

A Case Report of Coexisting Graves' Disease and Struma Ovarii

Ajalaya Teyateeti, M.D.*, Kobkun Muangsomboon, M.D.* , Malee Warnnissorn, M.D.**, Pawana Pusuwan, M.D.*

*Department of Radiology, **Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

ABSTRACT

A 72-year-old woman, known case of Graves' disease with anti-thyroid drug hypersensitivity was sent for radioactive iodine ablation prior to surgical resection of an ovarian tumor. Her 24-hour radioactive iodine thyroid uptake was normal. Thus, radioactive iodine whole body scan was performed to diagnose whether struma ovarii was the cause of thyrotoxicosis. The scan showed an iodine avid ovarian mass, which was pathologically proved to be struma ovarii. After surgical resection, she had persistent thyrotoxicosis leading to the conclusion of co-existing Graves' disease.

Keywords: Coexisting Graves' disease and struma ovarii, I-131 whole body scan, 24-hour I-131 thyroid uptake

Siriraj Med J 2016;68:265-270

E-journal: <http://www.tci-thaijo.org/index.php/sirirajmedj>

INTRODUCTION

Struma ovarii is a rare ovarian tumor that contains thyroid tissue. Most of struma ovarii patients present with tumor-related symptoms, but only a few patients have symptoms of hyperthyroidism (5-15%),¹⁻² because struma ovarii itself barely produces excessive thyroid hormone. Diagnosis of struma ovarii pre-operatively in a patient without significant symptoms of hyperthyroidism is therefore difficult. Moreover, even with presentation of hyperthyroidism, Graves' disease is still the most common cause whereas the ectopic thyroid tissue, like struma ovarii is diagnosed in very few patients.

This presented case report was coexisting Graves' disease and struma ovarii in a patient who

was planned for surgical resection of ovarian tumor, but had PTU hypersensitivity. Then, she was referred to the authors' hospital for ¹³¹I ablation. Struma ovarii was suspected as she had normal 24-hour ¹³¹I uptake and diagnosis was made later on, with ¹³¹I whole body scan. Co-existing Graves' disease was proved by TSH receptor antibody as the patient had no pathognomonic signs of Graves' disease.

CASE REPORT

A 72-year-old female visited the primary care unit with complaints of significant weight loss and fatigue which occurred over 3 months. Her physical examination revealed mild tachycardia and normal size of thyroid gland. No specific evidence of thyrotoxicosis or Graves's disease, such as ophthalmopathy or infiltrative dermopathy was observed. The only obvious finding was left leg edema without palpable abdominal or pelvic mass. The ultrasonography performed later on found a large left ovarian mass. The laboratory

Correspondence to: Pawana Pusuwan

E-mail: pawana.pus@mahidol.ac.th

Received 11 April 2016

Revised 25 April 2016

Accepted 28 April 2016

testing for investigation of the cause of weight loss and fatigue showed elevated thyroid hormone with suppressed TSH (FT3 17.2 pg/ml; normal 2.39-6.79, FT4 5.3 ng/dl; normal 0.58-1.64, TSH < 0.008 uIU/ml; normal 0.34-5.6) and elevated serum CA-125 of 54 U/mL; normal 0-35.

She was transferred to the cancer center, where the abdominal CT scan was done. The CT scan demonstrated a large mixed solid-cystic mass in her pelvic cavity, about 8.7x7.7x8.6 cm. The mass caused uterus displacement to the right pelvic cavity without significant intra-abdominal lymphadenopathy, omental thickening or peritoneal nodule (Fig 1). Malignant ovarian tumor was suspected and surgical resection was scheduled.



Fig 1. The post-contrast enhanced abdominal CT scan in coronal and axial views showed a large mixed solid-cystic mass in pelvic cavity that caused uterus displacement to the right. (solid portion; S, cystic portion; C, urinary bladder; B and intra-uterine device in the displaced uterus; arrow).

An endocrinologist gave her a high-dose propylthiouracil (PTU), dexamethasone and Lugol's solution to control thyrotoxicosis before the surgery. Twelve days later, she developed maculopapular rash along her extremities and low-grade fever. Laboratory testing showed normal complete blood count with improvement of thyrotoxicosis. (FT3 5.5 pg/ml; normal 2.0-4.4, FT4 5.3 ng/dl; normal 0.93-1.7, TSH < 0.01 uIU/ml; normal 0.27-4.2) Her liver enzymes slightly increased while the baseline test before starting PTU was normal (AST 78 U/L; normal < 40, ALT 111 U/L; normal < 40, ALP 304 U/L; normal 30-110). PTU was immediately withdrawn owing to high likeliness of PTU hypersensitivity and she was referred for radioiodine therapy.

Twenty-four hours ^{131}I uptake conducted for calculating dose of ^{131}I treatment at our hospital was 28.4% (normal range; 15-45%). The result of TSH receptor antibody was 2.6 IU/L (positive > 2 IU/L). Further investigation with ^{131}I whole body scan showed intense radiotracer uptake in her thyroid gland and in her pelvic cavity (Fig 2). Additional SPECT/CT imaging revealed an intense radioactivity in a large pelvic mass, compatible with struma ovarii of left ovary (Fig 3). Her thyrotoxic state was rendered to euthyroidism

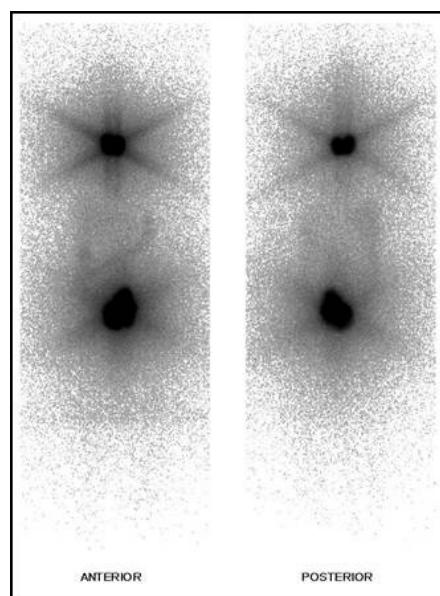


Fig 2. The ^{131}I whole body scan at 72 hours following oral administration of 2 mCi ^{131}I showed intense radiotracer uptake of the thyroid gland and in the pelvic region.

with 15 mg of methimazole daily. She underwent operation 2 months later.

An intraoperative pathology consultation showed a 12x8x6.5 cm solid and cystic left ovarian mass of soft, fleshy, glistening, light brown tissue with clear to straw colored content and focal hemorrhage, with a 3 cm locule containing yellow sebaceous material. Frozen section of the left ovarian mass was reported as “Struma ovarii”. Complete examination showed predominant component of benign thyroid follicles with an area

showing other mature teratomatous components (skin, fatty tissue, cartilage, and benign glands) accounting to 10%. (Fig 4)

Four days after the operation without anti-thyroid medication, her laboratory tests were FT3 1.05 pg/ml, FT4 0.68 ng/dl, TSH 0.59 uIU/ml and Tg 31.9 ng/ml (normal level of Tg 1.4-78.0 ng/ml). Thyroid function was re-evaluated with 24-hour ^{131}I uptake and ^{131}I thyroid scan (Fig 5). Results were initially normal; 24-hour ^{131}I uptake of 27%. Nevertheless, thyroid function tests slowly pro-

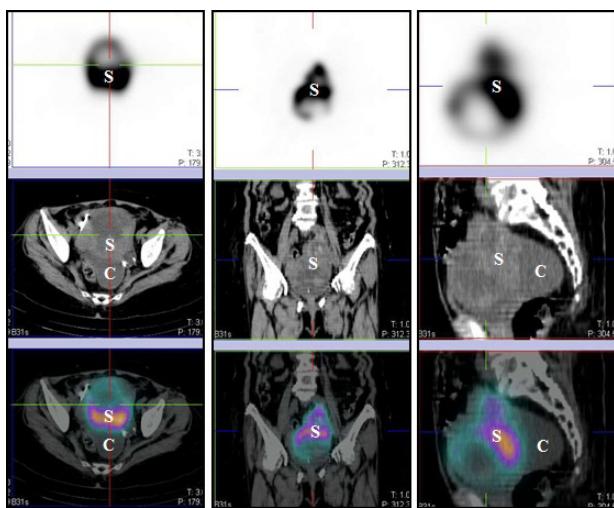


Fig 3. The SPECT/CT imaging of pelvis revealed ^{131}I activity in slightly enhancing area representing functioning thyroid tissue in the solid portion (S) of an ovarian mass. ^{131}I activity was not seen in cystic portion (C) of the mass.

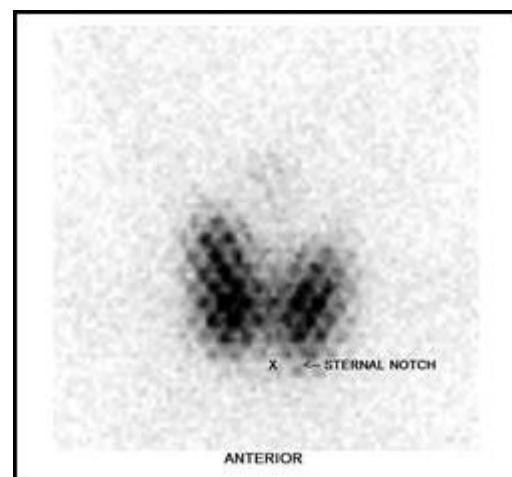
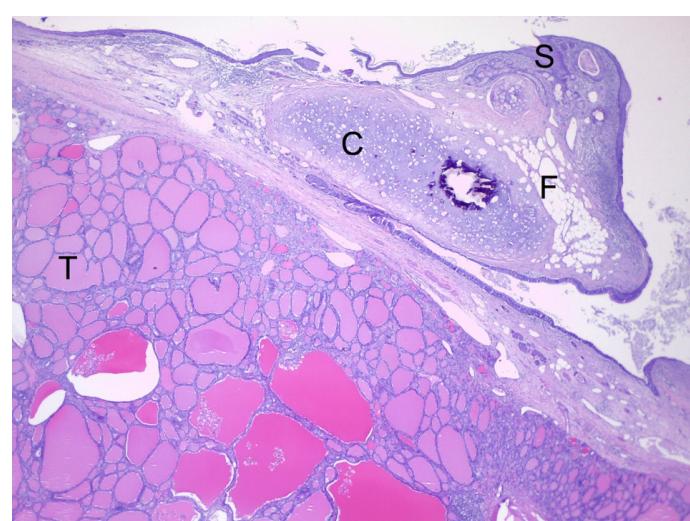


Fig 5. The ^{131}I thyroid scan (4-day post-operation) showed homogeneous radiotracer uptake in the normal size thyroid gland, consistent with normal 24-hour ^{131}I uptake of 27% (normal; 15-45%).



A



B

Fig 4. A) The cut surface of solid and cystic left ovarian mass showed soft, fleshy, glistening, light brown tissue (double arrow) with a locule containing yellow sebaceous material (*). B) Struma ovarii showed predominant mature thyroid tissue (T) with some other teratomatous components such as cartilage (C), fat (F), and skin (S).

gressed to overt thyrotoxicosis months later (FT3 5.14 pg/ml, FT4 2.08 ng/dl and TSH <0.014 uIU/ml). Endocrinologist sent her to evaluate the cause of persistent thyrotoxicosis. Instead of performing 24-hour ^{131}I uptake, ^{131}I whole body scan with 2 mCi ^{131}I was performed at that time due to suspicion of residual hyperfunctioning thyroid tissue in pelvic region. The ^{131}I whole body scan showed only radiotracer uptake at the thyroid gland without abnormal radioactivity in the other parts of the body (Fig 6). Thyrotoxicosis after removal of struma ovarii in this patient should be from hyperfunctioning thyroid gland. Methimazole 5 mg. daily was started to control symptoms of thyrotoxicosis. Two months later, she complained of weight gain and constipation. Her thyroid function test showed overt hypothyroidism. (FT3 1.29 pg/ml, FT4 0.38 ng/dl and TSH 66.03 uIU/ml). Methimazole was withdrawn, but subclinical hypothyroidism has persisted for about 1 year. Finally patient had hypothyroidism and low-dose thyroxine of 25 microgram daily was prescribed.

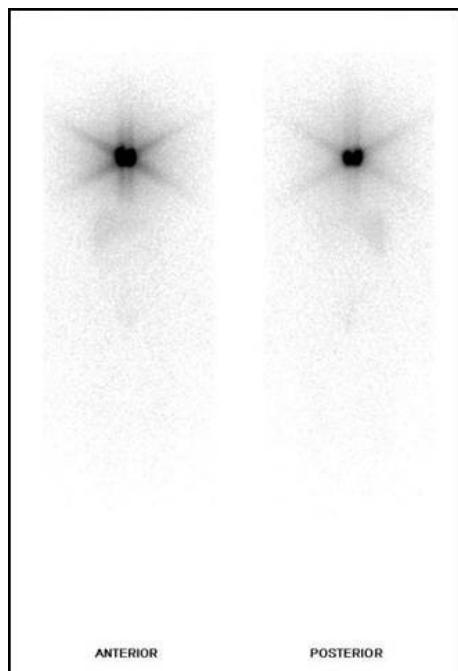


Fig 6. The post-operative ^{131}I whole body scan showed increased radiotracer accumulation in the thyroid gland. No abnormal radioactivity in the other part of the body was observed. These findings supported hyperthyroidism as a cause of persistent thyrotoxicosis.

DISCUSSION

Struma ovarii is a teratoma of ovary containing thyroid tissue similar to that of the thyroid gland. However, it rarely produces excessive hormone causing thyrotoxicosis. As reported in a few previous studies, pathophysiology of struma ovarii with thyrotoxicosis could be 1) hyperfunctioning struma ovarii alone, 2) hyperfunctioning thyroid with non-functioning struma ovarii, or 3) both hyperfunctioning struma ovarii and thyroid.³⁻⁷ Diagnosis of the first two causes are quite straightforward while the latter is relatively complicated. Fortunately, radiotracer used for thyroid imaging, such as $^{99\text{m}}\text{Technetium}\text{ pertechnetate}$ ³ or radioiodine help in differential diagnosis of the cause. Uptake of thyroid imaging tracer at cervical thyroid represents hyperthyroidism and that in pelvic region after exclusion of intense radioactivity in urinary bladder is struma ovarii. Even though, it can be mimicked by metastatic thyroid carcinoma at the ovary and radioiodine uptake in an ovarian cyst has been reported as well.⁸

Clinical presentation of patients with coexisting Graves' disease and struma ovarii in the previous case reports were varied.⁹⁻¹¹ Therefore, clues leading to diagnosis were different. Teale et al.,⁹ diagnosed coexisting struma ovarii in a patient with relapse Graves' disease following subtotal thyroidectomy by evidence of hypothyroidism after surgical resection of an ovarian tumor. Sitaswan et al.,¹⁰ reported a patient with Graves' disease who had persistent thyrotoxicosis following total thyroidectomy. Further investigation with 24-hour ^{131}I uptake showed low uptake and ^{131}I whole body scan performed later showed ^{131}I avid pelvic mass, consistent with struma ovarii. In a case report by Mimura et al.,¹¹ diagnosis was not as complicated as others. A patient with pre-existing Graves' disease, confirmed by TSH receptor antibody had a palpable pelvis mass, which was proved later to be struma ovarii. In this presented patient, even with obvious clinical presentation of thyrotoxicosis and ovarian tumor, concomitant hyperthyroidism remained the first differential diagnosis due to its higher incidence. She was referred for ^{131}I ablation due to PTU

hypersensitivity. The percentage of 24-hour ^{131}I uptake for calculating ^{131}I dosage was expected to be high, but the result was surprisingly normal. Her contrast-enhanced abdominal CT scan was done about 3 weeks before and she had been treated with Lugol's solution within the last 3 weeks. Iodine contents in these substances could potentially make ^{131}I uptake lower than it should be. However, as she had history of ovarian tumor, ^{131}I whole body scan was performed to exclude struma ovarii.

On ^{131}I whole body scan, there was intense uptake in pelvic region at which additional SPECT/CT imaging of pelvis proved that radioactivity was within the ovarian mass, which was suggestive of struma ovarii. ^{131}I whole body scan also showed unexpected intense ^{131}I uptake in the thyroid gland. According to the pathogenesis of struma ovarii, overproduction of thyroid hormone from ectopic thyroid tissue is supposed to suppress secretion of TSH from pituitary gland resulting in low radioiodine uptake of the thyroid gland. With this reason, presence of intense thyroid uptake on pre-operative ^{131}I whole body scan should be from co-existing hyperthyroidism.

Owing to clinical thyrotoxicosis and positivity of high specific thyroid antibody as TSH receptor antibody, Graves' disease was a prime diagnosis. Although physical examination showed neither thyroid enlargement nor any specific signs of Graves' disease, these are not uncommon for a patient with coexistence of struma ovarii and Graves' disease. According to studies by Smith¹² and Brown et al,¹³ incidence of thyroid goiter in patients with struma ovarii was only 16.3% and 41.7%, respectively.

In a struma ovarii patient, thyrotoxicosis results from ectopic thyroid tissue in ovary. Thus, symptoms will disappear after surgical resection of hormone-producing tumor. On the other hand, a major contributing factor of thyroid hormone overproduction in coexisting disease is circulating TSH receptor antibody which stimulates thyroid tissue in both ovary and thyroid.¹⁴ After surgical removal of struma ovarii, circulating TSH receptor antibody still exists. Persistence of thyrotoxicosis following surgery is consequently possible. Regarding to our patient, even though 24-hour

^{131}I uptake and ^{131}I thyroid scan performed 4 days after surgery were normal, serial laboratory testings finally revealed overt thyrotoxicosis 2 months later. The ^{131}I whole body scan done at the same period demonstrated increased radiotracer uptake of the thyroid gland without abnormal radiotracer accumulation in the other parts of the body. This proved the existence of hyperthyroidism. However, authors believed that the major source of excessive thyroid hormone in this patient was hyperfunctioning thyroid tissue in struma ovarii. Hormone produced from hyperfunctioning thyroid gland may be minority because 1) severity of post-operative thyrotoxicosis was only slight, 2) thyrotoxicosis gradually developed following surgical resection of struma ovarii, and 3) patient had no pathognomonic signs of Graves' disease – i.e. Graves' ophthalmopathy or diffuse enlarged thyroid gland.

In summary, diagnosis of coexistent struma ovarii and Graves' disease is rather complicated, but there are some clues. In elderly with ovarian tumor and thyrotoxicosis, struma ovarii should be a differential diagnosis. Radioiodine uptake and whole body scan should be considered. In case of struma ovarii alone, the 24-hour uptake should be low. However, 24-hour uptake may be normal or slightly high in a case of coexistent Graves' disease. On the radioiodine whole body scan, intense uptake in ovarian tumor is a diagnosis of struma ovarii and high uptake of the thyroid gland helps discriminate coexistent Graves' disease from struma ovarii alone. Lastly, thyrotoxic state could be persistent in coexisting disease, but should be resolved in struma ovarii alone.

REFERENCES

1. Yoo SC, Chang KH, Lyu MO, Chang SJ, Ryu HS, Kim HS. Clinical characteristics of struma ovarii. *J Gynecol Oncol* 2008;19:135-8.
2. Marcus CC, Marcus SL. Struma ovarii. A report of 7 cases and a review of the subject. *Am J Obstet Gynecol* 1961;81: 752-62.

3. March DE, Desai AG, Park CH, Hendricks PJ, Davis PS. Struma ovarii: Hyperthyroidism in a post-menopausal woman. *J Nucl Med* 1998;29:263-5.
4. Lazarus JH, Richards AR, Macpherson MJ, Dinnen JS, Williams ED, Owen GM, et al. Struma ovarii: A case report. *Clin Endocrinol* 1987;27:715-20.
5. Kempers RD, Dockerty MB, Hoffman DL, Bartholomew LG. Struma ovarii-ascitic, hyperthyroid, and asymptomatic syndromes. *Ann Intern Med* 1970;72:883-93.
6. Kung AWC, Ma JTC, Wang C, Young RTT. Hyperthyroidism during pregnancy due to coexistence of struma ovarii and Graves' disease. *Postgrad Med J* 1990;66:132-3.
7. Bayot MR, Chopra IJ. Coexistence of struma ovarii and Graves' disease. *Thyroid* 1995;5:469-71.
8. Nodine JH, Maldia O. Pseudostruma ovarii. *Obstet Gynecol* 1961;17:460-3.
9. Teale E, Gouldsbrough DR, Peacey SR. Graves' Disease and Coexisting Struma Ovarii: Struma Expression of Thyrotropin Receptors and the Presence of Thyrotropin Receptor Stimulating Antibodies. *Thyroid* 2006;16:791-3.
10. Sitaswan T, Hanamornroongruang S, Peerapatdit T, Thongtang N. Coexistence of Graves' disease and unilateral functioning Struma ovarii: a case report. *BMC Endocr Disord* 2015;15:68.
11. Mimura Y, Kishida M, Masuyama H, Suwaki N, Kodama J, Otsuka F, et al. Coexistence of Graves' Disease and Struma Ovarii: Case Report and Literature Review. *Endocr J* 2001;48:255-60.
12. Smith FG. Pathology and physiology of struma ovarii. *Arch Surg (Chicago)* 1946;53:603-26.
13. Brown WW, Shetty KR, Rosenfeld PS. Hyperthyroidism due to struma ovarii: Demonstration by radioiodine scan. *Acta Endocrinol* 1973;73:266-72.
14. Lefot G, Lommenges-Ducus M, Denechand M, Rivel J, Latapie J. Goitre ovation au cours d'une maladie de Basedow. *La Nouvelle Presse Medicale* 1981;10:2209-10.