Complete response after MAID treatment for advanced primary ovarian angiosarcoma: case report and literature review

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Summary:

The patient presented in this case report was a 45-year-old female, with a Stage IIIA ovarian angiosarcoma combined with mature teratoma, that underwent debulking surgery and achieved complete remission for 11 months after six cycles of MAID chemotherapy (mesna, adriamycin/doxorubicin, ifosfamide, and dacarbazine). Thereafter, she had tumor recurrence with peritoneal seeding and massive pleural effusion; hence she received chemotherapy again. Although she had been undergoing a series of chemotherapies, the tumor continued to progress. Hence, she refused further chemotherapy since September 2012. Unfortunately, she passed away in January 2013 due to severe dyspnea with wide spread tumor progression. She had the longestsurvival period (31 months) and complete remission period than the other advanced primary ovarian angiosarcoma cases ever reported in the literature.

Key words: Ovarian malignancy; Angiosarcoma; MAID.

Introduction

Sarcomas of the female reproductive tract are rare, especially those from the ovary [1, 2]. Primary ovarian angiosarcoma is even more rare. The authors present such a case treated in our hospital and also reviewed the literature.

Case Report

This previously healthy 45-year-old female patient was found to have ovarian tumors incidentally on June 24, 2010 and her initial transvaginal ultrasonographic examination revealed right and left ovarian tumors measuring 2.1 x 1.4 cm and 7.1 x 4.7 cm in size, respectively. Components of teratoma were found at left ovary. She underwent laparoscopic left oophorectomy on July 26, 2010. The left ovarian teratoma contained hair components. The uterus, right ovary, and bilateral tubes were grossly normal. The routine pathological examination revealed incidental presence of malignant components in the left ovarian tumor. Postoperative abdominal computer tomography (CT) work up revealed left para-aortic lymph nodes enlargement on August 3, 2010. She underwent debulking surgery (transabdominal hysterectomy, right salpingo-oophorectomy, pelvic lymph node dissection, para-aortic lymph node dissection, omentectomy, and appendectomy) on August 4, 2010. Postoperative levels of tumor markers in August 2010 showed elevated level of CA-125 (300.5 U/ml), but normal levels of AFP, CEA, SCC, β-hCG, and LDH. Microscopically, ovarian angiosarcoma was found along with teratoma. Malignant cells were present in ascites, omentum, and appendix. The Federation Internationale de Gynecologie et d'Obstetrique classification (FIGO) Stage was IIIA. The angiosarcoma showed irregular vascular channels lined by plump neoplastic endothelial cells (Figures 1 and 2), which were positive for endothelial markers with CD34 and CD31 immunohistochemical stain. She received six cycles of chemotherapy with MAID (mesna, adriamycin/ doxorubicin, ifosfamide, and dacarbazine) over the following five and a half months. The initial follow-up pelvic CT examinations in January and April 2011 both showed no tumor recurrence. In August 2011, mesentery fat became mildly enhanced on pelvic CT scan, but levels of tumor markers of AFP, CEA, β-hCG, and CA-125 (18.978 U/ml) were not elevated. Three month later, in November 2011, the level of CA-125 was significantly elevated to 182.3 U/ml and CT scan showed peritoneal tumor seeding and pleural effusion. Laparoscopic omental biopsy with pathological examination confirmed recurrence of angiosarcoma. Due to tumor recurrence with peritoneal seeding and massive pleural effusion, she received a series of chemotherapy: one cycle of chemotherapy with weekly paclitaxel, three more cycles of palliative chemotherapy with MAID, and six-month oral chemotherapy with vinorelbine. Although she had been undergoing the chemotherapy, the tumor continued to progress; hence, she refused further chemotherapy since September 2012. She passed away in January 2013 due to severe dyspnea with massive peritoneal tumor seeding and pleural effusion.

Discussion

In the literature, a total of 40 cases of primary ovarian angiosarcoma were reported. After a detailed review, only 26 cases had well-documented survival periods and treatment (surgery or chemotherapy) [1-20]. The other 14 cases lacked either or both of the aforementioned elements. In the former 26 cases, there were nine early-stage patients (Stages I and II) and 17 advanced-stage patients (Stages III and IV). Furthermore, the authors organized these 17 advanced-stage patients into Table 1 [4, 6-9, 11-

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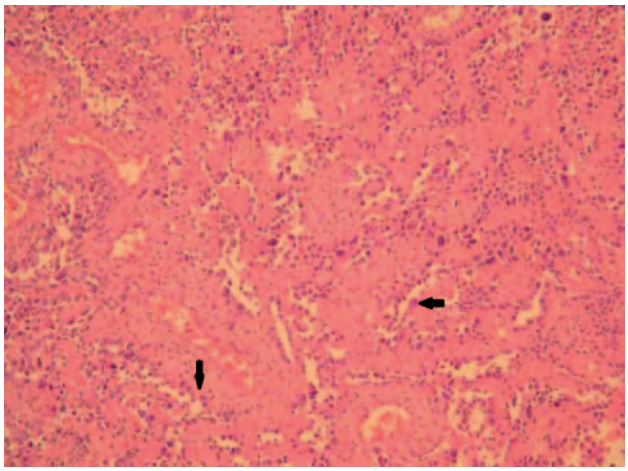

Figure 1. — Pathology (H & E stain 100X) section showing irregular slit-like vascular spaces lined by plump pleomorphic neoplastic endothelial cells (arrow).

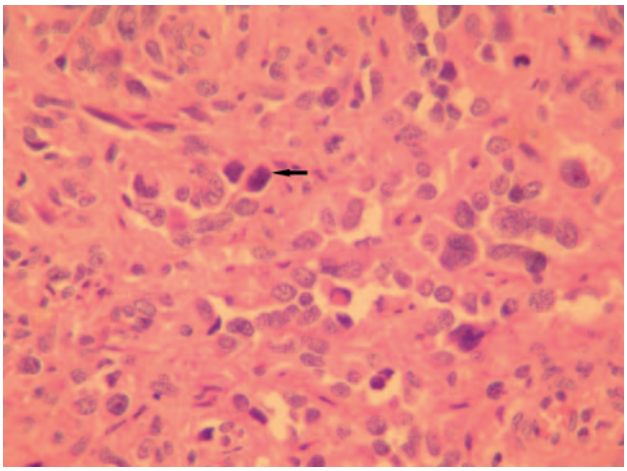

Figure 2. — Under high magnification, the neoplastic endothelial cells show marked variation of nuclear size, hyperchromatic nuclei, and high nuclear cytoplasmic ratio (arrow).

Table 1. — *The pathology, treatment, and outcome of advanced ovarian angiosarcoma.*

No.	Age (yrs)	Pathology	Stage	OP	C/T	Survival (months)	Reference
1	33	AS	IV	no#	none	2	[12]
2	67	AS	III	yes	none	1	[4]
3	77	AS+MC	III	yes	none	2.5	[15]
4	20-32*	AS	III	yes	none	2	[13]
5	20-32*	AS+MCT	III	yes	none	15	[13]
6	42	AS	III	yes	none	24	[14]
7	20-32*	AS+MCT	III	yes	none	30	[13]
8	35	AS	IV	yes	none	1	[14]
9	39	AS+MC	IV	yes	none	3	[18]
10	19	AS	III	yes	ADM & IFO X 6, then RT against enlarged mediastinal lymph nodes.	12	[8]
11	19	AS	IV	yes	ADM & IFO X 5, cisplatin & etoposide X 1	7	[7]
12	38	AS	IV	yes	ADM & IFO X 8	7	[17]
13	30	AS+MCT	III	yes	4 courses C/T, type not specified, s/p staging, followed by debulking surgery	9	[9]
14	25	AS	III	yes	ADM & IFO X 3	18	[11]
15	32	AS+MCT	IV	yes	high-dose ADM & IFO X 5, IFO X 4.	29	[6]
16	40	AS	III	yes	ADM & IFO X 6 (CR for 5 months), weekly paclitaxel	18+	[19]
17	23	AS	III	yes	MAID X 6 (CR for 8 months)	12+	[20]
18	45	AS+MCT	III	yes	MAID X 6 (CR for 11 months), Taxol X1, MAID X 3, VNR X 6	31	this case

* ages not individually reported; # autopsy; &: and; *OP*: operation; *s/p*: status post; *C/T*: chemotherapy; *AS*: angiosarcoma; *RT*: radiotherapy; *CR*: complete response; *MCT*: mature cystic teratoma; *ADM*: adriamycin (doxorubicin); *IFO*: ifosfamide; *VNR*: vinorelbine.; *MC*: mucinous cystadenoma.

15, 17-20]. Two of these nine early-stage patients, who did not receive adjuvant chemotherapy, were still alive with no evidence of disease in their 66th and 108th months after diagnosis [13]. Other four cases of these nine early-stage patients, who underwent adjuvant chemotherapy were still alive (survival period: 5+, 6+, 10+, and 10+ months, respectively), and two of these four cases had complete response [1-3, 10]. Other two cases of these nine early-stage patients were also still alive (survival period: 2+ and 14+ months, respectively), but their adjuvant chemotherapies were unknown [5, 14]. The last one of these nine early-stage patients died of septicemia on the 18th postoperative day [16]. Thus, early detection of ovarian angiosarcoma is a better prognostic factor regardless of utilization of adjuvant chemotherapy [2]. In Table 1, all these advanced stage patients were alive for less than 30 months, but the presented case was alive for 31 months. Eight of these advanced-stage patients and our patient, who underwent surgery and chemotherapy, had 12 months median survival. The other eight cases, which

underwent surgery alone, had 2.75 months median survival. The last one (Stage IV) who did not undergo surgery (just only autopsy) and chemotherapy remained alive for two months.

According to the retrospective analysis from Penel et al., doxorubicin-based regimens or weekly paclitaxel as first-line regimen may significantly improve the outcome of metastatic angiosarcomas [21]. Because tumor sensitivity to paclitaxel becomes lower if the primary site arises below the clavicle [22] and no visceral angiosarcoma achieved any response in the phase II trial in which paclitaxel was administered, a doxorubicin-based regimen still remains the first choice for those angiosarcomas that arise below the clavicle (including ovary). Thus, current recommended chemotherapy for ovarian angiosarcoma are MAID and ifosfamide/doxorubicin [23-25].

To date, including our case, only three advanced stage ovarian angiosarcoma cases received the MAID treatment and they also had complete response after MAID treatment [20, 26, and the present case]. Among these three advanced cases, first, Platt et al. described a case of complete resolution of Stage IV ovarian angiosarcoma with mature teratoma after five cycles of MAID chemotherapy, but no definitive sustained remission period was mentioned [26]. Second, Serrano et al. described a case of Stage IIIC ovarian angiosarcoma with complete response for eight months after six cycles of MAID chemotherapy [20]. Third, the present case, Stage IIIA ovarian angiosarcoma with mature teratoma, remained disease-free for 11 months after six cycles of MAID chemotherapy. Besides, the authors also found six advanced-stage ovarian angiosarcoma patients that had received doxorubicin and ifosfamide chemotherapy [6-8, 11, 17, 19], but only one case with Stage IIIC ovarian angiosarcoma, described by Guseh et al., had complete remission for five months after six cycles of doxorubicin and ifosfamide chemotherapy [19].

Although the significant morbidities of this MAID treatment were bone marrow toxicity and nadir sepsis with 5% treatment-related death rate [23, 25, 27], the above three advanced cases (including the present case) with MAID treatment were well-tolerated to this regimen. Therefore, taking into account the reported results and the present case, the MAID regimen may have better complete response (definitive sustained remission period: eight to 11 months) for advanced primary ovarian angiosarcoma with or without mature teratoma.

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