Brain metastasis of ovarian cancer after negative second-look laparotomy

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Summary

We present a case of ovarian carcinoma that had brain metastasis seven months after having a negative second-look laparotomy and 13 months after the onset of diagnosis. Despite intense multidisciplinary treatment with surgery, chemotherapy and radiotherapy, the patient died seven months after second-look laparotomy.

Key words: Ovarian carcinoma; Brain metastasis; Second-look laparotomy.

Background

Brain metastasis from ovarian cancer, a rare and highly dismal event, represents a major surgical challenge and requires intensive and often complex therapies. It develops mostly during or after postoperative chemotherapy. Although central nervous system involvement by epithelial ovarian carcinoma is rare, its incidence seems to be increasing, and this may be related to prolonged survival due to chemotherapy. It may also be predicted to occur early in the disease course due to a specific molecular genetic abnormality [1]. Despite a unique report of an unusually high incidence -11.6%- [2], the incidence of brain metastasis in the literature varies between 1.96% and 4.5% [3, 4, 5, 6].

We present a case of ovarian carcinoma that had brain metastasis seven months after having a negative second-look laparotomy and 13 months after the onset of diagnosis.

Case Report

A 50-year-old woman was referred to our department for second-look laparotomy (SLL) six months after being operated on sub-optimally in a city hospital for an ovarian cyst. In this preliminary operation, total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed assuming that the cyst was not malignant. In spite of the benign sonographic characteristics and clinical findings, the pathology report was "poorly differentiated endometrioid carcinoma". Although the case was accepted as stage Ia because the capsule was intact, six courses of carboplatin and paclitaxel in combination with radiotherapy were administered postoperatively in another oncology center since the surgical staging was not optimal.

The patient was referred to our department for SLL. The second-look surgery involved collecting multiple cytological specimens, omentectomy, appendectomy, iliac lymph node sampling, and multiple randomized biopsies of the peritoneal surfaces. SLL did not show any tumor implants macroscopically and all of the histologic results were negative. CA 125 value-48 U/ml- was a bit higher than the upper limit.

Seven months after SLL, the patient had headaches and motor weakness on her left side. Her neurologic examination revealed left hemiparesis, and anisocoria. Magnetic resonance imaging displayed multiple cystic and nodular lesions in the left temporal, left thalamic and deep right parietal regions (Figure 1a-1b) necessitating stereotaxic biopsy. Biopsy results revealed glandular malignant tumor cells due to carcinoma metastasis. Histology of the tumor cells was concordant with endometrioid ovarian carcinoma.

Paclitaxel, at dosages of 200 mg/m^2, and carboplatin at dosages of 400 mg/m^2, were administered every four weeks for ten courses in combination with radiotherapy. In spite of multidisciplinary treatment, the patient died seven months after SLL.

Figure 1a. — T1 weighted (TR: 390 ms/TE: 17 ms) contrast-enhanced axial image through the left temporal lobe revealing a 2 x 3 cm cystic enhancing mass and surrounding hypointense white matter edema. There is a little shift to the right side at the midline.

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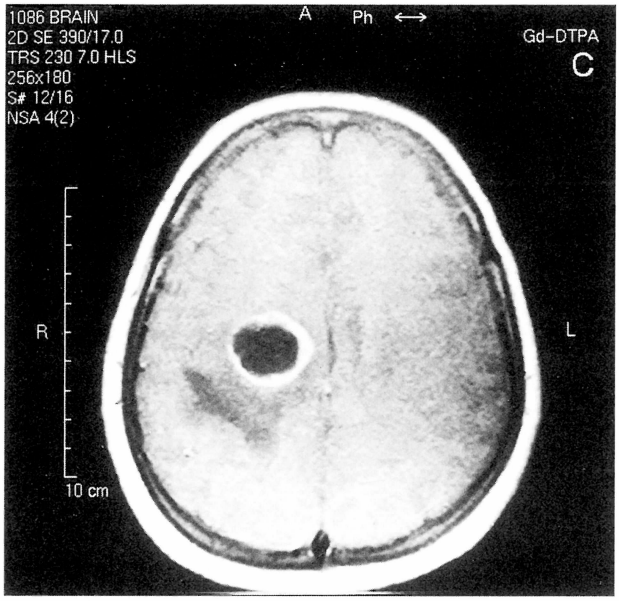

Figure 1b. — T1 weighted (TR: 390 ms/TE: 17 ms) contrast-enhanced axial image revealing a 2.5 x 2.5 cm cystic enhancing metastasis and hypointense edema behind it at the right corona radiata.

Discussion

Ovarian cancer is not the most common gynecologic cancer but it is the most lethal one. It accounts for over 50% of the deaths ascribable to gynecologic cancers [7]. The fact that there is not any ideal screening method for the disease and the late onset of the symptoms lead the patients to have advanced disease (stage III or IV) at the time of diagnosis and a high mortality rate. This reality increases the significance of surgical staging. Surgical staging is especially important for stage I and II patients who have a relatively high survival expectation. In 1989 the Gynecology Oncology Group reported that 4% of stage I cases have paraaortic and 11% have subclinical diaphragmatic metastases. These rates are 19.5% and 6% for stage II patients respectively [8]. Precise staging is the most important factor for the gynecologist for the prediction of the prognosis. Incomplete staging leads to an incorrect management and changes the expectant survival time.

Our case is a typical example of an incomplete staging and incorrect management. Peritoneal washings and lymphadenectomy are the lacking points. An intact capsule at histological examination was the reason to accept the case as stage Ia. Emergence of brain metastasis made us understand that the disease was a high stage ovarian cancer. Conversely, it would have been possible that the disease be accepted as stage Ia and chemotherapy would have been an unnecessary treatment. This would have been a great mistake as well.

Another aspect of the case is the occurrence of extensive brain metastases within a short time after cisplatin-based chemotherapy and negative SLL. We encountered only two reports concerning brain metastasis after negative SLL in the literature in the previous 15 years [9, 10]. The remaining articles regarding nervous system metastasis of ovarian carcinoma were related to the treatment of the disease. Despite reports of complete remission of the metastatic disease with multidisciplinary treatment combining surgery, chemotherapy and radiotherapy, our patient died seven months after the onset of neurological symptoms [11].

Cerebral metastasis of ovarian cancer may ensue single agent or combination chemotherapy. It is still an infrequent occurrence but, as the treatment for the disease produces more long-term survivors, such uncommon patterns of spread may become more frequent. Carboplatin is the recommended agent for the treatment of ovarian carcinoma metastatic to the brain [12]. Pharmacological studies enquiring the pharmacokinetics of carboplatin revealed low levels of carboplatin in the cerebrospinal fluid indicating that it does not cross the blood-brain barrier (BBB) sufficiently [13]. Paclitaxel also behaves in the same way [14, 15]. Co-administration of Cereport (RMP-7) – a selective bradykinin B2 receptor agonist-with carboplatin – may increase the permeability of the 'blood-brain tumor barrier' [16, 17]. Prophylactic central nervous system radiotherapy for patients achieving complete remission after systemic chemotherapy has also been recommended [18].

In our case with ovarian cancer, we encountered an unusual event - brain metastasis after negative second-look laparotomy. The fact that the patient had postoperative combination chemotherapy is another aspect of the disease process. Based on the pharmacological studies in the literature, our case may be an example that carboplatin and paclitaxel does not cross the BBB sufficiently.

Gynecologists dealing with a mass of ovarian origin must be capable of staging and should be aware of the principles of oncologic surgery. He should also consider performing frozen section. Brain metastasis should be kept in mind even if the second-look laparotomy results are negative. Hence, cranial imaging should be performed promptly in case of any neurological signs indicating brain involvement. A routine computerized axial tomography (CAT) scan of the brain may also be recommended for patients with ovarian carcinoma with prolonged survival.

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