Struma Ovarii Associated with Pseudo-Meigs’ Syndrome and Elevated Serum CA 125: A Case Report and Literature Review

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Abstract

The association of struma ovarii with Pseudo-Meigs’ syndrome and elevation of CA 125 has been reported in literature. Here we report a 55-year-old with benign struma ovarii who presented with ascites, small pleural effusion, suspicious left ovarian mass and elevated serum CA 125 level. Repeated cytology tests were negative for malignancy. The radiologic appearance was highly suggestive of an ovarian malignancy and due to her overall state of illness the patient received 3 cycles of chemotherapy. Chemotherapy had no impact on the rate of accumulation of ascites, CA 125 level or the size of the ovarian mass highlighting the need to reconsider the initial diagnosis. Diagnostic left oophorectomy revealed struma ovarii and was followed by resolution of the ascites and normalization of the serum CA 125. No recurrence of the ascites or of the tumor has been observed during the 5 months follow-up. Struma ovarii or other dermoid variants should be considered in the differential diagnosis in patients with ascites, pleural effusions and elevated CA125 level but with negative cytology. Diagnostic laparoscopic oophorectomy should also be considered within the standard protocol for diagnosis of indeterminate adnexal masses.

Keywords: Struma ovarii; Ascites; Ovarian cancer

Abbreviations: US: Ultrasound; MRI: Magnetic Radiology Image; CT: Computed Tomography; TSH: Thyroid Stimulating Hormone; CEA: Carcinoembryonic Antigen; TAH: Total Abdominal Hysterectomy; BSO: Bilateral Salpingo Ophorectomy; RSO: Right Salpingo Oophorectomy

Background

Struma ovarii is defined by the presence of thyroid tissue as a major component of an ovarian tumor. Most commonly, they occur as part of a teratoma, but may occasionally be encountered with serous or mucinous cystadenomas [1,2]. Pure struma ovarii is a variant where the tumour is composed entirely of thyroid tissue.

The vast majority of struma ovarii are benign; however, malignant transformation has been reported in 5-37% of cases, and even when these tumors are malignant they rarely metastasize [3]. Struma ovarii is most common between the age of 40 and 60 years [2]. The symptoms of struma ovarii are similar to other ovarian tumors and are nonspecific in nature. Approximately 5-15% of patients have hyperthyroidism [2,4]. The preoperative diagnosis is generally difficult and diagnosis is usually made upon histological examination of the tumor. Surgical resection remains the definitive treatment for benign disease, and surgery with adjuvant radioiodine therapy has been shown to be successful in treating metastatic and recurrent disease [1,5].

We report an unusual case of a 55-year-old morbidly obese woman who presented with left pleural effusion, ascites, left ovarian mass, and elevated CA 125 level, which was suspicious for an ovarian malignancy. However, failure to respond to 3 cycles of chemotherapy – especially in the absence of cytologic or histologic diagnosis of malignancy - raised the question of Meigs’ or pseudo-Meigs’ syndrome as one of the differential diagnosis despite absence of a radiologically demonstrable fibroma. The patient eventually underwent laparoscopic removal of the ovarian mass as a diagnostic and potentially therapeutic procedure given the failure to respond to chemotherapy. The pathologic diagnosis was struma ovarii. The postoperative period was uneventful. The relevant literature has been reviewed.

Case presentation

This is a case of a 55-year-old female who was admitted to a local hospital with abdominal distension and weight gain. She was para 2 with previous caesarean sections, has hypertension and was morbidly obese with a body mass index of 45 kg/m². One of her nephews had been diagnosed with thyroid cancer. An ultrasound showed gross ascites throughout the abdomen and a large complex cyst measuring 21×21×9 cm, the origin of which could not be identified. Subsequent CT confirmed large volume ascites and a complex cystic mass arising from the left ovary which was partly calcified and contained solid enhancing components which was highly suspicious for malignancy. Approximate dimensions were 15×14 cm. In addition, the CT showed small volume omental infiltration and a large para-umbilical hernia. There was extensive subcutaneous oedema typical of advanced ovarian cancer. The liver, kidney, spleen, pancreas, gallbladder and adrenals were normal and there were no enlarged lymph nodes. CT also demonstrated atelectasis in the lower lungs and small left pleural effusion. The patient underwent ultrasound guided drainage of the ascites. An omental biopsy was attempted but failed to produce diagnostic tissue and cytological examination of ascitic fluid showed no malignant cells.

She was then transferred to our hospital for further treatment in September, 2011. There were no symptoms or clinical signs suggestive of thyroid hormone imbalance. Physical examination revealed generalised oedema, slightly decreased air entry bibasally, large multilocular umbilical hernia and a large lymphedematous pannus in the lower abdomen. Due to morbid obesity, the ovarian mass was not palpable abdominally or vaginally.

The patient’s serum CA 125 level was 872 U/mL, while CEA (<1 ng/ml), CA19.9 (7 kU/L), and CA 15.3 (15 kU/L) levels were within the normal range. TSH was not measured. The case was discussed in the
The patient received three cycles of Carboplatin and Paclitaxel. Following drainage of the ascites and prior to initiation of chemotherapy, CA 125 level showed an initial fall to 284 U/mL, however no further fall was observed after 3 cycles of chemotherapy. Furthermore, she continued to collect recurrent ascites, the rate of accumulation of which had not changed since commencing chemotherapy. The total accumulation of ascites whilst on chemotherapy was more than 150 litres. Repeat CT scan showed no change in the size of the ovarian mass. In addition, what was previously reported as wispy omental infiltration on baseline scan was felt to be probably a reflection of oedema rather than malignancy. It was felt on review that this was most likely Meigs’ or pseudo-Meigs’ syndrome and a MRI was requested to further characterize the ovarian mass. The patient was surprisingly well and had managed to maintain her serum albumin at the level of about 25 g/L despite the large ascitic losses.

One of the major surgical obstacles in this patient was access to the lower abdomen through her large pannus which was felt to be unlikely to heal from a midline incision. The patient was therefore scheduled for a laparoscopic left oophorectomy or laparoscopic biopsy if the former was not feasible. At operation, there was no evidence of intraperitoneal spread of disease. The left ovarian mass appeared malignant with multiple cystic spaces. The right ovary and the uterus were normal. Left salpingo ophorectomy was performed and the specimen was placed in a fluid resistant retrieval bag (Espiner medical, Bristol, UK) and retrieved through an extended umbilical port incision after morcellation within the bag. The umbilical hernia was repaired and Tenckhoff peritoneal catheter was placed to manage any potential high volume recurrent ascites.

The patient recovered uneventfully and was discharged home on the 2nd postoperative day. The final pathology revealed features of struma ovarii with tissue predominantly composed of thyroid tissue with an admixture of large follicles distended by inactive colloid and smaller follicles lined by cuboidal/low columnar epithelium showing colloid scalloping. There was minimal cytological atypia or chemotherapy effect and no malignant elements were identified. There were no features to indicate a co-existent dermoid cyst of other germ layer-derived structures or a mucinous tumour.

Following surgery, there was an immediate and dramatic decrease in the rate of ascitic fluid production. Two months after surgery, the CA125 level dropped to the normal range and there was no clinical or radiological evidence of ascites. The Tenckhoff catheter was therefore removed under local anaesthetic. Thyroid function tests two months after the operation were normal. Presently, the patient is on follow-up with no recurrence of her symptoms.

**Discussion**

Meigs’ syndrome is defined as the triad of benign ovarian tumor (fibroma, thecoma, and granulosa cell tumor) with ascites and pleural effusion that resolves after resection of the tumor [6]. Pseudo-Meigs’ syndrome consists of pleural effusion, ascites, and benign tumors of the ovary other than fibromas. These benign tumors include those of the fallopian tube or uterus and mature teratomas, struma ovarii, and ovarian leiomyomas [7-9].

Struma ovarii is a rare ovarian tumor defined by the presence of thyroid tissue comprising more than 50% of the overall mass. It presents mainly during the 5th and 6th decades of life [2]; these of interest as teratomas are commoner in the younger age group. The majority of struma ovarii are benign and are usually unilateral. Malignant transformation is recorded in 5–37% of cases [3]. Despite containing thyroid tissue, only 5% of patients with struma ovarii have features of hyperthyroidism [4]. Ascites has been reported in approximately 15-20% of all cases [10] and this is rarely accompanied by an elevated serum CA125 level [11].

Several hypotheses have been postulated to explain the origin of the ascites, including transudation of the fluid through the tumor surface, repeated rotation of the tumor pedicle, obstruction of vessels or lymphatics by tumor, or the rich blood supply to the tumor [8,12,13]. The exact mechanism that accounts for the elevation of CA 125 is still unknown; a possible explanation is the irritation and subsequent inflammation of the pleura and peritoneum surface produced by tumour or the presence of free fluid in these spaces. Pleural effusion is thought to be caused by transport of ascites through the diaphragm or lymphatics, however, from the review of the literature it seems that there is no consistent relation between the volume of the ascites and the presence of pleural effusion (Table 1).

A MEDLINE search revealed many case reports describing benign struma ovarii presenting with ascites and elevated CA 125 level. Details of these reports were shown in table 1. All cases were initially thought to be malignant tumor. In all cases ascites disappeared completely and CA 125 normalized after tumor removal.

Apart from the case described by Amr and Hassan [14] where the patient was 31 years old, all the patients were over 40 with the majority in their 6th and 7th decade of life. The tumor size ranged from 4 to 23 cm (average 12 cm) in greatest dimension. Although the left ovary used...
| Author                      | Number of patients | Age (year) | Site | Size (cm) | Ascites volume (ml) | Clinical presentation                                         | CA 125 (U/mL) | Treatment                                                                 | Prognosis and follow up |
|-----------------------------|--------------------|------------|------|-----------|--------------------|----------------------------------------------------------------|--------------|---------------------------------------------------------------------------|--------------------------|
| Amr and Hassan [14]         | 1                  | 55         | R    | 12 x 9 x 6| 3,000              | Abdominal distension, right sided pleural effusion, ascites     | -            | TAH, BSO & partial omentectomy                                              | Well, 36 months          |
| Bethune et al. [15]         | 1                  | 62         | R    | 9 x 5 x 5 | 3,500              | Abdominal swelling, dyspnea, ascites & large bilateral pleural effusion | 1621         | TAH, BSO & infra-colic omentectomy                                          | Well, 5 months           |
| *Bokhari et al. [16]        | 1                  | 51         | R    | 15 x 6.5 x 11| -                  | Increasing abdominal girth, fatigue, dyspepsia, weight gain     | 1160         | TAH, BSO & appendectomy (frozen section performed)                         | -                        |
| Huh et al. [17]             | 1                  | 65         | R    | 5 x 4 x 4 | 20,000             | Abdominal distension, Dyspnea, moderate bilateral effusion, marked ascites, pulmonary embolism | 402          | TAH, BSO, appendectomy and omental biopsy (frozen section performed)       | Well, 4 months           |
| Hulow et al. [18]           | 1                  | 60         | L    | 7.5 x 6.8 x 4.7| 8,000             | Chest pain, cough, mild dyspnea, abdominal swelling, bilateral pleural effusion, ascites | -            | Laparotomy, BSO                                                            | -                        |
| *Jottkowitz et al. [19]     | 1                  | 79         | -    | -         | Several liters     | Abdominal distension, epigastric pain & ascites                 | 4670         | TAH & BSO, omentectomy & peritoneal biopsies (frozen section performed)     | -                        |
| *Leung and Hammond [11]     | 2                  | 60         | R    | 10        | 500                | Pelvic mass and small volume ascites                            | 224          | TAH & BSO and omentectomy (frozen section performed)                       | Well, 12 months          |
|                            |                    | 77         | L    | 8 x 10    | 4,000              | Pelvic mass & ascites                                          | 2,860        | TAH, BSO & left pelvic node sampling (frozen section performed)            | Well, 12 months          |
| Loizzi et al. [20]          | 1                  | 65         | R    | 12 x 7    | Few liters         | Abdominal pain, diffuse abdominal pain, marked right sided pleural effusion, ascites | 161          | Laparotomy with RSO                                                         | Well, 2 months           |
| *Loizzi et al. [3]          | 1                  | 83         | R    | 10 x 7 x 6.5| 3,000              | Abdominal distension, fatigue, anorexia, large amount of ascites | 1570         | TAH & BSO (Frozen section perfomed)                                        | -                        |
| Long et al. [21]            | 2                  | 53         | L    | 15 x 11 x 7| 4,100              | Abdominal distension, weight loss, ascites, left pleural effusion | 540          | TAH, BSO, & infracolic omentectomy (frozen section performed)               | Well, > 12 months        |
|                            |                    | 78         | L    | 12 x 10 x 5| -                  | Abdominal distension, weight loss, ascites & bilateral pleural effusion | 124          | TAH & BSO (frozen section performed)                                       | Well, 6 months           |
| Mantouvalos et al. [22]     | 1                  | 42         | L    | 15        | 2,000              | Abdominal pain and distension, dyspnea, cough, left sided pleural effusion, & ascites | -            | TAH & BSO                                                                 | -                        |
| *Mancuso et al. [23]        | 1                  | 31         | L    | 10 x 11 x 9| 300                | The pelvic mass was incidental finding. Ascites noted in the scan | 689          | Left salpingo-oophorectomy (frozen section performed)                       | -                        |
| Mitrou et al. [24]          | 1                  | 55         | L    | 22 x 23 x 10| 8,000              | Large pelvic mass, ascites, small left sided pleural effusion   | 3803         | TAH & BSO, infra-colic omentectomy & lymph nodes sampling                   | Well, 12 months          |
| Obeidat and Amarin [25]     | 1                  | 52         | R    | 10 x 15 x 8| 4,000              | Dyspnea, marked ascites and moderate right sided pleural effusion | 149          | TAH, BSO and omentectomy                                                   | Well, 1 month            |
| Paladini et al. [26]        | 1                  | 42         | R    | 11 x 7.3 x 8| 8,000              | Ascites, fever, diarrhea, vomiting and significant weight loss (hyperthyroidism) | 2,548        | RSO + ? TAH & LSO (frozen section performed)                               | Well, 6 months           |
Abdominal distention, ascites

| Author                  | Number of Patient | Age (year) | Size (cm)     | Clinical Presentation                                                                 | CA 125 (U/mL) | Treatment                                      |
|-------------------------|-------------------|------------|---------------|--------------------------------------------------------------------------------------|---------------|-----------------------------------------------|
| Zannoni et al. [31]     | 1                 | 66         | 9.5 x 5.6 x 7 | Abdominal swelling, fatigue, pelvic mass, ascites, right sided pleural effusion       | 1636          | TAH, BSO, omentectomy, sampling of pelvic lymph nodes (Frozen section performed)* |

*At histopathological analysis on frozen section, the diagnosis was “struma ovarii”.

| Author                  | Number of Patient | Age (year) | Size (cm)     | Clinical Presentation                                                                 | CA 125 (U/mL) | Treatment                                      |
|-------------------------|-------------------|------------|---------------|--------------------------------------------------------------------------------------|---------------|-----------------------------------------------|
| Lenehan et al. [13]     | 1                 | 55         | 6 x 5 x 4     | Epigastric pain, abdominal distension, change in bowel habits, & ascites             | -             | BSO (previous TAH)                            |
| Present case            | 1                 | 55         | 14 x 15       | A total of 150,000, Abdominal distension, ascites, left pleural effusion             | 872           | Laparoscopic left Salpingo-oophorectomy        |

*No pleural effusion prescribed
**Frozen section (DCG) was suggestive of adenocarcinoma, however, subsequent paraffin sections in the pathology department revealed benign a struma ovarii

Table 1: Benign struma ovarii associated with ascites & elevated CA125 level: reported cases.

**Frozen section performed**

Cases of malignant struma ovarii presenting as pseudo-Meigs’ syndrome with elevated serum CA 125 have been described. Zannoni et al. [31], reported a case of a 66-year-old woman who presented with ovarian mass, ascites, pleural effusion and elevated CA 125 levels. Optimal surgical staging was performed. Definitive histological examination revealed a malignant struma ovarii. This was followed by complete resolution of symptoms and rapid decline of both CA 125 and thyroglobulin levels to normal value. No adjuvant therapy was administered as the tumor was stage 1a with no evidence of lymphovascular space invasion. The patient remained under strict follow-up with periodic assessment of thyroglobulin and CA 125 level, CT scan and thyroid ultrasound (Table 2).

We describe an additional case of benign struma ovarii associated with pseudo-Meig’s syndrome and elevated CA 125, which shows analogies with the ones reported in the literature. However our case was novel in that the patient received chemotherapy preoperatively with no impact on the disease. In addition, most of the cases reported were to be described as the site of choice for struma ovarii, it seems to be distributed equally on both sides. Of the 25 cases described, there was one case of bilateral struma ovarii, 11 cases of right struma ovarii, 13 cases of left struma ovarii, and in one case the site was not reported. The ascites was more than 3 litres in the majority of cases. When measured, CA 125 was found to be elevated. Pleural effusions were found in 15 patients and there was no consistent relation between its existence and the volume of ascites. For example, Bethune et al. [15], reported a case of large bilateral pleural effusion although the ascites was only 3 litres, whilst no pleural effusion was reported by Mui et al. [12], although 8 litres of ascites was drained. In two cases features of hyperthyroidism were reported. In the majority of the cases there was no long term follow-up which needs to be further considered.
treated with hysterectomy and bilateral salpingo oophorectomy while our patient was treated with laparoscopic left salpingo oophorectomy in view of morbid obesity. The initial drop in the CA 125 noted after the drainage of the ascites supports the theory that the CA 125 elevation was likely to be caused partially by the ascites.

Conclusion

Struma ovarii are reported to be associated with clinical, radiologic and biochemical signs masquerading as ovarian malignancy. One should be aware of this diagnosis and consider it when a patient presents with ascites and elevated CA 125 with or without effusion but with negative cytology.

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