

## CASE REPORT

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# Cerebellum Metastasis in High Grade Serous Ovarian Cancer

Songül ALEMDAROĞLU<sup>a</sup>, Seda YÜKSEL ŞİMŞEK<sup>a</sup>, Fatih KÖSE<sup>b</sup>, Özlem ALKAN<sup>c</sup>, Hüsni ÇELİK<sup>a</sup><sup>a</sup>Department of Obstetrics and Gynecology, Başkent University Adana Dr. Turgut Noyan Application and Research Center, Adana, TURKEY<sup>b</sup>Department of Medical Oncology, Başkent University Adana Dr. Turgut Noyan Application and Research Center, Adana, TURKEY<sup>c</sup>Department of Radiology, Başkent University Adana Dr. Turgut Noyan Application and Research Center, Adana, TURKEY

**ABSTRACT** Brain metastasis is observed in increasing frequency along with the progress in treatment of epithelial ovarian cancer. When compared with brain parenchymal metastases, isolated cerebellum involvement has been reported more rarely. In our patient with advanced stage serous ovarian cancer, solitary cerebellum metastasis and leptomeningeal involvement were observed in the 50th month after the patient's diagnosis of ovarian cancer. When this metastasis was detected, the patient's ca 125 levels were normal. The patient has no systemic metastases. Owing to effective chemotherapeutic agents in ovarian cancer, such isolated metastases will be observed more. Multicentric studies on this subject are needed.

**Keywords:** Ovarian cancer; cerebellum metastasis

Central nervous system metastasis is the most common nervous system tumor in adults.<sup>1</sup> The most common cause in adults is metastasis from the lung, breast, melanoma.<sup>2</sup> Central nervous system metastasis is rare among gynecologic malignancies except choriocarcinoma.<sup>3</sup> Its frequency in ovarian cancer was reported as 2.2%. Because of systemic treatments and surgical techniques, in ovarian cancer in which high life expectancy has already been enabled, incidence of central nervous system metastasis has been reported in growing numbers.<sup>4</sup> Central nervous system metastases are mostly supratentorial and cerebellum localization is reported to be 10-15%. In this study, we aimed to present a case of brain metastasis with atypical location. We had been following-up the patient for 50 months because of high-grade serous ovarian cancer.

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## CASE REPORT

A 54-year-old patient was first admitted to our department in September 2014 because of pelvic swelling. The patient had no systemic disease in her medical history and her Eastern Cooperative Oncology Group performance status score was 1 (restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work). In the examinations, cancer antigen 125 (CA-125) value was observed to be 2,164 mg/dL and radiological evaluation was compatible with possible ovarian cancer with findings of bilateral ovarian mass along with peritoneal carcinomatosis. The patient underwent debulking surgery and no visible disease was attained. Pathological stage was International Federation of Gynecology and Obstetrics stage IIIC high-grade serous carcinoma. She was treated with adjuvant 6 cycles of carboplatin (AUC 5) and paclitaxel 175 mg/m<sup>2</sup> in 3 weeks. We did not operate poly ADP ribose polymerase inhibitors after the first cycle be-

**Correspondence:** Songül ALEMDAROĞLU

Department of Obstetrics and Gynecology, Başkent University Adana Dr. Turgut Noyan Application and Research Center, Adana, TURKEY

**E-mail:** songul\_aykul@hotmail.com



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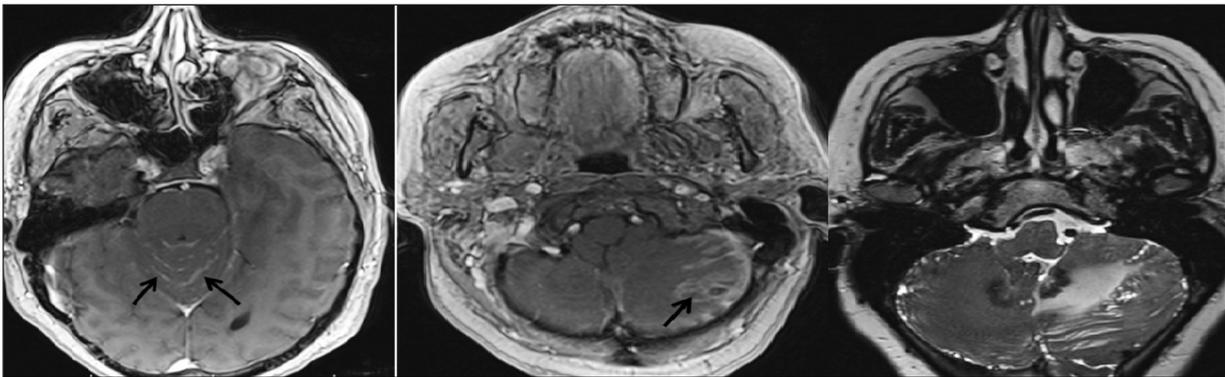
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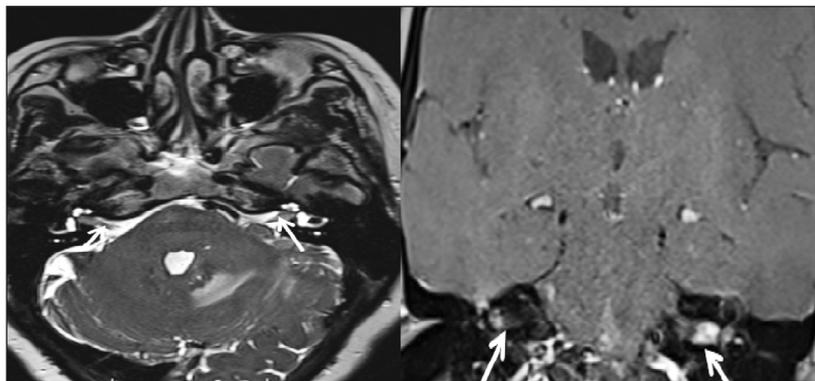
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cause it is not reimbursed in our country, Turkey. She was under surveillance with abdominal ultrasonography and CA-125 level every 3 months until March 2016 when asymptomatic abdominal recurrence with peritoneal carcinomatosis was detected. She was re-operated with no-visible disease and treated with 6 cycles of carboplatin (AUC 4)-liposomal doxorubicin 37.5 mg/m<sup>2</sup>-bevacizumab 7.5 mg/kg/3wk followed by bevacizumab maintenance 7.5 mg/kg/3wk. She developed hypertension along with significant headache at the 34<sup>th</sup> dose of bevacizumab along with high-grade proteinuria (>3.5 g/day). Bevacizumab was stopped to alleviate hypertensive attacks. During this time, it was observed that the levels of CA-125 was 1,253.6 IU/dL, abdominal ultrasonography and chest radiography were all normal. Genetic counselling was advised because of detection of BRCA-2 mutation during the follow-up of the patient. In the

same period, cranial magnetic resonance imaging (MRI) without mean distance of conformity examination was also seen to be normal when the patient had a strong headache. After 6 months, the patient was admitted to the emergency department with the complaint of imbalance. Cranial MRI showed a cerebellar mass and leptomeningeal enhancement of cerebellar folia and complex of seventh and eighth cranial nerves (Figure 1, Figure 2). The patient's level of CA-125 was found to be 24.2 IU/dL. Systemic metastasis was not detected in positron emission tomography-computed tomography. The patient underwent mass excision with neuronavigation. The pathological result was high-grade serous carcinoma. After the surgery, the patient received whole brain radiotherapy (WBRT). The patient's epileptic seizures after radiotherapy were not completely controlled by antiedema and antiepileptic therapy. She was admit-



**FIGURE 1:** a) Parenchymal metastatic lesion in the left cerebellar hemisphere at T1a axial contrast image. b) Vasogenic edema around the mass at T2a contrast image. c) Leptomeningeal involvement along vermicular folliculus.



**FIGURE 2:** T2A axial (a) and contrasted coronal T1A (b) images: due to leptomeningeal metastases, thickening and contrast enhancement in bilateral 7<sup>th</sup> and 8<sup>th</sup> cranial nerves.

ted to the emergency department with consciousness and shortness of breath. The patient was hospitalized at the intensive care unit and died due to neurological clinical progression.

## DISCUSSION

Metastasis of ovarian cancer is frequently detected in the abdomen through lymphatic or peritoneal spread. Its detection outside of the abdomen as a result of the hematogenous spread is quite rare. In a study were 4,277 patients with ovarian cancer were evaluated, the rate of central nerve system metastasis was reported to be 1.73%. However, in another retrospective evaluation in which 1,450 patients took part, this rate was determined to be 1.17%.<sup>5</sup> In a review containing 66 studies in which 591 brain metastasis were detected, the rate of cerebellum metastasis was reported to be 30%.<sup>6</sup> In more than half of these patients, extracranial disease was also observed.<sup>7</sup>

Although the value of CA-125, which is used very often ovarian cancer monitorization was within normal limits, in comparison to previous ones, it was detected higher (3.6 vs 24.2 IU/mL). The blood brain barrier is thought to inhibit the passage of the CA-125 molecules into the systemic bloodstream. There are studies reporting different levels of CA-125 in patients with brain metastasis. For this reason, in evaluating central nervous system metastasis, the patient's complaints, clinical findings, scanning methods are firstly used.<sup>8,9</sup> CA-125 elevation is found to be high in only 33% of patients with brain metastasis.<sup>8</sup> There is no research yet on the role of many new tumor markers in the early diagnosis of ovarian cancer, such as human epididymis protein 4, protease serine 8, folate receptor 1, kallikrein 6/7, glutathione S-transferase theta-1, in demonstrating brain metastasis.<sup>10</sup>

In a review of 56 studies involving 34,728 patients, the time interval between the diagnosis of ovarian cancer and brain metastasis was observed to be 24.8 months (11-46 months).<sup>9</sup> Patients with BRCA mutation were reported to have higher platinum sensitized disease, longer survival and disease-free survival.<sup>11</sup> In the study by Faluyi et al., in patients with ovarian cancer after breast cancer, while the risk of central nervous system metastasis was diagnosed

after 45.6 months on average, in patients without the diagnosis of breast cancer who were observed to be diagnosed with ovarian cancer, the risk of brain metastasis was 10.5 times higher.<sup>11</sup> Metastasis of ovarian cancer to the breast is reported more rarely.<sup>12</sup> In our patient, BRCA-2 mutation was diagnosed, and her mother was diagnosed with breast cancer. Cerebellum metastasis was observed in the 50<sup>th</sup> month after the patient's diagnosis of ovarian cancer.

An aggressive treatment plan for brain metastasis was performed in the patient. The patient underwent stereotactic surgery followed by whole brain radiotherapy (WBRT). The approach to the brain metastasis of gynecological cancer may be systemic chemotherapy, radiotherapy (WBRT, gamma-knife radiosurgery).<sup>13</sup> A multimodal approach, which is chosen according to the characteristics of the lesions, is associated with better results.<sup>14</sup> Multiple brain metastasis, presence of extracranial disease, age and monotherapy were stated as the most important factors related to overall survival in the Multicenter Italian Trials in Ovarian Cancer Group Study.<sup>15</sup>

In conclusion, owing to improved treatment methods, in the patients with high-grade ovarian cancer who have a significant increase in their life expectancy, brain metastases will be increasingly seen. With the BRCA-2 mutation and platinum sensitive stage high-grade ovarian carcinoma in our patient, although highly expected to respond well to multimodal therapy, probably leptomeningeal metastases, after the surgery-WBRT, intracranial metastases could not be survived. Unfortunately we lost our patient in a short term. By reporting this case, we aim that this type of patient is thought to contribute to development of a more diverse treatment approach.

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### Conflict of Interest

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members*

of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Songül Alemdaroğlu, Fatih Köse; **Design:** Songül Alemdaroğlu; **Control/Supervision:** Hüsnü Çelik, Özlem Alkan,

Fatih Köse; **Data Collection and/or Processing:** Songül Alemdaroğlu; **Analysis and/or Interpretation:** Songül Alemdaroğlu, Fatih Köse; **Literature Review:** Seda Yüksel Şimsek; **Writing the Article:** Songül Alemdaroğlu, Fatih Köse; **Critical Review:** Hüsnü Çelik, Özlem Alkan, Fatih Köse.

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