Italian Journal of
Gynæcology & Obstetrics
September 2023 - Vol. 35 - N. 3 - Quarterly - ISSN 2385 - 0868

Meigs syndrome secondary to adult granulosa cell tumour with elevated CA125 levels: a case report

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ARTICLE INFO

History
Received: 15 July 2022
Received in revised form: 09 September 2022
Accepted: 15 September 2022
Available online: 20 September 2023

DOI: 10.36129/jog.2022.65

Key words
Meigs syndrome; carbohydrate antigen 125 (CA125); adult granulosa cell tumour.

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ABSTRACT

Background. Meigs syndrome is defined as an ovarian tumour combined with ascites and hydrothorax. The underlying pathophysiology of ascites and pleural effusion in Meigs syndrome is not determined; however, these conditions will resolve after the resection of the ovarian tumour. Meigs syndrome with CA125 elevation is a rare benign condition, mimicking advanced ovarian cancer.
Case presentation. We report the case of a 44-year-old woman who presented with severe dyspnoea and distended abdomen. Her serum CA125 level was 948 IU/mL. Computed tomography (CT) scans revealed a large pelvic mass, ascites, and bilateral exudative pleural effusions. Considering the suspicion of ovarian cancer, the patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node dissection. Accordingly, an adult granulosa cell tumour, stage IA, was confirmed. Ascites with pleural effusions completely resolved after surgery. Meigs syndrome was finally diagnosed based on spontaneous resolution of the accumulated fluids after the removal of the ovarian tumour. Further, the postoperative CA125 level dropped to the normal range. The patient has remained disease-free for 2 years and is receiving follow-up examinations regularly without adjuvant treatment.
Conclusions. Meigs syndrome with elevated CA125 may lead to misdiagnosis of advanced ovarian cancer. If there is no evidence of malignant cells on cytology of the pleural effusion or ascites, Meigs syndrome should be considered.

INTRODUCTION

Meigs syndrome is defined as an ovarian tumour coupled with ascites and pleural fluids, which are spontaneously resolved after the removal of the ovarian tumour [1, 2]. The pathophysiology of ascites and pleural fluids in Meigs syndrome remains uncertain owing to the rarity of the disease occurring in approximately 1% of all ovarian tumours [3].

It is important to differentiate Meigs syndrome from ovarian cancer. Even though the clinical features of these diseases, including ovarian tumour, ascites, and hydrothorax are similar, prognoses are markedly different. Although Meigs syndrome is a benign condition, it is occasionally accompanied by elevation of carbohydrate antigen 125 (CA125) levels, a vital marker of ovarian cancer which accounts for 47% of all gynaecologic cancer-related deaths [4]. Accordingly, CA125 elevation in Meigs

syndrome is considered as a challenge in diagnosis. Moreover, such cases caused by adult granulosa cell tumour are extremely rare and only two cases have been reported to date [5, 6].
In this paper, we have reported a case of Meigs syndrome secondary to an adult granulosa cell tumour (AGCT) with CA125 elevation, mimicking advanced ovarian cancer.

CASE PRESENTATION

A 44-year-old woman with a history of two previous pregnancies presented to the emergency room with persistent dyspnoea and distended abdomen for 1 month. She complained of amenorrhoea for the last three months without any noted medical and surgical history. Physical examinations showed coarse breath sounds in both lung fields and a large palpable mass in the lower abdomen. Her serum CA125 level was elevated at 948 IU/mL.
An initial chest radiograph (**Figure 1**) revealed massive bilateral pleural effusion, which was more severe on the left side. Further, chest computed tomography (CT) scans demonstrated pleural thickening at dependent portions of both lungs and bilateral pleural fluids. Accordingly, diagnostic and therapeutic thoracentesis was performed and the presence of an exudative pleural fluid, was confirmed by a fluid to serum lactate dehydrogenase ratio of 0.8. The cytology of the pleural fluid was negative for malignancy. Ultrasonography showed a normal uterus with endometrial thickness of 7 mm. There was a large heterogenous solid mass that filled the lower abdomen, along with ascites. Further, abdominopelvic CT scans identified a multilobulated pelvic mass of 19 cm, presumed to be originated from the ovary (**Figure 2**). Considering clinical and radiological findings, ovarian cancer with pulmonary metastasis was suspected. The elevated serum CA125 level favoured a diagnosis of ovarian malignancy. Accordingly, pigtail catheters were placed to drain the bilateral pleural effusions and manage the persistent dyspnoea before performing the operation.
Based on the observations during the laparotomy, the uterus and the left adnexa were normal. The right ovarian mass measured 23 × 20 × 10 cm, and bloody ascites were present. Accordingly, cytoreductive surgery was performed because the ovarian malignancy could not be excluded. The patient subsequently underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph node dissection. On postoperative day 7, bilateral pleural effusions were completely resolved on chest radiography (**Figure 3**) and ascites disappeared simultaneously. The pathologic examination confirmed a diagnosis of adult granulosa cell tumour (AGCT) of the ovary. Further, the evaluation of ascites

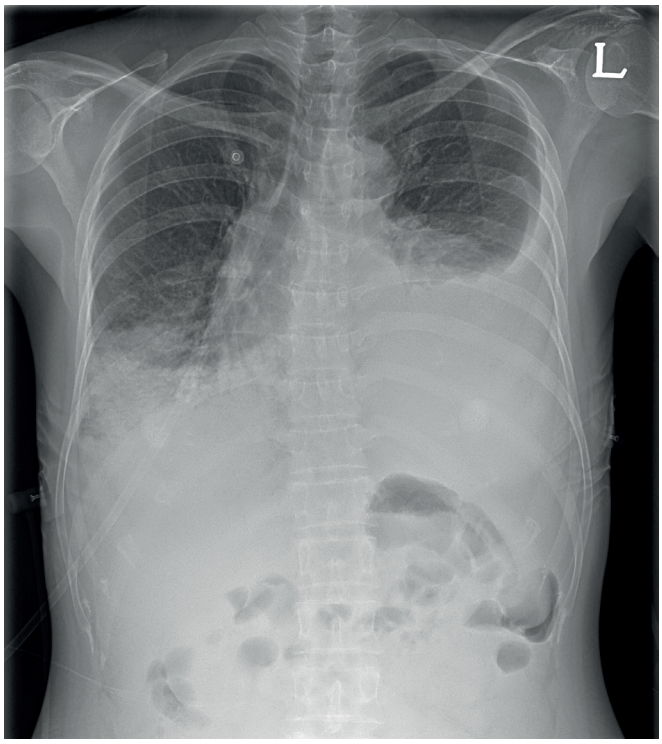

Figure 1. *Initial chest radiography revealed pleural effusions in both lung fields, which were more severe on the left side.*

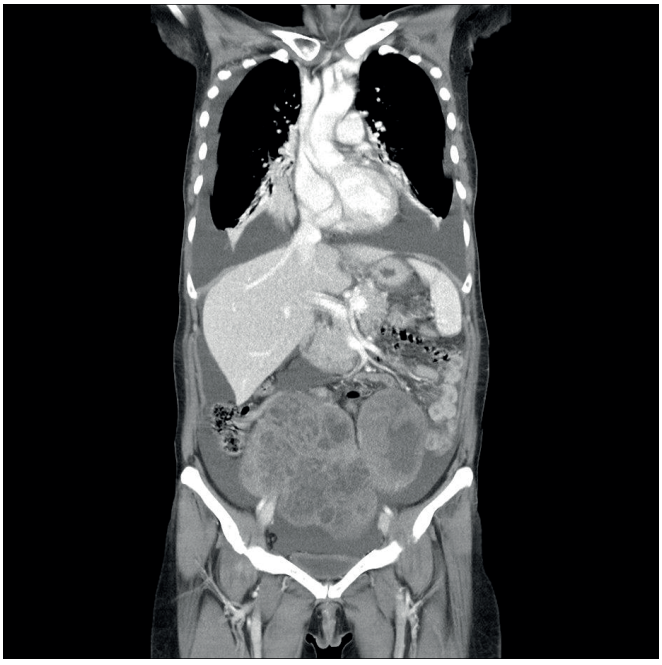

Figure 2. *Coronal plane of abdominopelvic and chest computed tomography (CT) disclosed a huge multilobulated pelvic mass. Ascites and bilateral pleural effusions were present.*

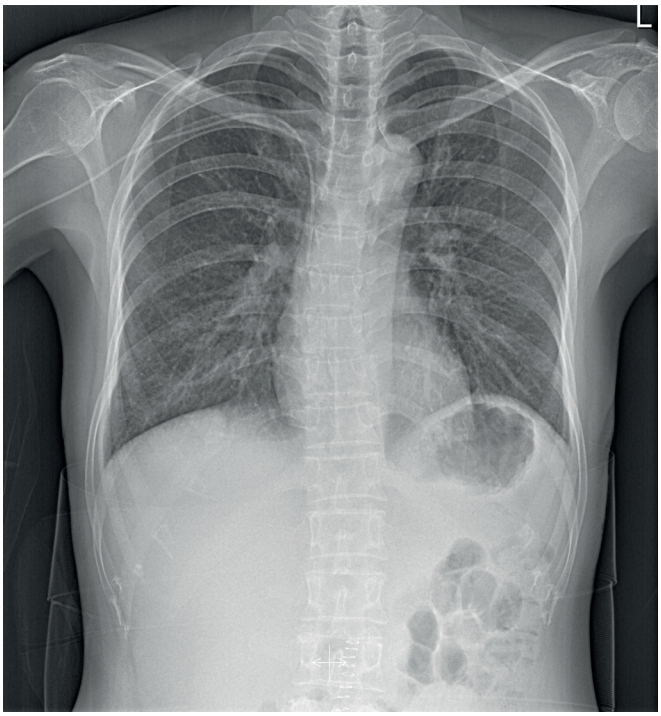

Figure 3. *A follow-up chest radiograph on postoperative day 7 revealed that bilateral pleural effusions were completely resolved.*

and the resected pelvic lymph nodes showed no evidence of malignancy. The stage of AGCT was IA based on the International Federation of Obstetrics and Gynecology classification. Meigs syndrome was finally diagnosed based on spontaneous resolution of the ascites and pleural effusion after removal of AGCT. Furthermore, the patient had developed pulmonary embolism and deep vein thrombosis as postoperative complications and was treated with 20 mg daily dose of rivaroxaban. The patient was discharged 15 days after the surgery in stable condition.

At 2 months postoperatively, the serum CA125 level had dropped to 22.4 IU/mL. Further, pulmonary thromboembolism and deep vein thrombosis were completely resolved after 6 months. The patient has remained disease-free for 2 years and ascites and pleural effusions did not recur. She is receiving regular follow-up examinations, consisting of clinical examination and periodic CT scans, without adjuvant therapy.

DISCUSSION

The underlying mechanisms for developing ascites and pleural effusion in Meigs syndrome are still unclear. However, several hypotheses have been proposed. The presence of ascites in patients with Meigs syndrome has been suggested to be caused by fluid leakage from the tumour itself, as well as the lymphatic blockage caused by tumour pressure on the abdominal and pelvic lymphatics [1]. Furthermore, the vascular endothelial growth factor is believed to contribute to the production of peritoneal and pleural fluids by enhancing capillary permeability [7]. Additionally, it is proposed that the cause of pleural effusion might be direct translocation of the ascites via diaphragmatic pores [8]. The pleural effusion is classified with Light's criteria as an exudate and is predominantly right sided [9].

CA125 is valuable in distinguishing between benign and malignant tumours in patients with pelvic masses. Approximately 80% of patients with advanced ovarian cancer have elevated serum CA125 levels beyond 30-35 IU/mL [10]. In this regard, the presence of ovarian tumours, together with ascites, pleural effusion, and an elevated CA125 level strongly suggest an ovarian cancer with peritoneal and pleural dissemination.

Nevertheless, the CA125 is also expressed by epithelial cells in the endocervix, endometrium, and fallopian tubes of normal adults [10]. It is also present in mesothelial cells of the pleura and peritoneum, particularly in the presence of inflammation and adhesions [11]. Approximately 1% of healthy women present increased CA125 levels (> 35 IU/mL) [10]. CA125 levels may increase in various benign conditions, such as benign ovarian tumour, uterine fibroids, and endometriosis [12]. Moreover, both non-malignant ascites and pleural effusion are associated with elevated CA125 levels. The mechanism and prevalence of Meigs syndrome with elevated CA125 levels remain unclear. It has been suggested that free fluids in peritoneal and pleural cavities may lead to irritation and subsequent inflammation, and result in production of excessive CA125 [13].

Granuloma cell tumours (GCTs) of the ovaries are pure sex-cord tumours and represent 2-5% of all malignant ovarian neoplasms [14]. Two distinguishable subgroups exist: AGCTs and juvenile granulosa cell tumours. AGCTs of the ovary are the most common type, comprising 90-97% of all GCTs, and mostly occur in middle-aged postmenopausal women [14]. Accordingly, the common manifestations are vaginal bleeding, palpable abdominal mass, and abdominal pain [15]. Further, menstrual irregularities and amenorrhoea have also been reported [15]. Most patients have one or more symptoms, but some patients (14.3-22.5%) are asymptomatic [16, 17].

Inhibin B and anti-mullerian hormone, formed in granulosa cells and secreted from GCTs, can be used

as tumour markers for predicting primary and recurrent diseases [18]. In addition to hormonal markers, efforts have been made to predict GCT by applying CA125, a peptide epitope of mucin, which is widely used as a vital biomarker for the screening, detection, and progression of epithelial ovarian cancer [19]. The study by Yesilyurt *et al*. [20] revealed that serum CA125 levels were significantly higher in patients with GCT than in those with benign ovarian cysts. Accordingly, in their study, the median CA125 level of patients with GCT was 64.5 ± 130.3 IU/mL. In contrast to this study, Lee *et al*. [16] reported that only 10 patients (9.8%) among 76 patients with AGCT had elevated preoperative serum CA125 levels beyond 35 IU/mL. Considering these observations, whether the serum CA125 levels increase in patients with GCT remains controversial. Further studies are needed to determine the clinical application of CA125 as an indicator for predicting GCT.

Meigs syndrome is a benign disease characterized by ovarian tumour, ascites, and hydrothorax. However, it occasionally presents with elevated CA125 which is an essential marker of ovarian cancer. Accordingly, it might be misdiagnosed as advanced ovarian cancer. The standard treatment of advanced ovarian cancer is cytoreductive surgery followed by adjuvant platinum-based chemotherapy [21]. In the first and second-line adjuvant chemotherapy in patients affected by ovarian cancer, the combined use of bevacizumab, an antiangiogenetic agent, significantly improves progression-free survival [21]. To achieve a personalized therapeutic strategy, it is necessary to preoperatively evaluate the conditions of gynaecologic cancer patients [22]. In our case, malignant cells were not found in ascites and pleural effusions, which is consistent with benign diseases such as Meigs syndrome. Physicians should consider the limitations of CA125 in differentiating benign and malignant ovarian tumours. For a precise diagnosis of Meigs syndrome, it is important to confirm the pathology of the ovarian tumour and postoperative resolution of ascites and pleural effusion. Misdiagnosis in patients with Meigs syndrome can delay the appropriate treatment and even lead to deterioration of the patient's condition.

CONCLUSIONS

Meigs syndrome with CA125 elevation caused by AGCT is extremely rare. Although elevated CA125 in AGCT is controversial, it should be noted that CA125 may be elevated in various benign conditions including Meigs syndrome. Excessive increased CA125 levels in Meigs syndrome may lead to the misdiagnosis of advanced ovarian cancer owing to similar clinical characteristics. Accordingly, if malignant cells are not detected in ascites and pleural effusion, Meigs syndrome should be considered despite CA125 elevation.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

H.Y.C., J.P.: Conceptualization, resources. H.Y.C.: Investigation, visualization, writing – original draft. J.P.: Methodology, project administration, writing – review & editing, supervision.

Funding

None.

Study registration

N/A.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

N/A.

Informed consent

The patient signed an informed consent form.

Data availability

Data are available under reasonable request to the corresponding author.

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