et al.* (2003) reported, that in the group of 16 patients treated surgically only, 8 recurrences were noted. All of them were successfully treated with therapy using radioiodine (DeSimone *et al.* 2003). Makani *et al.* (2004) recommended that 10-year period is a minimum needed for follow-up.

In women of childbearing age, a very important problem is to preserve fertility. Fertility sparing surgery should be considered in reproductive aged patients with minimal disease burden. Advanced changes require individual consideration in each case. Surgical treatment significantly reduces ovarian reserve, but also adjuvant radioisotope therapy with use of ^{131}I carries the risk of ovarian damage. Transient ovarian failure manifested in secondary amenorrhea with increased concentration of gonadotropins and the earlier occurrence of menopause in women with differentiated thyroid cancer treated with isotope ^{131}I have been noted (Ceccarelli *et al.* 2001; Raymond *et al.* 1989). In the case of malignant struma ovarii the damage might be greater due to the location of radioiodine absorbing lesions. In our patient serum FSH, LH and E2 suggested an iatrogenic menopause and the patient was treated with estrogen/progestin.

CONCLUSION

The case showed a rare manifestation of struma ovarii. Patient's young age, the presence of malignant variety of the disease with bone metastases are unusual respectively. Treatment of malignant struma ovarii needs to be individualized. Authors suggest that the management of malignant struma ovarii should be the same as differentiated thyroid cancer, so after surgical excision of ovarian neoplasm, we recommend thyroidectomy, radiotherapy with ^{131}I and levothyroxine suppressive therapy. Long-term follow-up for the detection of metastases or tumor recurrence by both serial serum

thyroglobulin examination and radioiodine whole body scan may be required in patients with this rare tumor.

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