Turk J Endocrinol Metab. 2021;25:243-248

Toxic Multi Nodular Goiter and Struma ovarii Coexistence: Report of a Rare Case

Toksik Multinodüler Guatr ve Struma Ovarii Birlikteliği: Nadir Bir Olgu Sunumu

Sahar Karimpour REYHAN, Roya SHIRZAD, Nooshin SHIRZAD*, Farid AZMOUDEH-ARDALAN**, Mahboobeh HEMMATABADI

Department of Endocrinology, Vali-Asr Hospital, Endocrinology and Metabolism Research Center, Imam Khomeini Complex Hospital, Tehran University of Medical Sciences, Tehran, IRAN
*Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, IRAN
**Department of Pathology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, IRAN

Abstract

Hyperthyroidism is a common disease that often presents with tremors, tachycardia, anxiety, and weight loss. Hyperthyroidism may be caused by several diseases. Ectopic hyperthyroidism that results from excess thyroid hormone synthesis arises from outside the thyroid gland. Struma ovarii is a famous form of this type of hyperthyroidism, which is extremely rare and arises from ectopic thyroid tissue in the ovarian neoplasm. Here, we present a case of a middle-aged woman with established thyrotoxicosis, who was referred owing to the recurrence of thyrotoxicosis after thyroidectomy. Finally, oophorectomy was performed, and she was diagnosed with Struma ovarii. Thus, the clinicians should consider Struma ovarii in women with thyrotoxicosis, without goiter or evidence of Graves' disease.

Keywords: Thyrotoxicosis; nodular goiter; struma ovarii

Özet

Hipertiroidizm, sıklıkla tremor, taşikardi, anksiyete ve kilo kaybıyla ortaya çıkan yaygın bir hastalıktır. Hipertiroidizme çeşitli hastalıklar neden olabilir. Aşırı tiroid hormonu sentezinin yol açtığı ektopik hipertiroidizm, tiroid bezi dışında bir odaktan kaynaklanır. Struma ovarii bu tip hipertiroidizmin en bilinen şeklidir, son derece nadir görülür ve yumurtalık neoplazmasındaki ektopik tiroid dokusundan kaynaklanır. Burada, tiroidektomi sonrası tirotoksikozun tekrarlaması nedeniyle sevk edilen orta yaşlı bir kadın olguyu sunduk. Hastaya ooforektomi yapıldı ve Struma ovarii teşhisi kondu. Guatr veya Graves hastalığı kanıtı olmayan tirotoksikozlu kadınlarda Struma ovarii akla gelmelidir.

Anahtar kelimeler: Tirotoksikoz; nodüler guatr; struma ovarii

Introduction

Hyperthyroidism is a common disease that often presents with tremors, tachycardia, high output heart failure, anxiety, and weight loss (1-3). Hyperthyroidism may be caused by several diseases. Ectopic hyperthyroidism, which results from excess thyroid hormone synthesis, arises from outside of the thyroid gland. Struma ovarii, a famous form of this type of hyperthyroidism, is commonly mostly

Address for Correspondence: Mahboobeh HEMMATABADI, Department of Endocrinology, Vali-Asr Hospital, Endocrinology and Metabolism Research Center, Imam Khomeini Complex Hospital, Tehran University of Medical Sciences, Tehran, IRAN
Phone: :98-21-66911294 **E-mail:** hemmatabadi55@yahoo.com

Peer review under responsibility of Turkish Journal of Endocrinology and Metabolism.

Received: 06 Jan 2021 **Received in revised form:** 28 Mar 2021 **Accepted:** 17 Apr 2021 **Available online:** 18 Jun 2021

DOI: 10.25179/tjem.2021-81052

a part of the multi-tissue proliferation of thyroid from all three embryonal germ layers and can secrete thyroid hormones that lead to hyperthyroidism. Approximately 5-8% of these tumors are clinically hyperthyroid. It could be benign or malignant, with 5-10% of cases being malignant (4,5).

Herein, we present a case of Struma ovarii where the patient was referred to our clinic owing to the recurrence of thyrotoxicosis after thyroidectomy.

Case Report

A 54-year-old woman was admitted to our hospital with the complaint of 16 kg weight loss, palpitation, fatigue, tremor, and increased appetite within the previous 6 months. She had a history of polyuria, nocturia, and lower abdomen discomfort during this period. Her menopause had occurred 2 years ago. She had a history of toxic multinodular goiter disease for 30 years, which had resolved with total thyroidectomy. The latter was performed the previous year due to goiter enlargement and thyrotoxicosis. After surgery, the patient was prescribed Levothyroxine 100 µg daily. Her past medical history revealed that the patient was diabetic and hypertensive. Both her mother and sister had a multinodular goiter. The patient was prescribed metformin 500 mg twice daily, levothyroxine 100 µg, losartan 50 mg, acetylsalicylic acid 80 mg daily, propranolol 20 mg three times daily, and amlodipine 5 mg daily. On physical examination, the patient's blood pressure was 140/90 mm/Hg, pulse rate 110 beats/min, and body mass index was 22.5 kg/m2. During her neck examination, the scar of thyroidectomy was observed without any evidence of lymphadenopathy. Abdominal examination revealed a palpable mass in the midline (approximately 16 cm in diameter). There were fine tremors in her hand fingers, and the muscle strength in upper and lower extremities was four-fifths.

Based on physical findings, a significant weight loss, large pelvic mass in her pelvic magnetic resonance imaging before surgery, and thyrotoxicosis state were detectedi (imaging and laboratory test results are summarized in Table 1 and Figure 1, Figure 2, Figure 3). Other biochemical investigations showed uncontrolled diabetes mellitus (FPG: 410; HbA1C: 10.1), anemia, and elevated serum alkaline phosphatase.

Table 1. Laboratory investigations of the introduced patient before and after tumor resection.

Biochemical parameters	After thyroidectomy (1 week later)	After adenexectomy	After adnexectomy (1 month later)
TT4 (mcg/dL)	27.8	2.6	7.8
TT3 (ng/mL)	2.29	<0.40	1.30
TSH (mIU/L)	<0.005	0.46	2.10
TGB (ng/mL)	>55		
Anti-hTG (kU/L	3.8		
Anti-TPO (kU/L)	4.1		

Next, the source of her thyrotoxicosis was determined. Ultrasonography of the patient's thyroid bed and cervical region, thyroid scan, and chest computed tomography (CT) scan revealed no evidence of thyroid gland remnant or ectopic thyroid in her neck and chest, with no evidence of factitious thyrotoxicosis (thyroglobulin level was increased). Scan study after intravenous injection of 10 mCi 99mTc pertechnetate was negative for functioning thyroid tissue in the thyroid bed and pelvis, possibly according to the significantly large and heterogeneous mass. Struma ovarii was suspected according to clinical findings, and surgical resection of the tumor was planned.

Preoperative management for prevention of thyroid storm was performed using methimazole 60 mg daily, dexamethasone 6 mg daily, cholestyramine powder 12 g daily, propranolol 80 mg daily, Lugol's iodine solution 24 drops daily, and lithium 900 mg daily owing to her resistant thyrotoxicosis. Also, insulin therapy using Lantus and Novorapid insulin was prescribed due to uncontrolled hyperglycemia. Finally, tumor resection was performed after clinical and laboratory euthyroidism (Figure 3).

The resected right salpingo-oophorectomy specimen was submitted to the pathology department in a fresh state for intraoperative histopathologic evaluation. It consisted of a lobulated pink brownish mass measuring 17×15×10 cm with an intact capsule and an attached fallopian tube measuring 11.5 cm in length and 0.5 cm in diameter. The dissected surface was multicystic com-

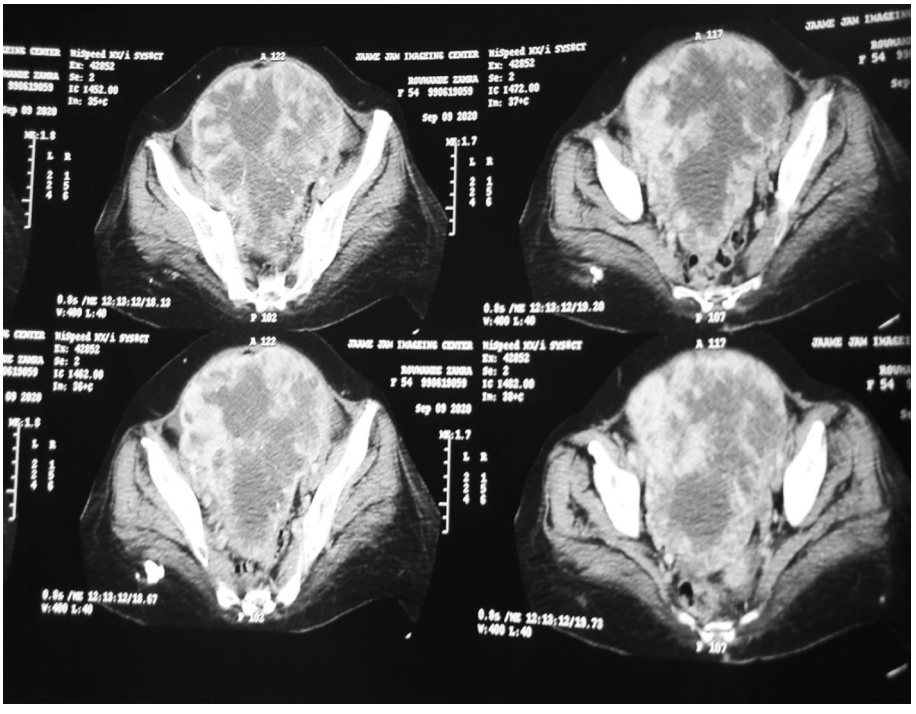

Figure 1. Pelvic magnetic resonance imaging shows enhanced multilocuolated solid mass at the anterior aspect of the uterus measuring about 199*164*116 mm with pressure effect on the uterus with posterior displacement due to primary ovarian tumor. There are no significant ascites or enlargement of the pelvic lymph or para-aortic nodes.

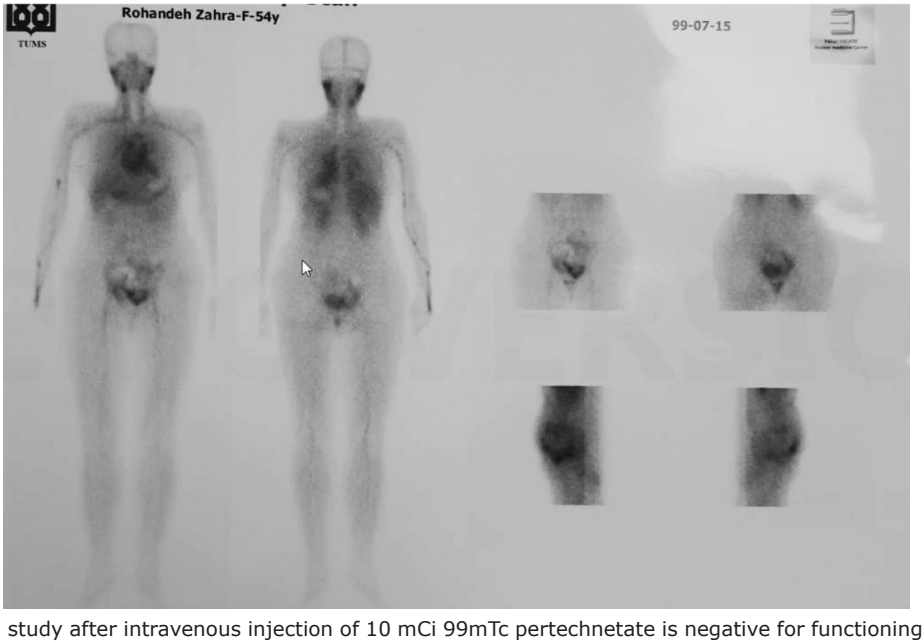

Figure 2. Scan study after intravenous injection of 10 mCi 99mTc pertechnetate is negative for functioning thyroid tissue in the thyroid bed and pelvis.

posed of cysts of varying sizes containing clear yellow-brownish fluid. The microscopic examination of multiple sections prepared from the mass showed exclusively thyroid tissue composed of follicles of different sizes lined by a layer of cuboidal bland-looking cells. The follicles contained colloids. There was no evidence of malignancy (Figure 4).

Figure 3. A very large well-circumference multilobulated right ovarian mass with cystic lesions.

Therefore, she was diagnosed with Struma ovarii.

On the follow-up visit after 1 week, the patient was in good condition and her thyroid function tests were: thyroid-stimulating hormone (TSH)=0.46 mIU/L, total thyroxine (TT4)=2.60 mcg/dL, and total triiodothyronine (TT3)=<0.40 ng/mL. Therefore, she was prescribed Levothyroxine 100 µg daily, and due to the well-controlled blood glucose levels, the patient's insulin dose was decreased. Finally, thyroid function tests were in the normal range after 1 month (Table 1).

URE 4: A) Low power scanning view shows exclusively thyroid tissue with areas of fibrous scarring (asterisk). Hematoxylin and eosin (H&E, x6) stain.

B) Follicles of variable sizes are depicted in this image. The follicles are lined by a layer of bland-looking cuboidal cells and containing pinks colloid (H&E, x400) stain.

Discussion

Overt thyrotoxicosis classic symptoms include tremor, tachycardia, heat intolerance, anxiety, weight loss, diarrhea, menstrual disorders, and gynecomastia (6). Common causes of thyrotoxicosis are Graves' disease; Hashitoxicosis; toxic adenoma; toxic multinodular goiter with increased radioiodine uptake; and disorders with near absent radioiodine uptake such as thyroiditis, factitious thyrotoxicosis, and ectopic sources of thyroid hormone secretions like Struma ovarii (7).

In general, serum TSH is suppressed and free T4 and/or T3 are elevated in hyperthyroid patients (8).

Struma ovarii is a mature thyroid tissue in ovarian teratomas, which consists of more than half of the overall tissue. The prevalence is about 2.7% of all ovarian teratomas and 1% of all ovarian tumors (9). It could be benign or malignant, and 5-10% of cases are malignant (4,5). The thyroid component is derived from an ovarian germ cell layer. In the literature review, there are cases of Struma salpingii, Struma uteri, and Struma testis (10).

Clinical manifestations of this rare disorder include abdominal pain, bloating, abnormal menses, pelvic mass, and thyrotoxicosis (11,12). Only 5-8% of cases are associated with clinical hyperthyroidism. These tumors are often diagnosed incidentally after surgery (9). The thyroid gland of these patients is not enlarged, and radioiodine uptake is low or absent in their thyroid gland; however, it often accumulates in their pelvis

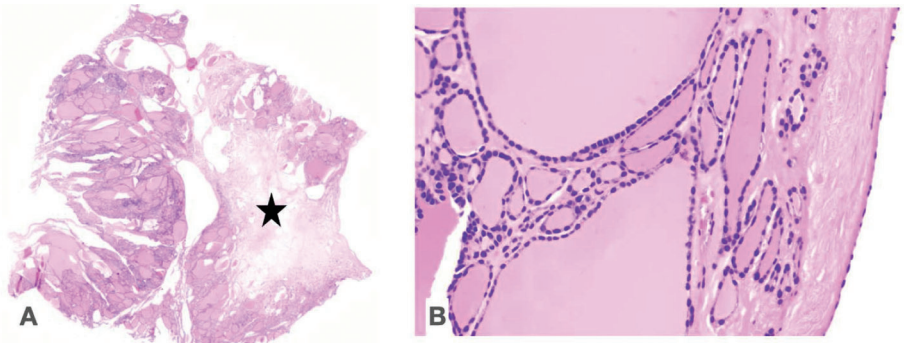

Figure 4. A) Low power scanning view shows exclusively thyroid tissue with areas of fibrous scarring (asterisk). Hematoxylin and eosin (H&E, x6) stain.
B) Follicles of variable sizes are depicted in this image. The follicles are lined by a layer of bland-looking cuboidal cells and containing pinks colloid (H&E, x400) stain.

(10,13). The negative T99 scan of our patient may be due to high vascularity of the tumor and high background in the pelvis; the condition reported previously (14). In this situation, we can perform an iodine scan; however, it might increase the risk of thyroid storm, particularly in our patient with severe thyrotoxicosis. Furthermore, a chest CT scan was performed to roll out the undiagnosed substernal goiter in this patient.

It is more often diagnosed in women aged between 22 to 70 years (15) and generally presents with a pelvic mass. Women with Struma ovarii and thyrotoxicosis rarely have goiter simultaneously (16). This could be explained as stimulation of thyroid tissue in the ovary by serum thyroid stimulating immunoglobulins or parallel formation of thyroid autonomous function in ovary along with toxic nodular goiter (17) and even rarely differentiated thyroid cancers could occur in struma ovarii (12). Surgical resection of the ovarian mass is the treatment of choice (18). Moreover, the patient had a manifestation of Struma ovarii after successful thyroidectomy that was clinically euthyroid after 6 months of follow-up and negative Technetium scan.

Struma ovarii should be considered in women with thyrotoxicosis, and careful abdominal physical examination should be performed before thyroidectomy in these patient groups.

Acknowledgements

We acknowledge all Hospital Staff who served the patient.

Source of Finance

The patient consented to the publication of her data and images.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Mahboobeh Hemmatabadi; Design: Mahboobeh Hemmatabadi, Nooshin Shirzad; Control/Supervision: Mahboobeh Hemmatabadi; Data Collection and/or Processing: Roya Shirzad; Analysis and/or Interpretation: Farid Azmoudeh-Ardalan; Literature Review: Sahar Karimpour Reyhan; Writing the Article: Sahar Karimpour Reyhan; Critical Review: Nooshin Shirzad; Materials: Mahboobeh Hemmatabadi.

References

1. Osuna PM, Udovcic M, Sharma MD. Hyperthyroidism and the heart. Methodist Debakey Cardiovasc J. 2017;13:60-63. [Crossref] [PubMed] [PMC]
2. Franklyn JA. The management of hyperthyroidism. N Engl J Med. 1994;330:1731-1738. Erratum in: N Engl J Med 1994;331:559. [Crossref] [PubMed]
3. Trzepacz PT, Klein I, Roberts M, Greenhouse J, Levey GS. Graves' disease: an analysis of thyroid hormone levels and hyperthyroid signs and symptoms. Am J Med. 1989;87:558-561. [Crossref] [PubMed]
4. LiVolsi VA, Baloch ZW. The Pathology of hyperthyroidism. Front Endocrinol (Lausanne). 2018;9:737. [Crossref] [PubMed] [PMC]
5. Kisakol G, Gonen S, Kaya A, Dikbas O, Sari O, Kiresi D, Gungor K, Karakurt F. Dual ectopic thyroid gland with Graves' disease and unilateral ophthalmopathy: a case report and review of the literature. J Endocrinol Invest. 2004;27:874-877. [Crossref] [PubMed]
6. Calissendorff J, Mikulski E, Larsen EH, Möller M. A prospective investigation of graves' disease and selenium: thyroid hormones, auto-antibodies and self-rated symptoms. Eur Thyroid J. 2015;4:93-98. [Crossref] [PubMed] [PMC]
7. Reid JR, Wheeler SF. Hyperthyroidism: diagnosis and treatment. Am Fam Physician. 2005;72:623-630. [PubMed]
8. Topliss DJ, Eastman CJ. 5: Diagnosis and management of hyperthyroidism and hypothyroidism. Med J Aust. 2004;180:186-193. [Crossref] [PubMed]
9. Rockson O, Kora C, Ramdani A, Basma A, Bouhout T, Serji B, El Harroudi T. Struma ovarii: two case reports of a rare teratoma of the ovary. J Surg Case Rep. 2020;2020:rjaa493. [Crossref] [PubMed] [PMC]
10. Chu YK. Ectopic thyroid on scintigraphy. Hong Kong J Radiol. 2018;21:143-149. [Crossref]
11. Roth LM, Talerman A. The enigma of struma ovarii. Pathology. 2007;39:139-146. [Crossref] [PubMed]
12. Middelbeek RJW, O'Neill BT, Nishino M, Pallotta JA. Concurrent intrathyroidal thyroid cancer and thyroid cancer in struma ovarii: a case report and literature review. J Endocr Soc. 2017;1:396-400. [Crossref] [PubMed] [PMC]
13. Young RH. New and unusual aspects of ovarian germ cell tumors. Am J Surg Pathol. 1993;17:1210-1224. [Crossref] [PubMed]
14. Yeh EL, Meade RC, Ruetz PP. Radionuclide study of struma ovarii. J Nucl Med. 1973;14:118-121. [PubMed]

15. Iranparvar Alamdari M, Habibzadeh A, Pakrouy H, Chaichi P, Sheidaei S. An unusual presentation of a papillary thyroid carcinoma in the struma ovarii in a 10 year-old girl: A case report. Int J Surg Case Rep. 2018;51:218-220. [Crossref] [PubMed] [PMC]
16. Anagnostou E, Polymeris A, Morphopoulos G, Travlos A, Sarantopoulou V, Papaspyrou I. An unusual case of malignant struma ovarii causing thyrotoxicosis. Eur Thyroid J. 2016;5:207-211. [Crossref] [PubMed] [PMC]
17. Mimura Y, Kishida M, Masuyama H, Suwaki N, Kodama J, Otsuka F, Kataoka H, Yamauchi T, Ogura T, Kudo T, Makino H. Coexistence of Graves' disease and struma ovarii: case report and literature review. Endocr J. 2001;48:255-260. [Crossref] [PubMed]
18. Rosenblum NG, LiVolsi VA, Edmonds PR, Mikuta JJ. Malignant struma ovarii. Gynecol Oncol. 1989; 32:224-227. [Crossref] [PubMed]