

Case Report

Long-term survival in an ovarian cancer patient with brain metastases

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Abstract

Background. Central nervous system (CNS) metastases from ovarian adenocarcinoma are uncommon. The long-term prognosis for these patients is poor, with studies reporting a mean survival of less than 12 months.

Case. We present a case involving a 57-year-old woman diagnosed and treated for primary ovarian cancer in 1994. She underwent optimal cytoreductive surgery and received adjuvant chemotherapy. In 1996, she was diagnosed with a right cerebellar metastatic lesion, and treated with surgery and whole-brain radiotherapy. She is currently 7 years post-treatment of her brain metastasis without evidence of recurrent disease.

Conclusion. Brain metastases from primary ovarian cancer are a relatively rare finding. These patients have a poor prognosis, with studies reporting a mean survival of 12 months. However, the patient in this report remains disease-free since her treatment for metastatic disease. Aggressive surgical and radiation treatment for patients with isolated CNS metastases is reasonable.

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Introduction

Ovarian cancer is the fifth most common cancer in women, accounting for nearly 14,000 deaths in 2001 [1]. Brain metastases resulting from primary ovarian cancer are rare [2]. However, there have been recent studies suggesting an increased incidence of brain metastases in patients with primary ovarian cancer [3,4]. Surgery, irradiation, and chemotherapy comprise the treatment regimen for prolonging survival, although the prognosis for these patients remains poor [5].

McMeekin et al. [6] examined the survival of 104 ovarian cancer patients with metastatic brain disease following a combination of surgery, irradiation, and/or chemotherapy. They reported a median survival of 6 months for all patients, regardless of the treatment modality. These results are more promising than that of Geisler and Geisler [5], who

reported a median survival of 3 months in ovarian cancer patients with concurrent metastatic brain disease.

There have been some studies that have encountered relative success in prolonging the life of these metastatic patients. Gabriele et al. [2,7] reported a mean survival of 17 months in a group of ovarian cancer patients with solitary brain metastases treated with surgery and radiotherapy. Additional studies examining the impact of irradiation on ovarian cancer patients with metastatic disease have reported patient survival results in the 2-year range [6,8]. Chemotherapy has also proven effective in treating brain metastases [2,8]. For example, Cormio et al. [2] described an ovarian carcinoma patient with brain metastases who survived 22 months following treatment with carboplatin.

Case report

A 50-year-old, right-handed, Caucasian woman was originally referred to our gynecologic oncology practice for treatment of an ovarian adenocarcinoma in April 1994. She presented with increased abdominal girth. The patient's preoperative serum CA-125 level was 150 U/ml. She

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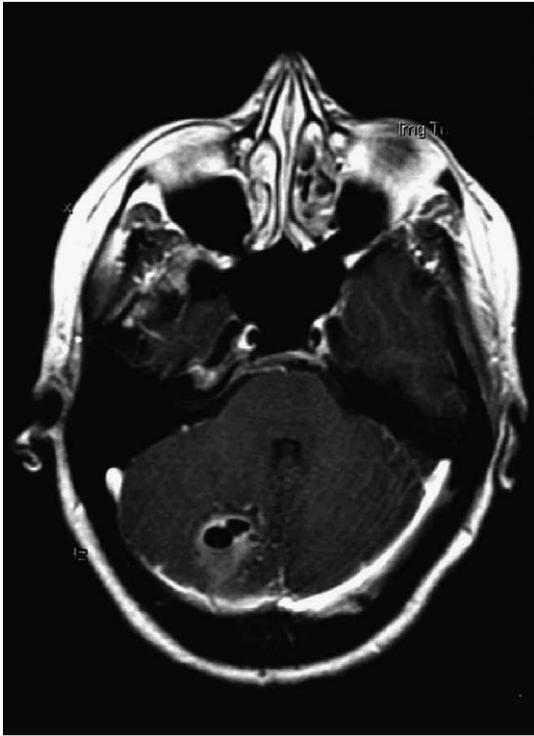


Fig. 1. MRI axial T1-weighted (TR = 400, TE = 26), post-gadolinium contrast exam through the posterior fossa demonstrating a biloculated rim enhancing lesion with an associated mass posteriorly within the right cerebellum, consistent with a metastasis.

underwent a proctosigmoidoscopy, laparotomy with en bloc total abdominal hysterectomy and bilateral salpingo-oophorectomy, modified pelvic posterior exenteration procedure with low rectosigmoid reanastomosis, and CUSA debulking from the diaphragm and peritoneal surfaces. There was no evidence of persistent intra-abdominal ovarian cancer based on the gross findings and frozen section examination. Final pathology revealed a poorly differentiated stage III C bilateral ovarian serous cystadenocarcinoma, with metastasis to the omentum, appendix, periaortic lymph node, and small bowel serosa. The patient subsequently received six courses of taxol (175 mg/m^2) and carboplatin (AUC = 5) commencing in April 1994. She exhibited a complete response to the chemotherapy, and by May 1994, her CA-125 level had declined to 4 U/ml. In November 1994, she underwent a second-look laparoscopy with lysis of adhesions, collection of multiple biopsies, and cytological washings that were negative for malignancy. She had thus achieved a complete clinical and surgical remission. The patient's medical history was significant for hypertension and hypothyroidism. Her medications include calan, premarin, and thyroxine. She denied tobacco or alcohol use.

Following primary treatment, the patient initially did well. She continued working full time and remained active. In July 1995, her clinical exam was unremarkable. She had a negative abdominal pelvic sonogram in October 1995, with the exception of cholelithiasis.

In July 1996, she presented with headaches, gait ataxia, and dysarthria, resulting in a consultation from a neurologist. She denied any weakness, syncope, visual or cognitive dysfunction, nor any seizure history. Her MRI in July 1996 revealed a 4-cm mass in the right cerebellar hemisphere with a cystic component (see Fig. 1). There was evidence of moderately severe mass effect involving the fourth ventricle. No other apparent lesions were noted. She underwent a gross total resection of the suboccipital mass in July 1996. The pathology revealed metastatic adenocarcinoma consistent with ovarian origin. In August 1996, the patient received adjuvant whole-brain radiation (3500 cGy) in 14 fractions to opposed lateral fields, which extended inferiorly to the first two cervical vertebrae. Subsequently, she was treated with a stereotactic boost (1000 cGy) to the right cerebellar tumor bed from August to September 1996.

The patient went on disability in July 1996 and has since retired. She complained of headaches and fatigue in October 1997, but her abdominal CT and MRI of the brain were negative. In November 1998, her headache complaints persisted with some reported visual disturbance. The patient had a CT and MRI of the brain, which were both unremarkable. She had a clinical exam in September 1999 and a follow-up MRI of the brain, which was negative. The patient complained of fatigue in August 2000 but her CT did not demonstrate any change in tumor status. In June 2001, the patient presented with right lower quadrant pain,

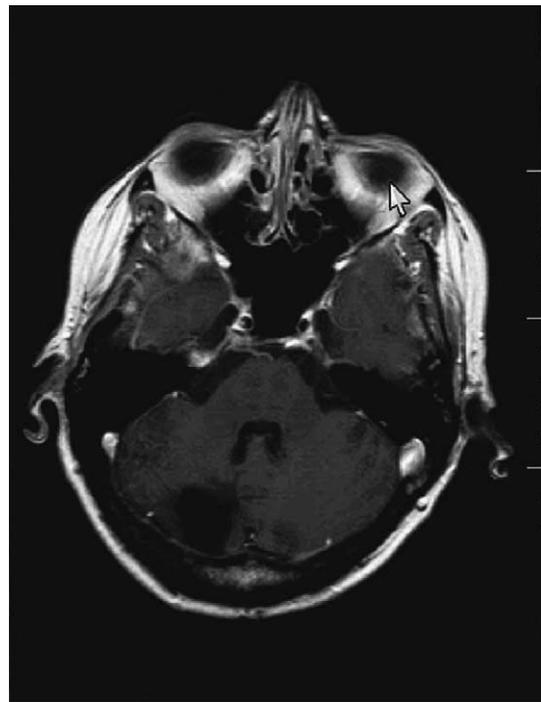


Fig. 2. MRI axial T1-weighted (TR = 627, TE = 17), post-gadolinium contrast exam through the posterior fossa demonstrating a 3-cm-diameter nonenhancing defect in the posterior aspect of the right cerebellar hemisphere in the post-surgical bed at the location of the previously demonstrated metastasis.

constipation, and memory deficits during clinical exam. Her MRI scan in February 2001 was unremarkable (see Fig. 2). In June 2002, the patient reported sciatic pain, constipation, and new onset left buttock pain during clinical exam. She underwent a PET scan for surveillance, which did not exhibit evidence of recurrent malignancy. The patient's serum CA-125 remains normal and she continues to be a pleasant and active individual.

Discussion

We report the status of an ovarian cancer patient who later developed metastatic brain disease. Brain metastases following ovarian cancer are uncommon, although reports have suggested that the prevalence rate may be increasing [4,5]. Currently, survival beyond 12 months is rare, although results may vary depending on the treatment regimen [6].

Metastatic brain disease originating from a primary ovarian carcinoma is treated with surgery, irradiation, and chemotherapy [8]. Ovarian cancer patient studies employing irradiation exclusively have exhibited a median survival of 2.5–4.5 months, and 10 months with combined irradiation and chemotherapy [5,9]. When surgery is involved with irradiation and chemotherapy, studies have reported a median survival of 20 months [9]. Surgery combined with innovative chemotherapy and stereotactic radiotherapy may prolong patient survival even further. Patients with solitary CNS metastases are probably the most likely to benefit from aggressive treatment.

The patient in this report has survived 9 years post-treatment for ovarian cancer and 7 years following treatment for metastatic brain disease. Her survival has far exceeded what has previously been reported. Hall et al. examined the long-term survival of a variety of cancer patients (e.g., ovarian, small cell, prostate) with metastatic brain disease, reporting a 7.8% actuarial survival rate for the ovarian cancer patients at 5 years. Cormio et al. [2] reported the results of a grade IV ovarian carcinoma patient who later developed brain metastases. The woman survived 22

months following carboplatin treatment for her brain metastases, eventually succumbing to recurrent pelvic disease.

We recognize the possibility that our patient had isolated CNS metastatic disease because the chemotherapy regimen used to treat her ovarian primary was unable to penetrate the blood–brain barrier. Many of the chemotherapies (e.g., carboplatin) are unable to permeate the blood–brain barrier, and thus cannot protect patients from the development of brain metastases [10]. Our patient had a solitary brain metastasis, which could have contributed to her protracted survival compared to patients with multiple lesions [8]. Aggressive treatment with surgery and/or radiation therapy is reasonable in this subgroup of recurrent ovarian cancer patients.

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