Rare disease

Papillary thyroid-type carcinoma arising from struma ovarii

Jerome Rebollos Barrera,¹ Leonido Andrade Manalo,² Frances lina Lantion Ang¹¹Department of Medicine, Philippine General Hospital, Manila, Philippines;²Department of Pathology, Philippine General Hospital, Manila, Philippines**Correspondence to** Dr Jerome Rebollos Barrera, jrom0330@yahoo.com**Summary**

Malignant transformation of benign monodermal teratoma is a rare presentation of struma ovarii. A 41-year-old Filipina presented with 1-year history of recurrent lower abdominal pain, abdominal swelling and vomiting. Ultrasound of the abdomen revealed a large cystic abdomino-pelvic mass densely adherent to the intestinal and uterine wall with moderate ascitis. The patient underwent total abdominal hysterectomy and bilateral salphingo-oophorectomy and histopathology showed papillary thyroid-type carcinoma arising from the left struma ovarii. She underwent total thyroidectomy, postoperative radioactive iodine ablation and maintained on levothyroxine suppressive therapy. She is now on regular follow-up for monitoring of possible tumour recurrence and metastasis.

BACKGROUND

Struma ovarii is a monodermal teratoma diagnosed when thyroid tissue is the predominant element (50%) of the ovarian tumour.¹ It is a rare condition, representing only less than 1% of all ovarian tumours.¹ Five to 10% of these tumours undergo malignant transformation, with papillary carcinoma and follicular carcinoma being the most common.¹ In a recent review, papillary carcinoma comprises about 51% (53/102) of the total thyroid-type malignancy of the struma ovarii reported from 1924 to 2008.² Due to the rarity of the disease, lack of uniform histological criteria for malignancy and protracted clinical course, its management is not also universally accepted by physicians. The aim of this paper is to present a rare case of papillary thyroid-type carcinoma arising from struma ovarii, and review the literature on the suggested consensus for diagnosis and management.

CASE PRESENTATION

A 41-year-old Filipina consulted at the Obstetrics and Gynaecology outpatient clinic of our institution with lower abdominal pain. She has been experiencing dull, recurrent pain at the lower abdomen associated with progressively enlarging non-tender mass and vomiting. She did not experience any bowel or urinary changes and her menstrual cycle was regular. The review of systems was unremarkable.

Her medical history included congenital cataract on the right and repeated consultations for recurrent abdominal pain. She is gravida 2 para 2. She had no family history of ovarian carcinoma or any gynaecologic and endocrine malignancies.

Physical examination showed stable vital signs. There were two firm, non-tender nodules on the right anterior neck each measuring 2 cm in diameter. There was no exophthalmos. The abdomen was globular with vague, non-tender mass on the left lower quadrant. She had normal reflexes and no finger tremors. The rest of the physical examination was unremarkable.

INVESTIGATIONS

Abdominal ultrasonography showed a large abdomino-pelvic mass measuring 12.5×12.1×8.3 cm with irregular cystic spaces within. The mass was densely adherent to the surrounding bowel loops and uterine walls with moderate amount of ascitic fluid, suggestive of malignant ovarian new growth. CT scan of the whole abdomen with contrast revealed a multi-lobulated mass at the pelvic region predominantly cystic with enhancing solid portion and calcification, suggestive of ovarian teratoma. Her CA 125 was slightly elevated at 41.3 U/ml (0–35 U/ml). The ultrasound of the neck revealed 11 thyroid nodules mostly hypoechoic and less than 1 cm in diameter, with two nodules greater than 2 cm in their largest diameter. There were no calcifications and increased vascularity noted. Her serum thyroid function tests (FT4-16.2 pmol/l (normal values=11–24 pmol/l), TSH-0.8 mIU/l (normal values=0.3–3.8 mIU/l) were normal.

She underwent exploratory laparotomy and total abdominal hysterectomy with bilateral salphingo-oophorectomy (TAHBSO). Intraoperatively, the left ovary was converted to a 10×7×6.5 cm multi-loculated, multi-septated mass which was densely adherent to the bowels posteriorly and to the uterus anteriorly. There was 200 ml of clear yellowish ascitic fluid and two mesenteric masses each measuring 1.5×1.0 cm.

On histopathologic examination, the large ovarian mass was a 10×7×6.5 cm struma ovarii which consisted of benign thyroid follicles with colloid and hyperplastic areas (figure 1) and predominantly malignant papillary architecture with thyroid follicles, fibrovascular cores and overlapping nucleoli (figure 2). On immunohistochemistry, the tumour cells were positive for thyroglobulin. The omentum, ascitic fluid, two mesenteric masses and the surrounding lymph nodes were negative for malignancy. The right ovary and uterus were unremarkable. Subsequently, she had total thyroidectomy for multi-nodular non-toxic goiter.

We considered her case as papillary thyroid-type carcinoma arising from struma ovarii and with multi-nodular non-toxic goiter.

Figure 1 Struma ovarii showing benign thyroid follicles in varying sizes containing colloid (orange arrow) with hyperplastic areas (H&E stain) (green arrow).

DIFFERENTIAL DIAGNOSIS

Before thyroid surgery, we considered papillary thyroid carcinoma with metastasis to the left ovary as differential diagnosis.

TREATMENT

After the TAHBSO, the patient was treated with platinum-based chemotherapy by the attending gynaecologist. We decided to discontinue this treatment modality as, on available data, it failed to improve mortality and morbidity outcomes.³⁻⁵

Radioactive iodine ablation at 100 mCi (3700 MegaBecquerels), and levothyroxine suppressive therapy at a dose of 1.6 ug/kg/day were given 6 weeks after the total thyroidectomy.

OUTCOME AND FOLLOW-UP

Whole body ¹³¹I scan, 7 days after the radioactive iodine ablation, revealed no residual functioning thyroid tissues. Repeat ultrasound of the abdomen, 6 months after TAHBSO, showed no evidence of ascites, tumour recurrence or metastasis. Her stimulated serum thyroglobulin was undetectable (0.1 ng/ml) confirming remission.

Currently, she is on suppressive dose of levothyroxine at 1.6 ug/kg. Thyroglobulin will be monitored every 6 months.

DISCUSSION

Struma ovarii is a rare form of teratoma characterised predominantly (>50%) of thyroid tissue in the ovary.¹ Barr bodies and 46 XX karyotype has been implicated to play a role in the parthenogenetic development of this type of mature teratoma.⁶ Its malignant conversion to thyroid-type carcinoma has been associated with BRAF mutation similar to that observed in the carcinoma of the thyroid gland.⁷

Actual occurrence of malignancy in the struma ovarii based on the available literature is confusing as some of the cases reported as malignant struma ovarii have been misdiagnosed. The term thyroid type – carcinoma is appropriate term because it specifies the histological type

Figure 2 Struma ovarii showing malignant papillary architecture with fibrovascular core (orange arrow) and overlapping nuclei (H&E stain) (green arrow).

(papillary, follicular, insular and anaplastic carcinoma) of struma ovarii.

Robboy *et al*⁸ reviewed one of the largest case reports and case studies from 1940 to 2008 and reported 88 malignant struma ovarii. Sixty patients had benign histological findings (mostly were adenoma) but were biologically aggressive. Twenty eight patients (32% of the reported cases) were histologically proven malignant, 20 of which were papillary carcinomas. Patients with papillary thyroid-type carcinoma were between 40 and 50 years of age at the time of diagnosis presenting with symptoms of abdominal pain, abdominal mass or vomiting. The tumours were white or tan, unilateral and confined to ovary with a median size of 13 cm. Our patient showed similar clinical and pathological presentations. She is 41 year old and presented with recurrent abdominal pain, abdominal mass and vomiting. The malignant tumour confined in the left ovary was 11 cm. In a similar case series,² 53 patients with papillary thyroid-type carcinoma (out of 102 confirmed histologically malignant struma ovarii) from 1924 to 2008 had similar manifestations.

Because there are no universally accepted criteria for diagnosis of thyroid malignancy in struma ovarii, most of the authors used the criteria for diagnosis of carcinoma of thyroid gland. In the 2003 World Health Organisation Classification of Tumours⁶ and in the review of Roth *et al*,⁹ it was suggested that the histologic criteria for diagnosis of papillary thyroid-type carcinoma should include enlarged, over-lapping, ground-glass, irregularly contoured nuclei lining papillary formations with fibrovascular cores or vascular invasion. However, not all of these features need be identified to establish the diagnosis. Nuclear features of primary thyroid carcinoma like grooves, intranuclear cytoplasmic inclusions, finely, granular chromatin and psammoma bodies are also present in papillary thyroid-type carcinoma of struma ovarii.⁹ Similar nuclear features are present in the follicular variant of papillary thyroid carcinoma; however, papillary architecture is absent.⁹ In our case, histopathologic review showed irregularly contoured nuclei lining papillary formations with fibrovascular cores confirming the diagnosis of classic type of papillary thyroid-type carcinoma.

Currently, there is still no universal therapy for this type of carcinoma. This is because no randomised controlled studies have been done comparing treatment modalities for thyroid-type carcinoma of struma ovarii and thus management is based on published case reports and case series. All cases of this type of carcinoma, however, were surgically managed by total abdominal hysterectomy with bilateral salphingo-oophorectomy, bilateral salphingo-oophorectomy or unilateral salphingo-oophorectomy. Few reviews looked at different therapies used in the management of this carcinoma after the removal of the mass with follow-up of their outcomes. In Desimone *et al.*³ review of 24 cases of thyroid-type carcinoma, those who underwent total thyroidectomy and radioactive ablation after surgical removal of the carcinoma had no disease recurrence even after 36 years. However, tumour recurrences were present in 50% of patients managed conservatively (surgery alone). Furthermore, Mircescu *et al.*⁴ showed the benefits of radioactive iodine ablation therapy even in patients already with tumour recurrence. In a review done on 54 'malignant struma', 11 of which were papillary thyroid-type carcinomas, none of the patients had clinical evidence of recurrent disease 7.3 years after conservative treatment. Available reports³⁻⁵ also failed to show beneficial roles of chemotherapy and radiotherapy used for the treatment of primary ovarian carcinoma, in the treatment of papillary thyroid-type carcinoma. Thus, several authors^{1 3 10 11} recommended that the criteria for diagnosis, treatment and follow-up of thyroid-type carcinoma of struma ovarii should be similar with that of primary thyroid carcinoma. Yassa *et al.*¹² on the other hand suggested that treatment after surgery should be according to the aggressive activity of the tumor. Those classified as low risk (≤ 2 cm and confined to ovary and no worrisome histologic findings should be managed with thyroxine therapy, pelvic imaging, and periodic measurements of serum thyroglobulin. While those classified as high risk (larger carcinomas, disease outside the struma ovarii and with more aggressive histologic features) should be treated with total thyroidectomy, radioactive iodine ablation and levothyroxine suppression therapy.

Like primary thyroid carcinoma, papillary thyroid-type carcinoma arising from struma ovarii has good prognosis with 5- and 25 -year survival rate of 92% and 79%, respectively.⁸ The average time to first tumour recurrence for papillary carcinoma is 4 years but may appear as late as 21.4 years after the surgery.² Factors predictive of aggressive clinical course are the following (1) tumour size >10 cm, (2) more than 80% strumal tissue affected by carcinoma and (3) extensive papillary carcinoma histology like necrosis, ≥ 5 mitoses per 10 high power field and marked cytological atypia.² Metastasis is not uncommon and is not limited locally as there were reports of lung¹³ and hepatic metastases.¹⁴ In our case, although the mass is confined to the ovary with no evidence of distance metastases, long-term follow-up is indicated as recurrence is likely in tumour with size >10 cm.²

As of now, with limited evidence from case reports and case series, diagnosis and management of patients with thyroid-type carcinoma arising from struma ovarii

particularly papillary carcinoma should be based on the recommended guideline for diagnosis and management of well-differentiated thyroid carcinoma.

Learning points

- Struma ovarii is diagnosed when thyroid tissues is the predominant element ($>50\%$) of the ovarian tumour.
- Papillary thyroid-type carcinoma arising from struma ovarii should only be considered if the histologic finding of the tumour is similar to that of papillary carcinoma of the thyroid gland.
- Surgical removal of the struma ovarii remains the initial definite treatment for all thyroid malignancies arising from struma ovarii.
- Further management of papillary thyroid-type carcinoma of struma ovarii is similar with that of papillary carcinoma of thyroid gland which includes: (1) total thyroidectomy (2) postoperative radioactive iodine ablation and (3) levothyroxine suppressive therapy.
- Thyroglobulin every 6 months should be done to monitor any tumour recurrence.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. Devaney K, Snyder R, Norris HJ, *et al.* Proliferative and histologically malignant struma ovarii: a clinicopathologic study of 54 cases. *Int J Gynecol Pathol* 1993;**12**:333–43.
2. Roth LM, Miller AW3rd, Terman A. Typical thyroid-type carcinoma arising in struma ovarii: a report of 4 cases and review of the literature. *Int J Gynecol Pathol* 2008;**27**:496–506.
3. Tavassoli F, Devilee P. Pathology and genetics of tumours of breast and female genital organs. In: *World Health Organization Classification of Tumours*. Lyon: IAP Press 2003.
4. Schmidt J, Derr V, Heinrich MC, *et al.* BRAF in papillary thyroid carcinoma of ovary (struma ovarii). *Am J Surg Pathol* 2007;**31**:1337–43.
5. Robboy SJ, Shaco-Levy R, Peng RY, *et al.* Malignant struma ovarii: an analysis of 88 cases, including 27 with extraovarian spread. *Int J Gynecol Pathol* 2009;**28**:405–22.
6. Roth LM, Terman A. The enigma of struma ovarii. *Pathology* 2007;**39**:139–46.
7. DeSimone CP, Lele SM, Modesitt SC. Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and I131 therapy. *Gynecol Oncol* 2003;**89**:543–8.
8. Mircescu H, Gariépy G, Bélanger R, *et al.* Papillary carcinoma within struma ovarii: a case report with literature review. *The Endocrinologist* 2001;**11**:413–20.
9. Shaco-Levy R, Bean SM, Bentley RC, *et al.* Natural history of biologically malignant struma ovarii: analysis of 27 cases with extraovarian spread. *Int J Gynecol Pathol* 2010;**29**:212–27.
10. Makani S, Kim W, Gaba AR. Struma Ovarii with a focus of papillary thyroid cancer: a case report and review of the literature. *Gynecol Oncol* 2004;**94**:835–9.
11. Mattucci ML, Deller A, Guerriero A, *et al.* Malignant struma ovarii: a case report and review of the literature. *J Endocrinol Invest* 2007;**30**:517–20.
12. Yassa L, Sadow P, Marqusee E. Malignant struma ovarii. *Nat Clin Pract Endocrinol Metab* 2008;**4**:469–72.
13. Ruel IF, Fierrard H, Vercellino L, *et al.* Pulmonary metastasis of struma ovarii: a case report. *Clin Nucl Med* 2010;**35**:692–4.
14. McDougall IR. Metastatic struma ovarii: the burden of truth. *Clin Nucl Med* 2006;**31**:321–4.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Barrera JR, Ang FL, Manalo LA. Papillary thyroid-type carcinoma arising from struma ovarii. *BMJ Case Reports* 2012;10.1136/bcr.03.2012.6145, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>