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From a clinical case to a review of literature: Struma ovarii associated with ascites and high serum CA125

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Abstract

Struma ovarii is a rare dermoid tumor of the ovary (1% of all ovarian tumors and 2,7% of ovarian teratomas), with more than 50% of the overall tissue being thyroid. Approximately one third of the cases present ascites. Pseudo-Meigs syndrome has been reported in fewer than 10 cases and 5-8% present thyroid hyperfunction. However, only 26 cases reported the association of ascites or pseudoMeigs' syndrome, elevated cancer antigen 125 and benign struma ovarii in the literature. The authors submit a case of benign struma ovarii that presented as a pelvic mass with ascites and highly elevated CA 125 serum levels and an extensive literature survey on this topic.

Keywords: Struma ovarii, CA125, ascites, ovarian tumor

Introduction

First described in 1899 by Boettlin[1], Struma ovarii represents a rare dermoid tumor of the ovary (1% of all ovarian tumors and 2,7% of ovarian teratomas[2]), with more than 50% of the overall tissue being thyroid[3].Typically occurs between the ages of 40 -60 and rarely occurs before puberty.[4] Approximately one third of the cases present ascites; pseudo-Meigs syndrome has been reported in fewer than 10 cases and 5-8% present thyroid hyperfunction.[4] However, only 27 cases reported the association of ascites or pseudo Meigs' syndrome, elevated cancer antigen 125 and struma ovarii in the literature.

The authors submit a case of benign struma ovarii that presented with a pelvic mass, ascites and highly elevated CA 125 serum levels.

Case presentation

A 42-years old female patient with no prior medical history presented to Fundeni Clinical Institute surgical department with gross abdominal distension and diffuse abdominal pain that started 3 months ago and had gradually getting worse.

Physical examination reveals an overweight (BMI 29.69) otherwise healthy-looking patient with gross abdominal distension with dullness to percussion and no abdominal tenderness, hepato-splenomegaly, or palpable abdominal mass. She reports normal bowel movement and physiological mictions. External pelvic examination is normal, and the internal pelvic examination shows normal vaginal walls and cervix. Bimanual palpation exposes a mass that compresses the left lateral and posterior fornices and is fixed on the adjacent planes. Digital rectal examination reveals a left-anterior external compression but otherwise normal. No other pathological findings were found.

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Management

Initial laboratory workup was normal, except CA125 that was 1700 UI/ml with normal range of 0-35 UI/ml.

An abdominal ultrasound showed grade III ascites and tumoral left ovarian cystic mass with heterogeneous tissue structure.

A CT scan of the thorax, abdomen and pelvis was performed revealing the left ovarian cystic mass with approximately 60 mm diameter, and heterogenous structure through the presence of tissular areas. The tumor had blurred margins and was in contact with the middle rectum. Grade III ascites was confirmed with no peritoneal carcinomatosis. The right ovary was of normal aspect and no additional tumors were detected.

A colonoscopy showed extrinsic compression on the middle rectum with normal mucosa, otherwise normal up to the caecum.

The case was discussed with the hospital tumor board and it was decided to carry out surgery in order to perform a biopsy and frozen section histopathological examination depending on which the surgery will be adapted. Surgery associated risks were presented to the patient and a written informed consent was obtained.

Intraoperatively, approximately 6 liters of clear ascites had been collected not before some samples being obtained in order to perform cytology and microbiology examination. At the abdominal cavity inspection, a large cystic left ovarian tumor was observed that had no rectal involvement and was adherent to the anterior wall of the recto-uterine pouch. No other macroscopic or palpatory pathological findings were noted. A left oophorectomy was performed, and the surgical specimen was sent to frozen section histopathological examination. The cytology of the ascites was negative for malignancy and the frozen section histopathological examination revealed: the resected specimen - ovary was enlarged 7/6/6 centimeters with lobulated aspect on cut surface with cystic area and compact with soft green-brown tissue; microscopically there were cellular regions composed of numerous microfollicular acini, sertoliform tubules as solid areas in which the cells have eosinophilic cytoplasm. Those areas were separated by oedematous and fibromatous stroma (Fig.1). No further surgical intervention was performed.

Post-operative recovery was uneventful; the patient was discharged 5 days after.

Outcome

At one-month follow-up, the surgical wound was healed, and the patient had no ascites at the abdominal ultrasound. The laboratory workup was normal with CA125 level of 20 UI/ml. The immunohistochemistry was performed and the tumoral cells were positive for CK7 (Fig.2), TTF1 (Fig.3), PAX8, negative for CK20, Chromogranin, Synaptophisin, CDX2, and Ki67 (Fig.4) was 5-7% positive nuclear staining in tumoral cells.

The final histopathological result and the immunohistochemistry result concur the diagnosis of benign struma ovarii. Further laboratory workup showed a normal serum-level of thyroid hormones with a TSH (thyrotropin/ thyroid stimulating hormone) level of 6.85 µUI/ml (normal range 0.27-4.2 µUI/ml), being detected with subclinical hypothyroidism. The patient was referred to the endocrinologist and entered a follow-up program for early detection of overt hypothyroidism.

At six-month follow-up, the patient had no other symptoms, an abdominal ultrasound was performed, with no additional findings. No additional thyroid-hormone substitution was needed, given the normalization of the TSH level.

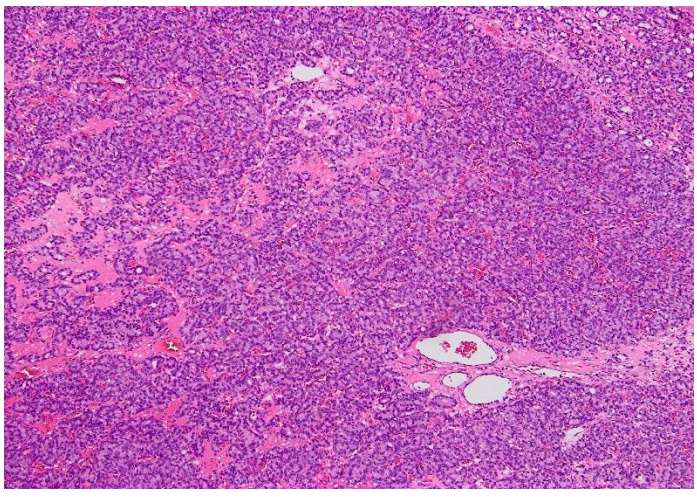

Figure 1. HE, x100, struma ovarii, with microfollicular and solid areas

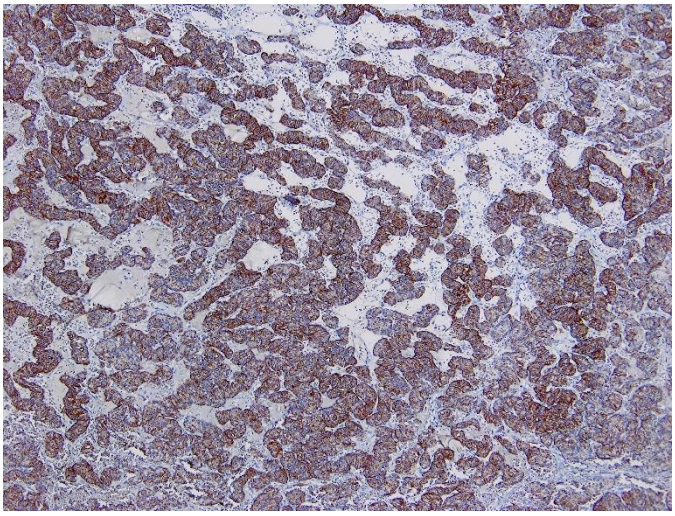

Figure 2. Immunohistochemical stain, CK7 positive tumoral cells

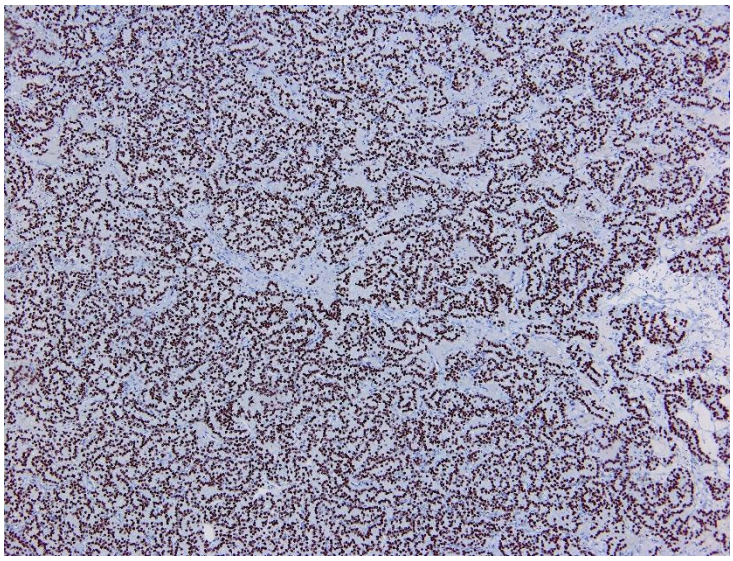

Figure 3. Immunohistochemical stain, TTF1 positive tumoral cells

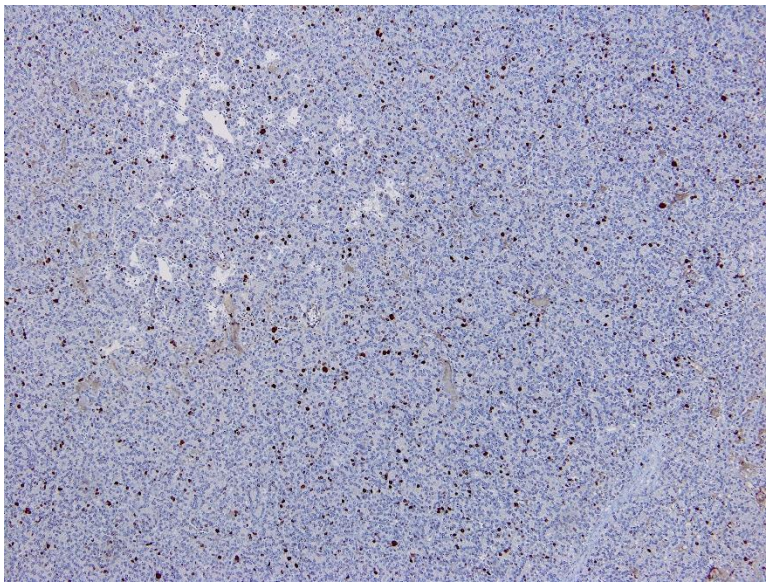

Figure 4. Immunohistochemical stain, Ki 67 5-7% nuclear positive in tumoral cells

Literature Review

A computerized advanced search was performed on PubMed (Public/ Publisher MEDLINE) electronic database using the following criteria: "struma ovarii" & "ascites" or "pseudo Meigs' syndrome" & "CA125" on 25 February 2020 and identified 31 case reports/ literature reviews. Search was not limited by publication date but was restricted to English literature. Nevertheless, 4 case reports didn't associate elevated CA125 with struma ovarii and ascites or pseudo Meigs syndrome and where excluded.

The results are reported in Table 1.

Table 1. Literature review of cases of struma ovarii with ascites or pseudo-Meigs' syndrome and elevated CA 125 levels

Author	**Year**	**No. of patients**	**Age**	**Site (left/ right)**	**Presenting Symptomes**	**Ascites Volume (ml)**	**Tumor size (cm)**	**CA125 (µg/ml)**	**Coexisting thyroid disease**	**Treatment**
Jotkowitz and Gee[5]	1993	1	79	NA	Abdominal distension	Several liters	NA	4670	Absent	TAH, BSO, omentectomy& peritoneal biopsies (frozen section performed)
Leung and Hammond [6]	1993	2	60	R	Nonspecific symptoms	500	10	224	Absent	TAH, BSO and omentectomy (frozen section performed)
			77	L	Abdominal distension	4000	8x10	2860	Absent	TAH, BSO & left pelvic node sampling (frozen section performed)

Bethune et al.[7]	1996	1	62	R	Dyspneea, abdominal distension	3500	9x5x5	1621	Absent	TAH,BSO& infracolic omentectomy
Mancuso et al.[8]	2001	1	31	L	Lower abdominal pain	300	10x9	689	Absent	LSO (frozen section performed)
Long et al.[9]	2001	2	53	L	Abdominal distension	4100	15x11x7	540	Absent	TAH, BSO & infracolic omentectomy (frozen section performed)
			78	L	Abdominal distension, cachexia	NA	12,2x10 x5,2	124.9	Absent	TAH& BSO(frozen section performed
Huh et al.[10]	2002	1	65	R	Abdominal distension, dyspneea	20000	5x4x4	402	Hypothyr oidism	TAH, BSO, appenddectomy and omental biopsy (frozen section performed)
Loizzi et al.[11]	2002	1	83	R	Abdominal pain, distension	3000	10x7x6, 5	1570	Absent	TAH &BSO (frozen section performed)
Bokhari et al.[12]	2003	1	51	R	Abdominal distension	NA	15x6,5x 11	1160	Absent	TAH,BSO& apendectomy (frozen section performed)
Zannoni et al.[13]	2004	1	66	L	Abdominal distension	5500	9,5x5,6x 7	1636	Absent	TAH,BSO, omentectomy, sampling of pelvic lymph nodes , peritoneal biopsy (frozen section performed)
Rim et al.[14]	2005	1	50	L	Abdominal distension	3000	4x4	878,67	Absent	TAH &BSO (frozen section performed)
Guida et al.[15]	2005	1	42	R	Abdominal distension	4000	9,1x7,7	2548	Graves disease	TAH &BSO
Loizzi et al.[16]	2005	1	65	R	Dyspnea, abdominal pain	Few liters	12x7	161	hyperthyr oidism	RSO
Uehara and Sawada[17]	2007	1	67	L	Abdominal distension, dyspneea	NA	7x7	2086	Absent	TAH &BSO

Obeidat et al.[18]	2007	1	52	R	Abdominal distension, dyspnea	4000	10x15x8	149	Absent	TAH, BSO & omentectomy
Paladini et al[20].	2008	1	42	R	Abdominal distension, cachexia	8000	11x7,3x8	2548	Basedow syndrom unresponsive to medication- total tyroidectomy=> persistent hyperthyroidism	RSO (frozen section performed)
Mui et al.[21]	2009	1	56	L	Abdominal distension	8210	6x5x4	5218	Nontoxic multinodular goiter	TAH,BSO& omentectomy (frozen section performed)
Rana et al.[22]	2009	1	70	R&L	Abdominal distension, dyspneea	NA	L 7,5x5,5x4 R 2x1,5x1	284	Absent	TAH,BSO &patial omentectomy
Jiang et al.[23]	2010	1	46	R	Abdominal distension, fatigue	6000	20x18x15	1230	Absent	TAH&BSO (frozen section performed)
Obeidat et al.[24]	2012	1	55	L	Abdominal distension	6142 /day	14x15	872	Absent	LSO (frozen section performed)
Mostaghel et al.[25]	2012	1	72	R	Dyspnea	700	9,5x12	607.4	Absent	TAH,BSO& omentectomy (frozen section performed)
Anastasilakis et al.[26]	2013	1	49	R	Abdominal distension	moderate	18x12x10	404.7	Graves disease	TAH & BSO
Diavatis and Papanikolaou [27]	2016	1	75	L	Abdominal pain	NA	6,34x5,91	264	Absent	TAH,BSO&omentectomy (frozen section performed)
Yadav et al.[28]	2017	1	55	L	Abdominal distension	680	6x5x3,5	258	Absent	LSO (frozen section performed)
Fujiwara et al.[29]	2018	1	50	L	Abdominal distension	3300	10x8x7	1237	Absent	TAH & BSO (frozen section performed)

Present case	2020	1	42	L	Abdominal distension	6000	4x6	1700	Absent	LSO (frozen section performed)

The data from these 28 cases including our case was analyzed using Microsoft Office Excel.

The median age (years) was 58.85 years with a minimum of 31 years and a maximum of 83 years. Also, one patient presented with bilateral struma ovarii and one case didn't mention the side. For the rest, 12 (46.15%) cases were localized on the right ovary and 14(53.84%) on the left ovary.

82,1% of the patients presented with abdominal distension, 25 % presented dyspnea, 10,7% with abdominal pain. Other symptoms were fatigue, cachexia and nonspecific. Coexisting thyroid disease was present in 6 patients (21,4%).

Only one case (Zanonni et al.[13]) of malignant struma ovarii was associated with ascites and high levels of CA125, all others were benign struma ovarii.

Even though frozen section histopathological examination was performed in 71,4% of the cases, extensive surgery was performed in 78,57% of cases.

Discussion

Struma ovarii is a rare ovarian tumor (1% of all ovarian tumors) that is often diagnosed on the histopathological report and sometimes further immunohistology is needed in order to deliver an accurate diagnosis, given the fact that on radiological examination the characteristic features are not straightforward interpreted. Frequently, it is misdiagnosed as ovarian neoplasm and unnecessarily extensive surgery is performed.

Meigs syndrome is characterized by the triad of benign solid ovarian tumor (most frequent fibromas, cystadenoma, granulosa cell tumor or thecoma), ascites and pleural effusion that resolves after the resection of the tumor. Pseudo-Meigs syndrome consists of the same triad with the difference that the benign tumor is other than those in Meigs syndrome.[24]

Serum Cancer Antigen 125 is a tumoral marker originating from fetal coelomic epithelium: Mullerian epithelium, pleura, pericardium and peritoneum. Even though high levels of CA125 are associated with ovarian carcinoma, it can be raised in various other gynecological pathologies: endometriosis, acute pelvic inflammatory disease, fibromatosis,[30] and non-gynecological: acute peritonitis, acute/ chronic pancreatitis, hepatitis, cirrhosis, renal failure, autoimmune disease.[31]

Every single case in which the suspicion is towards malignancy should be addressed to the local/hospital tumor-board for a patient-centered treatment planning. In order to avoid meaningless surgical procedures, the surgeon should have prior histopathological confirmation of the malignancy or intraoperative biopsy with frozen section histopathological result in order to further advance with the intervention. In this case, by doing the frozen section histopathological examination, the patient received the standard of care for this type of pathology. Even though this type of tumor and clinical presentation is rare, suspicion of malignancy should always be present. The surgical standard of care for benign struma ovarii is salpingo-oophorectomy of the affected side.

Furthermore, after the histopathological department establishes the diagnoses, the patient should be referred to an endocrinologist to assess the thyroid function. If malignant struma ovarii is discussed, the patient should be referred to a surgeon specialized in endocrine surgery in order to undergo a total thyroidectomy followed by radioiodine ablation therapy and subsequent oncological evaluation.

Conclusion

Struma ovarii is a rare tumor, with only 27 cases of struma ovarii associated with high levels of CA125and ascites or Pseudo-Meigs' syndrome reported in the literature. In this case not only the patient had struma ovarii and high levels of CA 125 but was accompanied by grade III ascites, similar with ovarian carcinoma, making the therapeutical decision more difficult.

Abbreviation List

BSO -bilateral salpingo-oophorectomy

CA125 – cancer antigen 125

CK7- cytokeratin 7

HE- hematoxylin and eosin stain

HE4 – human epididymis protein 4

Ki67-cellular marker for proliferation

L -left

LSO – left salpingo-oophorectomy

NA- non assessed

R -right

RSO – right salpingo-oophorectomy

TAH – total abdominal hysterectomy

TTF1- thyroid transcription factor-1

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Patient consent: The patient consent was obtained.

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