Bone Metastasis as the Initial Presentation in One Case of Ovarian Cancer With Two Components of Endometrioid Adenocarcinoma and Adenosarcoma

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Ovarian cancer with bone metastasis is relatively rare (about 1.2%) [1], compared with direct extension, transperitoneal seeding and lymphatic spread. Bone metastasis of ovarian cancer is mostly found during recurrence, and is very rare at the initial diagnosis with only a few cases reported [2]. We report a case with the initial diagnosis of advanced ovarian cancer with thoracispinal metastasis, and discuss the differential diagnosis and clinical course.

A 48-year-old women gravida 2, para 1, had suffered from mid-back pain for 4 months. She had iron-deficiency anemia because of menorrhagia. She visited a gynecologic clinic for regular Papanicolaou tests and pelvic examinations annually. The only abnormal finding was adenomyosis using ultrasound in October 2005. She did not have changes in appetite, decreased body weight or bowel movement changes. However, her back pain had been present since October 2005. She visited a neurologic clinic in our hospital in February 2006, and an osteolytic lesion in the pedicle of T7 was noticed on an X-ray film of the spine. High signals in the pedicles of T7 and L3 and soft tissue around T7 on magnetic resonance imaging were found (Figure 1). Her CA 125 level was 102.22 U/mL and CA 199 was 98.3 U/mL. She underwent T2–T8 laminectomy and excision of a tumor in February 2006. Pathologic findings revealed metastatic poorly differentiated carcinoma with glandular differentiation. Postoperative follow-up revealed normal findings on chest X-ray, panendoscopy and colonofiberscopy, and a large left ovarian multicystic tumor measuring approximately 15 × 10 cm adhered to her uterus and adenomyosis of the uterus on the computed tomography scan (Figure 2).

In March 2006, she underwent exploratory laparotomy, and a left ovarian cystic tumor measuring approximately 14 × 11 × 8 cm, which adhered to her uterus, bowel, retroperitoneum and left fallopian tube, and some ascites, were found intraoperatively. The frozen pathology during the operation revealed ovarian malignancy. Abdominal total hysterectomy, bilateral salpingo-oophorectomy, bilateral pelvic lymph node dissection and infracolic omentectomy were performed. There was no residual tumor in the abdominal and pelvic cavity after surgery. Grossly, the left ovary showed a huge unilocular cystic tumor, which measured 6.5 × 5.0 × 2.0 cm after cystic content evacuation, with a polypoid solid nodule protruding from the cystic wall into the cystic cavity. The final microscopic finding showed: (1) left ovarian adenosarcoma with predominant rhabdomyosarcomatous differentiation over the solid part, and grade I endometrioid adenocarcinoma with squamous differentiation over the cystic part with deep, irregular invasion over the gland (Figure 3); (2) multiple lymph node metastasis; and (3) carcinoma *in situ* of the cervix. Based on the histologic and immunohistologic findings (i.e. positive for CK7, focally patchy positive for p16, negative for CK20 and TTF-1), the lesion in the vertebral body was consistent with a metastatic lesion from ovarian endometrioid adenocarcinoma.

Under the diagnosis of ovarian cancer with thoracispinal metastases, she received palliative radiotherapy for bone metastasis, and systemic chemotherapy with one cycle of carboplatin (area under the curve, 6 mg/mL · min) and paclitaxel (175 mg/m^2) initially. The chemotherapy regimen was then changed to six courses of doxorubicin (50 mg/m^2) and ifosfamide

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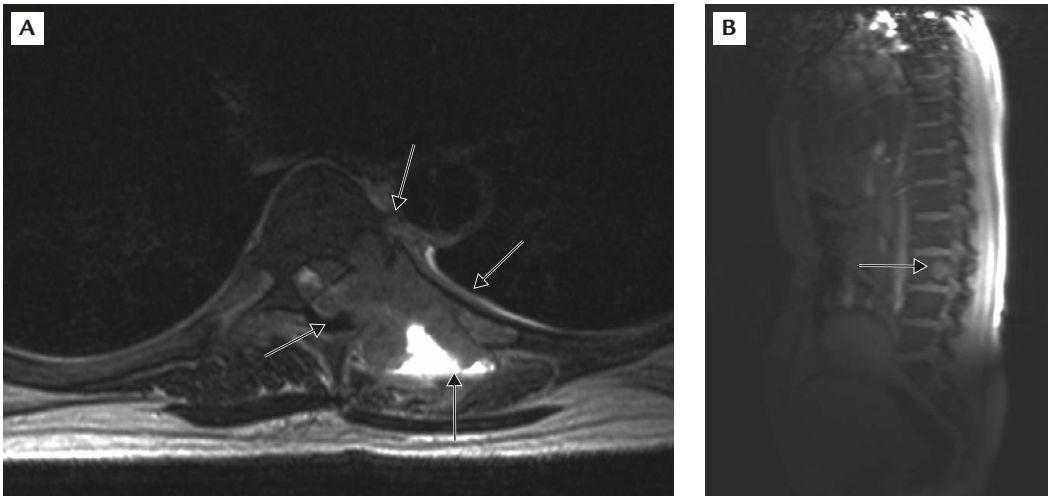

Figure 1. (A) Magnetic resonance imaging of the thoracic spine revealed a bone lesion (arrows) at T7 with epidural involvement; (B) another bone lesion was found at L3 (arrow).

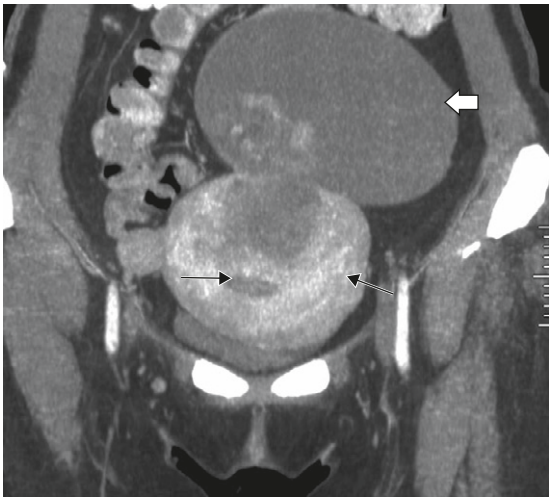

Figure 2. Abdominal and pelvic computed tomography scan revealed a huge heterogeneous mass (large arrow) adhered to the right superior aspect of uterus. Tumor invasion to the deep myometrium was also found (small arrows).

(5 g/m^2) for 21 days per cycle (from April 5, 2006 to July 20, 2006) because of her anaphylactic reaction to paclitaxel. Progressively decreased values of CA 125 (from 102.22 U/mL in February 2006 to 43.7 U/mL in July 2006) were noted. However, an emergency operation with posterior decompression, instrumentation and fixation at T5 to T9 was performed for multiple thoracolumbar spinal compression fractures and impending paraplegia in October 2006. In addition, a large amount of ascites and a huge pelvic tumor were found. Nonetheless, this patient refused further chemotherapy and received palliative therapy only. She died from septic shock in November 2006.

Ovarian epithelial malignancies usually spread by direct extension, transperitoneal seeding or lymphatic spread. Distant metastases present only in 8% of the patients at the time of diagnosis, and 22% of the patients present with distant metastases during the course of the disease [1]. Ovarian epithelial malignancies metastasize to the skeletal system at an incidence of only 0.7–14% (Table) [1–12], and bone metastasis is a late stage issue, which is rare at the initial diagnosis [2]. Only a few cases with bone metastasis have been reported at the initial presentation in patients with ovarian cancer [10,13]. We also performed a retrospective chart review from January 2005 through December 2006 in our hospital, and only our current case was found to have an initial presentation with bone metastasis among 90 ovarian cancer patients.

The median time to development of bone metastasis after the diagnosis of stage I–III ovarian cancer was 74 months (range, 68–80 months) [1]. Therefore, bone metastasis in this case may reflect its aggressive nature despite the status of grade 1 endometrioid adenocarcinoma. Bone metastases in patients with ovarian carcinoma are usually associated with symptoms of bone pain. The lesions tend to be focal and osteolytic, rarely osteoblastic [14]. The vertebral bodies are the most common site of metastasis, followed by the ribs, clavicle, skull, and femur [11]. In addition, the osteolytic spinal lesions of this case were similar to the most common findings of the bone lesions resulting from ovarian cancer metastasis. All histologic types of ovarian cancer can metastasize to the bones, and the most frequent is epithelial ovarian carcinoma. Serous cystadenocarcinoma (15%) had been reported as the most common histologic type of gynecologic cancer with bone metastasis, followed by mucinous cystadenocarcinoma (12%) and endometrioid adenocarcinoma (10%) [4]. However, no reports were available in the literature that mentioned bone metastasis in patients with ovarian adenosarcoma.

The mean survival interval was 7.5 months (range, 6–39 months) in patients with bone metastasis of

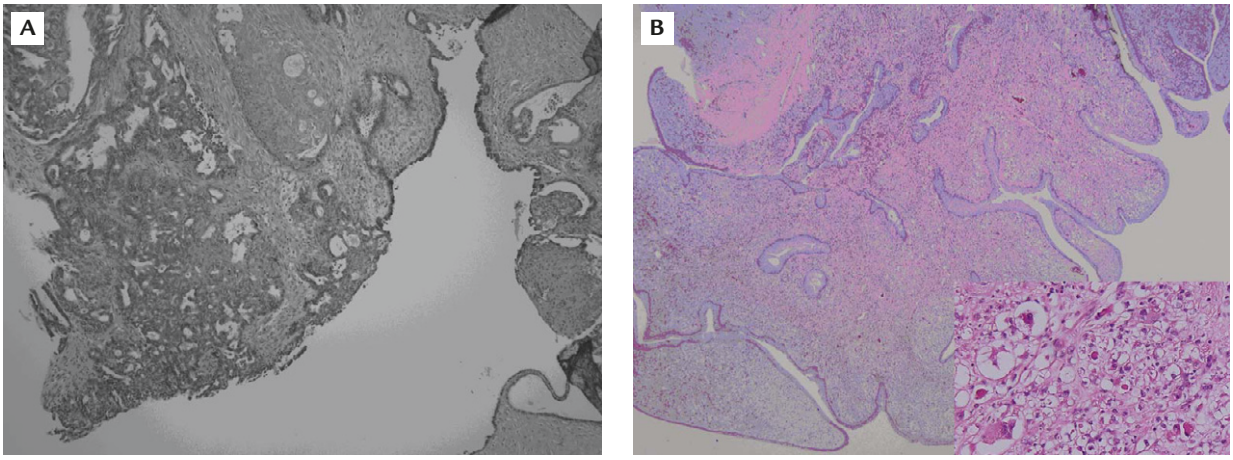

Figure 3. The pathologic picture of the left ovarian cyst: (A) the cystic wall was composed of grade 1 endometrioid adenocarcinoma (hematoxylin and eosin, 100×); (B) the solid component of the cyst was composed of adenosarcoma with predominant rhabdomyosarcoma (hematoxylin and eosin, 20×; insert, from the same section: hematoxylin and eosin, 200×).

Table. Literature review of the incidence of bone metastasis in cases of ovarian cancer

Year	Author	Patients (*n*)	Bone metastasis		Total, *n* (%)
			Antemortem detection (*n*)	Postmortem detection (*n*)	
1949	Allan and Hertig [3]	243	0	0	0 (0)
1966	Bergman [4]	86	0	12	12 (14.0)
1974	Julian et al [5]	87	0	3	3 (3.4)
1978	Brufman et al [6]	143	1	0	1 (0.7)
1982	Mettler et al [2]	106	4	0	4 (3.8)
1987	Dauplat et al [7]	255	3	1	4 (1.6)
1988	Dvoretsky et al [8]	100	0	11	11 (11.0)
1988	Karkavitsas [9]	37	0	0	0 (0)
1989	Rose et al [10]	381	0	43	43 (11.3)
1990	Abdul-Karim et al [11]	113	2	4	6 (5.3)
1992	Kumar et al [12]	130	4	0	4 (3.1)
2003	Cormio et al [1]	162	0	2	2 (1.2)
2007	Chen et al (this study)	90	1	0	1 (1.1)
	Total	1,933	15	76	91 (4.7)

ovarian cancer [7,11,12]. The survival interval of 10 months in this case was within the reported range.

Metastatic bone tumors in women mostly originated from breast cancer, followed by lung, kidney and thyroid cancer. Metastatic bone tumors which originate from gynecologic cancer are rare [15,16]. However, we recommend a careful investigation, such as pelvic examination, Papanicolaou test and ultrasound of pelvic organs, in women with metastatic bone lesions to avoid missed or delayed diagnosis and treatment.

In conclusion, we present a rare case of ovarian cancer with two components of endometrioid adenocarcinoma and adenosarcoma with an initial presentation of bone metastasis. Poor prognosis was noted despite aggressive treatment.

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