Recurrent ovarian cancer metastatic to the bone: Case report

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In patients with gynecologic malignancies, bone metastases are unusual and generally occur in a more advanced stage of the disease with extended local invasion of the primary site and/or parenchymal metastasis. In ovarian cancer, the main route of spread is intraperitoneal implantation and loco-regional invasion, whereas extraperitoneal spread usually implies advanced disease. Bone metastasis from ovarian cancer is rare and occurs in approximately 1% of primary or recurrent disease. The prognosis of cases with bone metastasis is poor. We report a patient with metastases to the sternum and a rib after prolonged treatment and a patient with recurrent ovarian cancer metastatic to the sacrum 8 months after primary treatment.

Key Words: Recurrent ovarian cancer, Bony metastasis

Case Report

Case 1

A 47-year-old woman with clinical stage IIIC ovarian carcinoma underwent primary cytoreductive surgery in our hospital. In 1999, she was admitted to our department and underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy, and multiple biopsies. The pathologic examination established the histologic diagnosis of a serous cystadenocarcinoma. Postoperatively, she received adjuvant chemotherapy with four cycles of paclitaxel and carboplatin, and one cycle of cyclophosphamide and...
cisplatin. The patient had remained disease-free for approximately 2 years, but in November 2005 she complained of an enlarged mass in the supraclavicular area bilaterally. A needle aspiration cytology of a supraclavicular lymph node revealed metastatic adenocarcinoma. She began radiation therapy to the neck and a 2nd line chemotherapy with Camtobell (six cycles), leading to progression. Subsequently, she received a 3rd line chemotherapy with paclitaxel and cisplatin. In December 2006, right axillary lymphadenopathy developed and the patient received palliative radiotherapy with cisplatin chemotherapy (six cycles) leading to complete remission of the axillary lesion. The patient remained disease free for 1 year. In May 2008, the patient complained of a tender mass on the lower chest and a chest CT showed a round mass with a soft tissue density in the mid-body of the sternum extending to left 3rd and 4th ribs (Fig. 1A). Sequential fine needle aspiration biopsies were performed and the pathologic result revealed metastatic adenocarcinoma. A bone scan revealed multiple bone metastases, including the sternum and rib (Fig. 1B). Palliative radiotherapy was performed to alleviate dyspnea. Two months later, she developed numbness and pain in the right arm and complained of a subcutaneous nodule in the right breast. The patient refused further treatment and she is currently undergoing hospice care at home.

Case 2

61-year-old woman with FIGO stage IIIC ovarian cancer underwent primary cytoreductive surgery in our hospital. In April 2007 she underwent a total abdominal hysterectomy with a bilateral salpingo-oophorectomy, bilateral pelvic and para-aortic lymph node dissection, total omentectomy, low anterior resection, multiple biopsy, peritonectomy, and appendectomy. The pathologic examination established the histologic diagnosis of a poorly differentiated endometrioid adenocarcinoma of the left ovary with multiple lymph nodes metastases. The patient received post-operative adjuvant chemotherapy with nine cycles of paclitaxel and carboplatin. The patient remained disease-free for 8 months. In August 2008, she complained of decreased sensation of the left lower extremity and pelvic pain. A lumbar MRI revealed loss of the fatty marrow signal with enhancement of the sacrum and both iliac bones, suggesting multiple bony metastases (Fig. 2A). Subsequently, she complained of headache, nausea, and vomiting. A bone scan revealed multiple bone metastases (Fig. 2B). A brain MRI showed a 4 cm peripheral enhancing mass in the left cerebellum and a 1 cm enhancing nodule in the left temporal lobe. The patient declined further treatment and received conservative treatment.
Fig. 2. (A) Lumbar MRI reveals loss of fatty marrow signal with enhancement suggesting bony metastasis to the sacrum and iliac bones. (B) Bone scan reveal multiple bony metastases.

Discussion

The final endpoint for most patients with epithelial ovarian cancer is death by intra-abdominal metastasis or intestinal obstruction, but rarely has hematogenous or lymphatic spread to other organs, such as the liver, pleura, lungs, skin, brain, and spleen been reported, while metastasis to the bony skeleton is extremely rare; in fact, most clinical series have reported an incidence of < 4%. Burns et al. reported that bone metastasis occurs in only 1% of ovarian cancer patients, with the exception of dysgerminomas. The mode of spread appears to be hematogenous, although no definite route has been documented in the literature. Ovarian cancer frequently spreads by direct invasion, implantation, or lymphatic dissemination to the peritoneum, pelvic, and para-aortic lymph nodes. The liver is commonly involved with recurrent ovarian cancer. Liver metastasis has a frequency of approximately 9.4% among patients who present with recurrent ovarian carcinoma and comprises about 20% of all distant metastases from ovarian cancer. Epithelial ovarian cancer can spread beyond the pelvis and abdomen. This disease has significant potential for distant metastasis, like other adenocarcinomas. Bone metastasis from epithelial ovarian cancer is anecdotal and has been reported rarely in the literature. The mode of spread appears to be hematogenous in bony metastasis, although no definite route has been documented in the previous literature.

In an autopsy series, Dauplat et al. analyzed 336 patients with distant metastasis from ovarian cancers. Of these, four patients had bone metastases, two of which were localized to the thoracic vertebra, 1 to the clavicle, and 1 had bone marrow involvement. The median time to development of bony metastasis ranged from 13~49 months. Rose et al. studied the metastatic pattern in 428 women in an autopsy series and correlated different histologies with sites of metastasis. The incidence of bony metastasis was 0.06~0.19% with epithelial histology. There was no difference in the spread pattern with different histologic subtypes. Brufman et al. found only 1 case in 143 patients involving the lumbar vertebrae. Mettler et al. confirmed bone metastases in 4 of 106 patients by bone scan. Autopsy data revealed bone metastases in 6~15% of cases. Bergman et al. observed bone metastases at autopsy in 8 of 54 patients with serous cystadenocarcinoma, 1 in 8 cases of mucinous carcinoma, and 2 in 20 cases of endometrioid adenocarcinoma. In all these cases, the involved bone areas included the pelvis, the vertebrae, the femurs, and the skull.
are few reports of chest wall involvement, including the sternum or the rib, as in our first case.\textsuperscript{1,10} Of bone metastases from different gynecologic carcinomas involving 305 patients, 113 involved patients with ovarian cancers. The most common site observed was the thoracic vertebra, followed by the clavicle and axial skeleton. Bone metastases were correlated with advanced anatomic stage, histopathologic type, and grade.\textsuperscript{11} Lymphadenopathies within the pelvis and para-aortic regions were associated with a greater incidence of bone metastasis as compared to those without lymphadenopathy.\textsuperscript{5}

The increasing occurrence of such unusual distant metastases from ovarian cancer possibly reflects the increased survival due to improved systemic and palliative therapy. Our first case developed bone metastasis after prolonged chemotherapy. Some authors suggest that platinum-based chemotherapy may be associated with mutagenic changes in the clinical setting, which may result in a more aggressive tumor cell if therapy is not successful.\textsuperscript{9} It has been implied that the differences observed in metastatic patterns between those patients treated with platinum versus those who were never treated with platinum may be biologically meaningful.\textsuperscript{12}

In our cases, both patients had widespread disease. Despite the active treatment, prognosis of cases with bone metastases is poor. It has been reported that the median survival after the clinical diagnosis of bone metastasis is only 4 months.\textsuperscript{4} The management remains controversial, depending on the location and the extent of spread. Unfortunately, our two patients declined further treatment after the diagnosis of bone metastases, although the prognoses are expected to be poor regardless of treatment efforts.

In summary, we describe unusual two cases of recurrent ovarian cancer metastatic to the bone. The management is difficult and response to treatment is poor in these cases with recurrent ovarian cancer metastatic to bone.

참고문헌

임소이 외 2인. Recurrent ovarian cancer metastatic to the bone

= 국문초록 =

부인암에서 골전이는 드문 편이며 일반적으로 진행된 병기에서 국소적으로 병이 퍼짐되었거나 다른 정기로 전이되었을 때에 질 발생한다. 난소암에서 암세포가 전파되는 주 경로는 복막내 착상, 국소적 침습이 있으며 복막외로 전파되는 경우는 병이 진행된 상태임을 의미한다. 난소암에서 발생한 골전이는 드문 것으로 일차성 또는 재발성 난소암의 약 1%에서 발생한다. 골전이가 발생한 경우의 예후는 매우 좋지 않다. 저자들은 난소암으로 오랫동안 치료한 후 흉골과 뼈골에 전이된 1예와 일차 치료 8개월 후 천골에 전이된 1예를 문헌고찰과 함께 보고하고자 한다.

중심단어: 재발성 난소암, 골전이