

Struma Ovarii In Our Series: A Retrospective Study

Kliniğimizde Struma Ovarii Olguları: Retrospektif bir inceleme

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ÖZET

Objective: To evaluate clinical and pathological features of struma ovarii cases retrospectively.

Material and Methods: The present study included 8 patients reported with pathology of struma ovarii in the medical records. Archive slides were reviewed for diagnostic confirmation, regarding patterns and accompanying thyroid pathologies. Extraovarian dissemination of thyroid tissue, presence of accompanying other ovarian pathologies and that how many cases were composed of pure thyroid tissues were investigated. The clinical features were determined by screening the patient files. Data such tumor size and lateralization were obtained from the pathology reports.

Results: The age of the patients ranged between 45-85 years. The most common hospital admission complaint was palpable mass. Five patients had right ovarian struma ovarii. The tumor diameter ranged between 9-15 cm. Tumor was limited by ovary in all the cases. All the struma ovarii cases demonstrated follicular pattern in the microscopic examination. No thyroid-associated malignancy was encountered. Tumor was composed of pure thyroid tissue in 6 cases. We assessed two cases as proliferative struma ovarii. Recurrence was detected during follow-ups in none of the cases.

Conclusion: Struma ovarii is the most commonly seen ovarian monodermal teratoma and mostly benign. The presence of malignancy associated with thyroid should be eliminated by a careful histopathological examination in order not to hinder the chance of additional treatment.

Key words: struma ovarii, monodermal teratoma, germ cell tumor

ABSTRACT

Amaç: Struma ovarii olgularının klinik ve patolojik özelliklerini retrospektif olarak değerlendirmek

Gereç-Yöntem: Bu çalışmaya tıbbi kayıtlarda struma ovarii tanısı olan 8 hasta dahil edildi. Arşiv preparatları tanı confirmasyonu, izlenen paternler ve eşlik eden tiroid patolojileri için gözden geçirildi. Tiroid dokusunun over dışı yayılımı, eşlik eden diğer over patolojilerinin varlığı ve kaç tümörün saf tiroid dokusundan oluştuğu araştırıldı. Klinik özellikler hasta dosyaları taranarak belirlendi. Tümör boyutu ve lateralizasyon gibi veriler patoloji raporlarından elde edildi.

Bulgular: Hastaların yaşı 45-85 arasında değişmekteydi. En sık hastaneye başvuru şikayeti ele gelen kitleydi. Beş hastada sağ overde struma ovarii saptadık. Tümör çapları 9-15 cm arasında değişmekteydi. Tüm olgularda tümör overler ile sınırlıydı. Tüm struma ovarii olguları mikroskopik incelemede foliküler patern gösterdi. Altı olguda tümör sadece tiroid dokusundan oluşuyordu. Tiroidle ilişkili malignite ile karşılaşılmadı. İki olguyu proliferatif struma ovarii olarak değerlendirdik. Hiçbir olguda takiplerde nüks saptanmadı.

Sonuç: Struma ovarii en sık görülen overyan monodermal teratomudur ve çoğunlukla benignidir. Tiroid ile ilişkili malignite varlığı, ek tedavi şansını engellemek için dikkatli bir histopatolojik inceleme ile ekarte edilmelidir.

Anahtar Kelimeler: Struma ovarii, monodermal teratom, germ hücreli tümör

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INTRODUCTION:

Germ cell tumors make up approximately 15-20% of all ovarian tumors and a major part of germ cell tumors are teratomas (1). Struma ovarii (SO) is the most common ovarian monodermal teratoma (2) and represents 0.5-1% and 2-5% of all ovarian tumors and teratomas, respectively (3, 4). Besides normal-appearing thyroid follicles with microscopically varying sizes, different histological patterns also have been identified. These include diffuse, trabecular and pseudotubular patterns as well as small clusters of tumor cells (2). Thyroid tissue may be found in 5-20% of the mature teratomas, however, the presence of thyroid tissue more than $\geq 50\%$ of overall tumor is required to be termed as SO. Also the presence of thyroid tissue below 50% with accompanying thyroid-associated malignancy is adequate to diagnose SO (5, 6, 7). SO cases are mostly benign while malignancy rate is 5-10% (4, 6, 8). Malignant SO makes up 0.01% of all ovarian tumors (8). A case with characteristics of thyroid carcinomas is diagnosed to be malignant SO (9). The most common malignancy is papillary thyroid carcinoma (PTC) followed by follicular carcinoma (FC) as the most common second malignancy (4, 5). Roth et al. have identified "highly differentiated follicular carcinoma of ovarian origin (HDFCO)" which is the extraovarian dissemination of normal-appearing thyroid tissue and this entity was previously known as peritoneal strumosis (5). SO may be detected in all age groups, particularly between 4th-6th decades of the lifespan (1, 8).

We have aimed to retrospectively analyze the struma ovarii cases diagnosed in our hospital.

MATERIALS-METHOD:

The present study included 8 patients reported with pathology of SO between 2006-2017 in the medical records saved in Medical Faculty Hospital of Hatay Mustafa Kemal University. Archive slides were reviewed for diagnostic confirmation. The diagnosis was based on the presence of tumor tissue comprising of $\geq 50\%$ thyroid tissue or $< 50\%$ thyroid tissue accompanied with thyroid-associated malignancy (5). The slides were analyzed in terms of patterns (follicular/diffuse/trabecular/pseudotubular/small clusters of tumor cells) and accompanying thyroid pathologies (tumoral/non-tumoral) if present. The diagnosis of papillary thyroid carcinoma (PTC) was based on the nuclear characteristics of PTC while the diagnosis of follicular carcinoma required the presence of lymphovascular or capsular invasion without nuclear characteristics of PTC. The diagnostic term "proliferative SO" was used in the presence of tightly packed thyroid follicles or papillary structures without nuclear characteristics of PTC. We have evaluated the cases regarding the presence of extraovarian dissemination of thyroid tissue and accompanying other ovarian pathologies as well as that how many cases included thyroid tissues. Data such as patient age, patient complaint for hospital admission, thyroid hormone levels, CA125 levels, radiological features of the tumors (solid/cystic), type of the performed surgery and presence of recurrence were reviewed by screening the patient files. Data such tumor size and lateralization (right/left ovary?) were obtained from the pathology reports.

The present study was approved by Hatay Mustafa Kemal University Board of Ethics on Noninvasive

Table 1. The Clinical features of Tumors

Case No	Age	Symptoms	Radiology	Surgical Procedure	Tumor Location	Tumor Size (cm)
1	46	None	NRR	TAH+BSO	Left	10
2	74	Pelvic mass	Heterogenous mass	TAH+BSO	Right	11
3	74	None	NRR	Right USO	Right	11
4	54	Pelvic mass	Cystic mass	TAH+BSO	Left	14
5	64	Abdominal pain	NRR	TAH+BSO	Left	12
6	45	Vaginal bleeding	Cystic mass	TAH+BSO	Right	10
7	85	Pelvic mass	Heterogenous mass	TAH+BSO	Right	15
8	46	Pelvic mass	Cystic mass	TAH+Right USO	Right	9

NRR: no radiologic report

Table 2. The Microscopic Features of Tumors

Case No	Age	Symptoms	Radiology	Surgical Procedure
1	Follicular	None	Mature cystic teratoma in the right ovary	SO
2	Follicular	Cartilaginous tissue	None	SO
3	Follicular	Mature adipose tissue	None	SO
4	Follicular	None	None	Proliferating SO
5	Follicular	None	None	SO
6	Follicular	None	Mature cystic teratoma and corpus luteum cyst in the left ovary, serous cyst in the right ovary	SO
7	Follicular	None	Mature cystic teratoma in the left ovary, serous cystadenoma in the right ovary	SO
8	Follicular	None	None	Proliferating SO

Clinical Human Studies Ethics Committee (Dated: 04.06.2020 - Approval No: 02).

RESULTS:

We analyzed totally 8 cases of struma ovarii. The ages of the patients ranged between 45-85 years while mean age±standard deviation was 61±15.48 years. Palpable mass, abdominal pain and vaginal bleeding were the baseline complaints in 4, 1 and 1 patients for admission to the clinic, respectively. No complaint was reported in two patients. Thyroid hormone levels of the patients before surgery were unavailable in the medical records; thyroid function tests were postoperatively performed in only one patient and resulted slightly elevated T4 level. CA125 value of 1 patient could be reached from the medical records and that was within normal limits. The ultrasonographies (USG) of the patients revealed multiloculated cystic mass in the adnexal field of three patients while two patients had heterogeneous masses. USG examinations of the three patients could not be obtained. The surgical procedures such as total abdominal hysterectomy+bilateral salpingo-oophorectomy (TAH+BSO), TAH+right salpingo-oophorectomy (USO) and right USO were performed in 6, 1 and 1 patients, respectively. Five patients (62.5%) had right ovarian SO while left ovarian SO was detected

in 3 (37.5%) patients. Mean tumor diameter±standard deviation was 11.5±2.07 (ranging between 9-15 cm). The clinical features of the tumors were summarized in Table 1. All the SO cases demonstrated follicular pattern under the microscopic examination. Various sizes of follicular structures including colloids were encountered as lined by uniform thyrocytes (Figure 1, 2). Tumor was composed of pure thyroid tissue in 6 (75%) cases whereas thyroid tissue accompanied with cartilage and mature adipose tissue were also present in 1 and 1 cases, respectively. Tumor was limited by ovary in all the cases; we detected no extraovarian dissemination. No thyroid-associated malignancy (PTC or FC) was encountered. We evaluated two cases (25%) to be proliferative SO (Figure 3). In the analysis of the accompanying ovarian pathologies; we have identified contralateral ovarian mature cystic teratoma, ipsilateral ovarian serous cyst and ipsilateral ovarian serous cystadenoma in the ovary in 3, 1 and 1 cases, respectively. The microscopic characteristics of tumors were summarized in Table 2.

The mean follow-up period (mean±standard deviation) was 72.87±31.71 (ranging 34-118) months in our 8 cases. The follow-up duration of two cases with proliferative SO were 74 and 100 months, respectively. Recurrence was detected during follow-up periods in none of the cases.

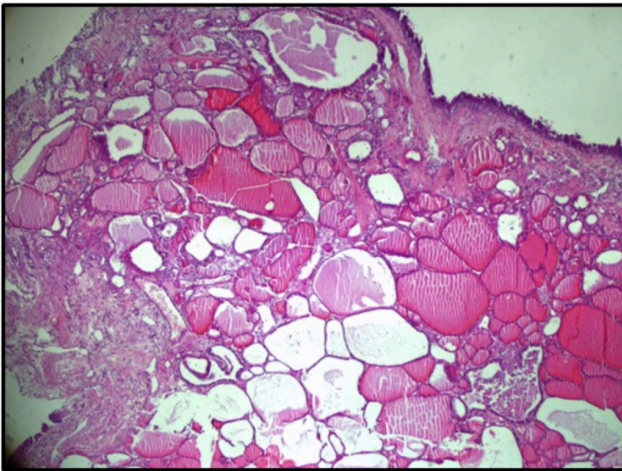


Figure 1: Various sizes of follicular structures including colloids (H+E, x40)

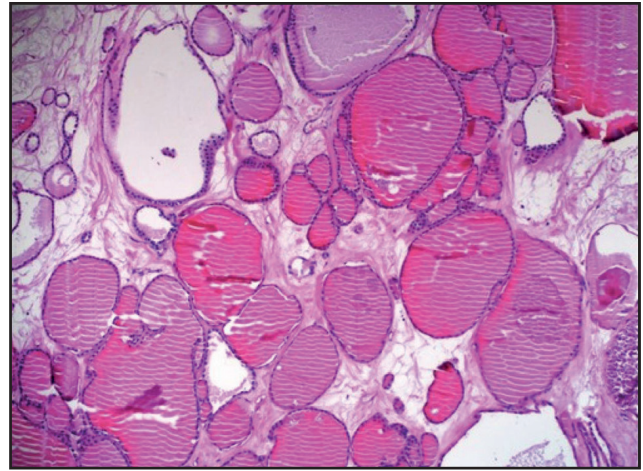


Figure 2: Various sizes of follicular structures including colloids (H+E, x100)

DISCUSSION:

SO is defined as the ovarian goitre that completely or predominantly includes thyroid tissue ($\geq 50\%$). This diagnostic term also involves the mature teratoma cases accompanied with thyroid-associated malignancy (5). It has been first identified in 1889 by Boettlin (9,10). SO may be detected in all age groups, particularly between 4th-6th decades of the lifespan (1,8,9). It is usually observed unilaterally accompanying contralateral mature cystic teratoma and cystadenoma may be present in some cases (11, 12). All of our cases were also unilateral and tumor was localized in the right ovary in 62.5% of the cases. In our study, we have analyzed the ovaries with respect to accompanying pathologies. We have encountered contralateral ovarian mature cystic teratoma, ipsilateral ovarian serous cyst and ipsilateral ovarian serous cystadenoma in the ovary of 3, 1 and 1 cases, respectively. Age of the patients ranged between 45-85 years in our study. That age range was higher compared with the studies in literature.

The patients mostly apply to the clinic with the complaint of unilateral palpable mass, whereas some patients may have acute abdomen, vaginal bleeding or menstrual irregularity (4, 13). On the other hand, 40% of the patients are asymptomatic (13). Ascites or pleural effusion (Pseudo-Meigs Syndrome) may be detected in some patients, laboratory examination may manifest hyperthyroidism and elevated levels of serum CA125 (6, 11). CA125 has a low clinical importance since it may increase in both benign and malignant SO cases. Increased serum CA125 level is due to presence of ascites rather than tumor in the patients with SO (14). The symptoms and findings of thyrotoxicosis

were determined in only 5-8% of the cases despite dominance of thyroid tissue (1, 7). In our case series, the most common cause for hospital admission was unilateral palpable mass consistently with the literature. None of our cases indicated a symptom of hyperthyroidism, because, thyroid function tests were not performed preoperatively. CA125 value of 1 patient could be reached in the medical records and found within normal limits.

Malignant SO cases are encountered in the 5th-6th decades of the lifespan. The patients are mostly asymptomatic, the most common admission cause is unilateral palpable mass (3, 4). The findings of hyperthyroidism such as weight loss, fatigue, heat intolerance, tremor and tachycardia are rare (9). The clinical picture of ascites and pleural effusion is more commonly associated with benign SO, however, it may be observed in also malignant SO cases, although rare (13). Also, we have analyzed our case series with respect to accompanying malignancy, none of our cases manifested a finding in favor of malignancy.

SO cases are usually macroscopically cystic, they may include also solid fields. Their outer surface is usually smooth and section surface appears shiny due to inclusion of thyroid tissue (6, 12). Microscopic images show various sizes of follicles that include colloid and are lined by a single-row epithelium. The use of diagnostic term "proliferative SO" is recommended in the presence of crowded and tightly packed thyroid follicles without malignant characteristics (12). Different histological patterns of SO also have been described. Those include diffuse, trabecular and pseudotubular patterns as well as small clusters of tumor cells. Follicular

pattern is a differentiated form. Other patterns do not include colloids and follicular formation and are the dedifferentiated forms because of these characteristics (2). All the cases in our series had a follicular (micro or macro) pattern and two (25%) of our cases had proliferative SO.

The most common malignancy which develops associated with SO is PTC followed by FC (1,4,5). The fact whether diagnostic criteria for PTC and FC which develop in the thyroid gland are valid in the diagnosis of the tumors developing associated with SO is controversial (1,5,15). The rarity of these lesions and absence of an uniform criterion create difficulty in diagnosis of these lesions (3, 12). Nevertheless, many studies have defended the diagnostic validity of the diagnosis based on the histopathological criteria for the thyroid carcinoma that develops in the thyroid gland (16). Approximately 5-23% of the malignant SO cases metastasize; the most frequent metastatic target is abdominal cavity, however, metastases may be encountered in also liver, lung, brain, bones and contralateral ovary (1, 17). On the other side, HDFCO is a rarely seen thyroid-type carcinoma developing associated with SO and characterized by the presence of benign-appearing thyroid follicles that spread over the ovaries. It is biologically malignant because of its metastatic potential (18). All genetic anomalies specific for cancer types developing from thyroid gland have been identified also for the thyroid cancers developing associated with ovarian teratomas. These genetic anomalies include the point mutations on BRAF, HRAS and NRAS, loss of heterozygosity in the PTEN gene region and RET/PTC rearrangements (13).

The treatment of malignant SO is controversial. Radical surgery is necessary in the postmenopausal

women or women without fertility expectancy. On the other hand, conservative treatment should be performed in the women who expect pregnancy; however, this treatment option is possible only if the disease is unilateral in the absence of invasion or metastasis (1). Radioactive iodine treatment is recommended after surgery in the patients with a tumor larger than 4 cm in diameter, extraovarian dissemination and aggressive histological features. Thyroidectomy should be performed prior to this treatment in these patients (19). Thyroidectomy is performed to confirm histological normality of thyroid tissue and increase the efficacy of radioactive iodine treatment (17, 20). The target of radioactive iodine treatment is ablation of thyroid remnants and destruction of the metastatic foci (1). The prognosis of benign SO and non-metastatic malignant SO is good. Thyroglobulin is used as a tumor marker in the follow-up of malignant cases (6). Surgery was applied to all cases in our series; no additional treatment was applied while no malignancy was detected. Recurrence was detected during follow-up period in none of the cases.

CONCLUSION:

Struma ovarii cases are the most commonly seen ovarian monodermal teratomas and mostly benign. Thyroid tissue may be found in 5-20% of the mature teratomas, however, thyroid tissue constitute more than $\geq 50\%$ of overall tumor to be termed as SO. The presence of thyroid tissue below 50% is adequate to diagnose SO if accompanied with thyroid-associated malignancy. The presence of malignancy associated with thyroid should be ruled out by a meticulous examination to preserve the option of an additional treatment.

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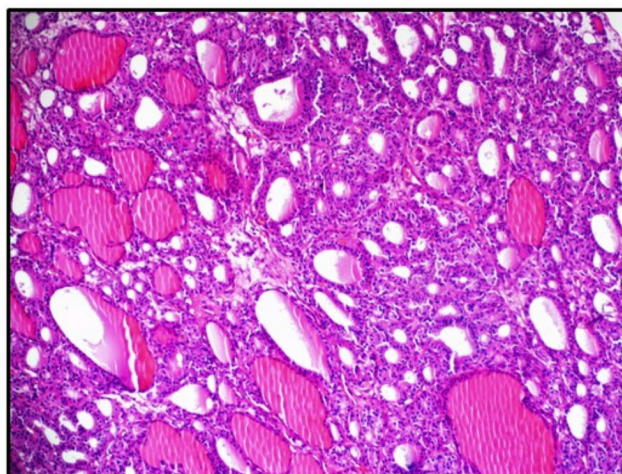


Figure 3: Tightly packed thyroid follicles (H+E, x40)

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