Primary ovarian angiosarcoma - review of the literature and report of a case with coexisting chylothorax

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Summary

Background: Primary ovarian angiosarcoma is a very rare gynaecologic malignancy with poor prognosis and uncertain, up-to-date, treatment options. Its exact diagnosis is challenging for surgeons and difficult for pathologists. There are only a few cases reported in the international literature.

Case: We report a case of primary pure ovarian angiosarcoma with coexisting chylothorax which is, to the best of our knowledge, the first reported case. An extensive review of the literature analyzing all clinical and pathological parameters related to this condition is presented.

Result: In spite of all therapeutic efforts, surgical and medical, prognosis of ovarian angiosarcoma remains very poor in most cases.

Conclusion: Primary ovarian angiosarcoma is a rare and aggressive malignancy. The report of such cases is interesting in order to exchange knowledge and experience, and possibly to further improve our diagnostic and therapeutic capabilities.

Key words: Ovary; Primary angiosarcoma; Chylothorax, MAID chemotherapy.

Introduction

Angiosarcomas are rare soft tissue sarcomas which generally arise in the skin or subcutaneous tissues in areas exposed to sunlight. Primary ovarian angiosarcomas are exceedingly rare, and only 25 cases of primary ovarian angiosarcomas have been reported so far [1-17]. We present herein a case of a primary ovarian angiosarcoma associated with chylothorax. This unusual clinical presentation of ovarian angiosarcoma has, to the best of our knowledge, not previously been reported.

Case Report

A previously healthy 29-year-old woman, gravida 0, presented with mild abdominal distension and pain of one month's duration. On pelvic examination a mobile, non tender soft mass was palpated in the right lower abdominal quadrant.

Transvaginal ultrasonography revealed an 8 x 6 x 5 cm right ovarian mass, which consisted of solid and cystic areas and a small volume of free intraperitoneal fluid. The uterus and the left ovary appeared normal. MRI of the abdomen showed a right adnexal tumor with no signs of intra- or retroperitoneal spread. The chest X-ray was clear. Serum CA125 was 230 U/ml, while AFP, CEA, CA15-3 and CA19-9 were normal.

Exploratory laparotomy was undertaken revealing a right ovarian mass of 8 x 6 cm and approximately 500 ml of serous ascites. There were no palpable nodes. The right ovary was removed and, as a malignant tumor was diagnosed upon frozen section, omentectomy and a left ovarian biopsy were also performed.

Cytology of peritoneal washings was negative for tumor cells. The final histology report noted that the findings were indicative of angiosarcoma. Histological slides and tissue blocks were sent for a second opinion to the referral centre for female genital system pathology in Mannheim, Germany, where a diagnosis of angiosarcoma of the ovary was confirmed. Microscopic examination showed a tumor composed of vasoformative and solid areas. Anastomosing vascular channels were lined by atypical endothelial cells and contained red blood cells. The solid areas consisted of anaplastic pleomorphic cells, with high mitotic activity. Necrosis and hemorrhage were focally present (Figures 1 and 2). Immunohistochemical analysis for vimentin, CD31 and CD 34, showed strong positivity in neoplastic cells, consistent with a vascular tumor phenotype. Remnants of normal ovarian cortex were apparent. The fallopian tube was free of tumor.

The tissues from the left ovary and the omentum were negative for malignancy.

The patient was readmitted four months later. At that time, CA125 was 781 U/ml. An abdominal MRI scan showed ascites, right pleural effusion and possible metastatic foci around the sigmoid and rectum, and the serosa of the urinary bladder. A chest CT scan showed a large right pleural effusion with atelectasia compatible with pressure from the effusion but no signs of parenchymal tumor infiltration. Also, a breast MRI scan was normal, excluding a primary angiosarcoma arising from that site. Cytology of the pleural fluid was positive for poorly differentiated malignant tumor cells. The macroscopic view of this fluid was opalescent and pearly, with a consistency of 8590 cells/μl, 60% lymphocytes, 30% polymorphonuclear leucocytes, 4,93 g/dl leucoma, 2,91 g/dl albumin, LDH 456 U/l and 57 mg/dl glucose, indicative of chylothorax. The patient had a permanent chest drainage tube which yielded 750-1500 ml of chyle daily. She was put on total non-fat parenteral nutrition and commenced treatment with somatostatin, which temporarily reduced daily chest drainage to 150-360 ml. As another chest

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Table 1. — *Summarized review of the literature (blank spaces where there is no information from the authors).*

Author	Age	Main symptoms	Tumor markers	Uni-bilateral	Size (cm)	Pure	Coexisting ovarian pathology	Associated findings	Metastasis	Stage	Adj. chem.	Survival
Evtushenko N.T.	7	–	–	–	not	Available	–	–	–	–	–	–
Ongkasuwan C.	77	Vomiting, peritonitis		Unilat.		No	Mucin. cystadenoma	Ascites		Unknown		2 months
Patel T.	42	Abd. pain & distension, DIC		Unilat.		Yes		Haemo-peritoneum	Hypogastric pleural effusion	Unknown		18 days
Bouchi J.	21	Fever, dyspnea		Bilat.		Yes			Lungs	IV	Yes	Death after 2nd chemotherapy
Cunningham M.	19	Abd. discomfort		Unilat.	12	Yes		Haemothorax para-aortic nodes, lungs	Omentum,	IV	Yes	7 months
Nara M.	33	Non productive cough, hemoptysis	CA 125 normal	Unilat.		Yes		Alveolar hemorrhage	Lungs	IV	No	Some months
Nielsen G. (7 cases)	20-32	Abd. pain, distension		6 Unilat. 1 Bilat.	6-13	5 pure 2 non	Dermoid cysts			I (4 cases) III (3 cas.)	No	2 months-9 years
Lifschitz-Mercer B.	25	Abd. distension, weight loss		Unilat.		Yes		Ascites		I	Yes	18 months later still alive
Nucci M. (3 cases)	27-42	Abd. pain	CA 125 normal	Unilat.	3.5-14	Yes		Ascites (2 cas.)		I-V		1-24 months
Furihata M.	46			Unilat.		Yes				Unknown		9 months
Platt J.S.	40	Abd. pain, breath shortness		Bilat.	11x9x9	No	Teratoma	Pleural effusion, ascites	Omentum, mesenterium, bowel serosa	IV	Yes	5 cycles chemoth. Still alive
Jylling A.	37			Unilat.		No	Mucin. cystadenoCa			Unknown		
Twu N.-F.	38	Cough, hemoptysis	CA 125: 70.9 U/ml	Bilat	11x6 10x9	Yes		Ascites	Omentum, lungs	IV	Yes	7 months
Pillay K.	45	Abd. distension		Unilat.	22x10	Yes		Ascites		IV		3 months
Davidson B.	19	Abd. pain, distension		Unilat.	18x15	Yes		Ascites	Peritoneal cavity Paraaortic nodes	IV	Yes +Radio	12 months
Jha S.	28	Abd. pain, distension		Unilat.	20x25	Yes			Sigmoid, abd. wall (recurrence)	IV	Yes	7 years later still alive
Quesenberry C.	31	Abd. distension, urinary frequency	CA 125 normal	Unilat.		Yes				Ic	Yes	10 months later still alive
Our case	29	Abd. distension and pain	CA 125 230 U/ml	Unilat.	8x6	Yes		Chylothorax, ascites	Peritoneal cavity, lungs	IV IV	Yes (1 cycle)	6 months

CT scan suggested parenchymal pulmonary metastasis, thoracoscopic pleurodesia was performed, and chemotherapy with MAID (mesna, doxorubicin, ifosfamide, dacarbazine) was initiated. However, the patient died of tumor progression shortly after completion of only one cycle of chemotherapy.

Discussion

Primary ovarian angiosarcoma is an extremely rare lesion of high malignant potential. A literature search in Medline using the key words "angiosarcoma" and "ovary" turned up only 25 published cases of primary ovarian angiosarcomas [1-17] (Table 1). It is noted that there are also secondary ovarian angiosarcomas which are metastatic from other sites, e.g., the breast.

Although ovarian angiosarcomas may occur during a wide age range (7-77 years), they are most commonly found during the reproductive period, as in our case.

The most often reported presenting symptoms such as abdominal distension and pain are non-specific. Further associated clinical findings are variable amounts of ascites, pleural effusion, and alveolar haemorrhage [2, 8, 9, 13-15]. In our paper, the association of ovarian angiosarcoma with chylothorax is reported for the first time.

While malignancy may be suspected preoperatively, the exact nature of these tumors can only be established by thorough histological and immunohistochemical examination of the resected tumor specimen.

The majority of ovarian angiosarcomas are unilateral, and only four of the 25 reported cases were reported as bilateral [4, 7, 11, 13].

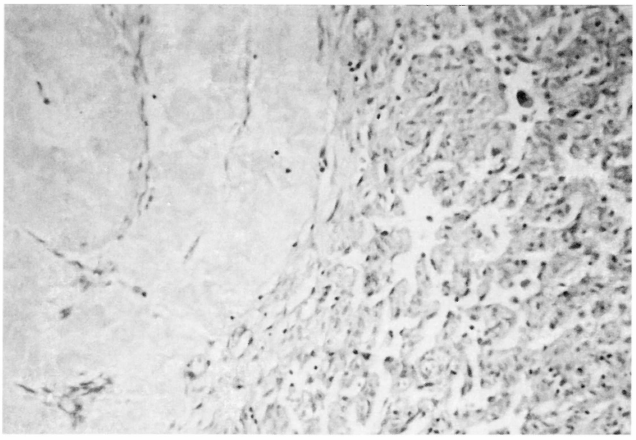
The size of the ovarian tumor reported in this paper (eight cm) is well within the reported size range (3.5-25 cm).

As in the current case, most reported cases of ovarian angiosarcomas were histologically pure angiosarcomas (20/25 cases) [3-10, 13-17]. Rarely, mixed neoplasms have been described consisting of angiosarcoma and mucinous cystadenoma [2], mucinous cystadenocarcinoma [12], and dermoid cyst [7, 11]. One complex mixed neoplasm consisting of ovarian angiosarcoma, mucinous cystadenoma, a borderline tumor, and cystadenocarcinoma has also been reported [12].

While seven of the 25 reported cases of ovarian angiosarcoma were limited to one or both ovaries, 13/25 cases presented with extra ovarian tumor spread (Stage III-IV) [4-7, 9, 11, 13-16].

Metastatic disease has been described in the lungs,

g. 1



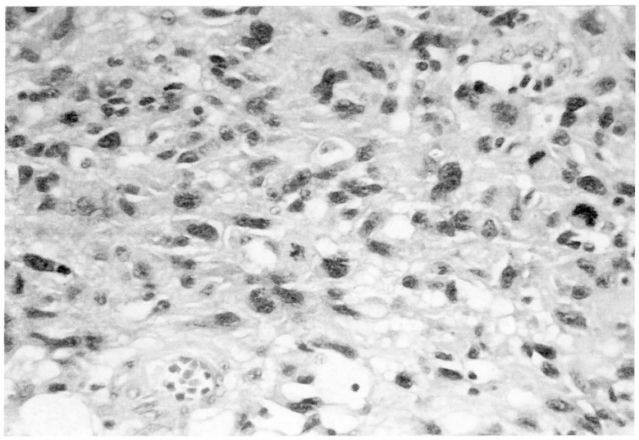


Fig. 2

Figure 1. — A corpus albicans of the ovary (left) and part of the angiosarcoma (right) with complex anastomosing channels (hematoxylin-eosin stain, original magnification x 200).
Figure 2. — Angiosarcoma of the ovary with mostly solid architecture and cells with high nuclear pleomorphism (mitosis in the center) (hematoxylin-eosin stain, original magnification x 400).

omentum, bowel, peritoneal cavity and paraortic nodes. Uncontrollable chylothorax in the current case was possibly, as no autopsy was undertaken, the result of metastatic infiltration of the major thoracic duct.

In four of the 25 cases, no information about tumor stage was given [2, 3, 10, 12]. The first published case report of ovarian angiosarcoma was written in Russian, and no information about tumor stage is given in the English abstract of that paper [1]. Primary ovarian angiosarcoma is most likely derived from the ovarian vasculature. Other histogenetic theories such as origin in mixed mullerian tumors, dermoid cysts or other germ cell tumors have also been proposed [8]. Because of the rarity of the disease, optimal management has not been defined. MAID (mesna, doxorubicin, ifosfamide, dacarbazine), as in our case, has been used as a therapeutic option in many cases, however, prognosis remains poor in most instances. Only one case with Stage I disease with nine years survival after surgical treatment has been reported [7]. Usually death occurs within a few months after the initial diagnosis.

In conclusion, primary ovarian angiosarcoma is an extremely rare aggressive malignancy. In spite of all therapeutic efforts, prognosis is very poor in most cases.

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