



Ovarian Cancer with Leptomeningeal Involvement

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Abstract

Ovarian cancer usually spreads locally. Leptomeningeal involvement is very rare with poor prognosis. We reported two cases with leptomeningeal metastasis. 51-year-old woman who was diagnosed with serous papillary ovarian carcinoma metastatic to liver and spleen, FIGO (International Federation of Gynecologists and Obstetricians staging system) stage IV. She received multiple courses of chemotherapy due to increase in Cancer Antigen-125 (CA-125) but there was no pathological metabolic activity in Positron Emission Tomography-Computed Tomography (PET-CT). After her last chemotherapy she presented with neurological signs. In her cranial Magnetic Resonance Imaging (MRI), pathological findings consistent with leptomeningeal metastases were obtained. Cerebrospinal fluid cytology was compatible with adenocarcinoma metastasis. One dose of intrathecal methotrexate and dexamethasone were applied. Nevertheless she died 3 days after the first administration of intrathecal treatment. The second patient was 58-year-old woman who was diagnosed with ovarian carcinoma FIGO stage IIIC. She received 6 cycles of carboplatin and paclitaxel. After initial treatment she followed up in remission until she had neurological symptoms. In May 2016, she had headache and difficulty in walking. Her cranial MRI revealed metastatic mass in right cerebellar hemisphere. She underwent cranial surgery for metastatic mass and received 6 cycles of carboplatin and paclitaxel she had not any other organ involvement except cerebellum. In December 2016, she experienced sudden vision loss and eyelid edema. Her new cranial MRI reported leptomeningeal involvement. Her PET-CT reported no pathological 18F-fluorodeoxyglucose (18F-FDG) uptake. Seven doses of intrathecal methotrexate (12 mg) and dexamethasone (8 mg) were applied. Her bevacizumab, gemcitabine and cisplatin therapy is still ongoing.

Keywords

Leptomeningeal involvement, Ovarian carcinoma, Neurological sign

Introduction

Ovarian carcinoma ranks fifth in cancer deaths among women and is the most common cause of deaths due to gynecological cancers. Central nerve system metastasis is rare; also leptomeningeal metastasis is very rare. There are a limited number of cases with isolated leptomeningeal metastasis due to ovarian carcinoma in the literature. We aimed to present two cases with ovarian carcinoma and leptomeningeal metastasis.

Case Report

A 51-year-old woman who had total abdominal hysterectomy history (the operation did not include ovaries and fallopian tubes) because of myoma uteri presented with abdominal distention, loss of appetite and constipation in June 2010. In her abdominal ultrasound and Computed Tomography (CT) revealed right adnexal mass which extended presacral area, ascites, liver metastasis and omental thickening. CA-125 was > 5230 U/

mL. In August 2010, she underwent bilateral salpingo-oophorectomy, pelvic lymph nodes dissection, omentectomy, splenectomy, appendectomy and partial liver resection (tumoral infiltration to spleen discovered during surgery). The pathology results of removed tissues were serous papillary ovarian carcinoma. Subsequently she received 8 cycles of carboplatin and paclitaxel. 6 months after the first line chemotherapy her abdominal computed tomography revealed progression of peritoneal implants and in her laboratory evaluation CA-125 was 2500

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U/mL. Her chemotherapy changed with liposomal doxorubicin. She received six cycles of liposomal doxorubicin. In her control CT after three cycles of chemotherapy, partial remission was obtained; after six cycles of treatment, PET-CT showed pathological metabolic activity in peritoneal implants, subcapsular area of liver and aortocaval lymph nodes and CA-125 was 2578 U/mL. Her treatment changed with gemcitabine and cisplatin. After 12 cycles of chemotherapy CA-125 level decreased (CA125:58 U/mL) and PET-CT revealed no evidence of pathological metabolic activity. One month later, CA-125 level increased (278 U/mL) and bevacizumab and topotecan were started. CA-125 levels decreased (CA-125:146 U/mL) in first six cycles of chemotherapy, but when tenth cycle of chemotherapy was applied CA-125 level increased (CA125:2484 U/mL) despite of obtaining no pathological metabolic activity in PET-CT and paclitaxel and carboplatin was applied again. CA-125 level decreased to 700 U/mL after 3 courses of chemotherapy. One month later, after her last chemotherapy she presented with headache and vomiting. In her cranial Magnetic Resonance Imaging (MRI), pathological findings that compatible with leptomeningeal metastasis was obtained. Then, lumbar puncture was performed. Opening pressure was high. One of two cytology's of Cerebrospinal Fluid (CSF) was reported as adenocarcinoma metastasis. Intrathecal methotrexate (12 mg) and dexamethasone (4 mg) were applied. We planned performing this regime twice a week; unfortunately she died 3 days after receiving the first dose of intrathecal chemotherapy.

The second patient was 58-year-old woman who had total abdominal hysterectomy with bilateral salpingo oophorectomy for ovarian carcinoma, FIGO stage IIIC [1] in 2012. She received 6 cycles carboplatin and paclitaxel chemotherapy after operation and followed up in remission between 2012-2016. In 2016 she had neurological signs; headache and difficulty in walking. In her cranial MRI there was a mass in right cerebellar hemisphere which was suspicious for metastasis. She underwent cranial surgery for metastatic mass and received 6 cycles of carboplatin and paclitaxel (Because we got remission with initial treatment, we applied carboplatin and paclitaxel again when metastatic mass revealed). She had no organ involvement. In December 2016, she experienced sudden vision loss and eyelid edema. Her new cranial MRI reported leptomeningeal involvement. There was not recurrence in cranial operation area and any newly developed metastatic mass in cranial MRI. There was no pathological 18F-fluorodeoxyglucose (18F-FDG) uptake in her PET-CT. Seven doses of intrathecal methotrexate (12 mg) and dexamethasone (8 mg) was applied. Then bevacizumab, gemcitabine and cisplatin therapy started. Her treatment is still ongoing.

Discussion

Ovarian carcinoma is the most common cause of deaths due to gynecological cancers and 5-year relative survival rates approximately 45% [2]. Ovarian carcinoma usually spreads locally. Distant metastasis is rare without intraabdominal organ involvement [3]. Central nervous system involvement due to epithelial ovarian carcinoma is estimated 1-2% [4]. Leptomeningeal involvement is quite rare. Leptomeningeal involvement is usually seen in advanced stages and with widespread systemic involvement [5]. There are a limited number of cases of isolated leptomeningeal metastases in the literature [3,6-8]. Despite the increase in tumor marker (CA-125) level in our cases, there was no evidence of systemic involvement in imaging studies.

The most common symptoms associated with leptomeningeal involvement are headache and mental status changes [9]. Mental status changes include confusion, loss of alertness, disorientation, defects in judgment or thought, unusual or strange behavior, disruptions in perception, psychomotor skills and behavior. Symptoms related to cranial nerve or spinal nerve involvement can also be seen [9]. Cranial MRI may be helpful in diagnosis, but the specificity is low compared to the lumbar puncture [6]. Leptomeningeal involvement is diagnosed by cytologic examination of the cerebrospinal fluid obtained by lumbar punching. Only 50% of cases can be diagnosed by first examination [3]. Similarly, our first case was diagnosed by the second CSF examination. MRI can support leptomeningeal involvement in patients whose CSF cytology is negative [10].

Survival of ovarian carcinoma is prolonged with current treatments. This increases the likelihood of metastasis in more rare regions. Elevated CA-125 could be an indicator of this despite imaging techniques does not reveal metastasis.

Survival due to leptomeningeal involvement is rather short. Similar to the limited number of cases in the literature, we planned to use intrathecal methotrexate in our cases [6,11].

As a result, although ovarian carcinoma is one of the common gynecologic cancers, leptomeningeal involvement is very rare. The possibility of leptomeningeal involvement in patients with central nervous system involvement as well as ovarian carcinoma with elevated tumor markers should be kept in mind.

References

1. Prat J, FIGO Committee on Gynecologic Oncology (2014) Staging classification for cancer of the ovary, fallopian tube, and peritoneum. *Int J Gynaecol Obstet* 124: 1-5.
2. Cancer Facts and Figures 2016. American Cancer Society.

3. Delord JP, Fizazi K, el Hajj M, et al. (1998) Isolated leptomeningeal metastasis from ovarian carcinoma: an unusual event. *Eur J Cancer* 34: 758-759.
4. Pietzner K, Oskay-Oezcelik G, El Khalifaoui K, et al. (2009) Brain Metastases from Epithelial Ovarian Cancer: Overview and Optimal Management. *Anticancer Res* 29: 2793-2798.
5. Kolomainen DF, Larkin JM, Badran M, et al. (2002) Epithelial ovarian cancer metastasizing to the brain: a late manifestation of the disease with an increasing incidence. *J Clin Oncol* 20: 982-986.
6. Hiromitsu Yamakawa, Haruko Ariga, Akemi Enomoto, et al. (2009) Meningeal dissemination from an ovarian carcinoma with effective response to intrathecal chemotherapy. *International Journal of Clinical Oncology* 14: 447-451.
7. Shlomit Yust-Katz, Samuel Mathis, Morris D Groves (2013) Leptomeningeal metastases from genitourinary cancer: The University of Texas MD Anderson Cancer Center experience. *Med Oncol* 30: 429.
8. Gordon AN, Kavanagh JJ Jr, Wharton JT, et al. (1984) Successful treatment of leptomeningeal relapse of epithelial ovarian cancer. *Gynecol Oncol* 18: 119-124.
9. Pace A, Fabi A (2006) Chemotherapy in neoplastic meningitis. *Critical Reviews in Oncology Hematology* 60: 194-200.
10. Straathof CS, de Bruin HG, Dippel DW, et al. (1999) The diagnostic accuracy of magnetic resonance imaging and cerebrospinal fluid cytology in leptomeningeal metastasis. *J Neurol* 246: 810-814.
11. Goto Y, Katsumata N, Nakai S, et al. (2008) Leptomeningeal metastasis from ovarian carcinoma successfully treated by the intraventricular administration of methotrexate. *Int J Clin Oncol* 13: 555-558.