Gynecologic Oncology Reports 32 (2020) 100540

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Case report

Metastatic brain disease in early stage ovarian cancer: A case report

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ARTICLE INFO

Keywords:
Early stage ovarian cancer
Brain metastasis
Early metastatic disease

ABSTRACT

Ovarian cancer rarely metastasizes to the brain. If it does, it is more likely to occur with advanced stage carcinomas, more than one year after diagnosis, and rarely presents as a single lesion. Early detection, treatment, and close follow-up is essential to optimize prognosis and prevent long-term disability. This case presents a 54-year-old female with a previously diagnosed & treated stage 1a, grade 3 ovarian cancer who presented with a complaint of persistent headache. Imaging demonstrated a singular brain lesion. She underwent mass resection with pathology consistent with metastatic ovarian cancer. This was only 18 months after her primary diagnosis, demonstrating the importance of close surveillance and heightened awareness of metastatic disease.

1. Introduction

In 2018, there was predicted to be approximately 22,240 new cases of ovarian cancer and 14,070 ovarian cancer deaths in the US (Torre et al., 2018). Epithelial ovarian cancer is the most common type of ovarian cancer and the one of the most common causes of gynecological cancer related deaths (Jayson et al., 2014). One quarter of all ovarian cancers are diagnosed at stage I (Torre et al., 2018). The incidence of brain metastases in ovarian cancer is estimated to be between 0.29 and 5% and often coincide with extracranial metastasis (Ushijima, 2010; Pectasides, 2006). More commonly, brain metastasis occurs in stage III and stage IV and are histologically grade 3 (Pectasides, 2006). We present a rare case of a patient with stage IA, grade III endometrioid ovarian cancer who developed a single brain metastatic lesion (See Schemes 1a–4).

2. Case

The patient is a 54-year-old G3 P2-0-1-2 with significant past medical history of endometrioid ovarian cancer (stage Ia, grade 3) who presented to the emergency department with a primary complaint of left-sided headache. She had been experiencing *retro*-orbital headaches for the last several months without other neurological deficits. Review of systems was otherwise negative.

Her physical examination was within normal limits. Due to the persistent nature of the patient's symptoms and significant history, a head CT was performed. This demonstrated a left frontal 2.4 × 2.4 cm lobe mass with surrounding edema. An MRI was subsequently performed which demonstrated a heterogeneously enhancing circumscribed 2.5 cm mass within the left anterior frontal region with extensive vasogenic edema, mass-effect and midline shift. A CT of the chest, abdomen, and pelvis were negative for any metastatic disease.

The patient underwent menopause at age 49 with menarche at 13. She had 2 healthy pregnancies. She never used tobacco, did not have any history of hormonal replacement therapy and had no significant family history. As previously mentioned, the patient did have a recent history of endometrioid ovarian cancer (stage Ia, grade 3). After surgical intervention (total abdominal hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection, appendectomy, and omentectomy), the patient underwent 6 cycles of Paclitaxel (Taxol) and Carboplatin (Carbo). She declined any genetic or germline mutation testing. The patient did follow-up as directed with her gynecological oncologist. Other than a complaint of headache, the patient did not have any other significant symptoms or findings during these visits. The patient had undergone a head CT and PET/CT skull in the interval between her surgical intervention and current presentation. No abnormalities were found.

She was admitted to the hospital with continued close monitoring. She was started on intravenous steroid therapy along with antiseizure medications. A serum CA-125 was 7 unit/mL, which was unchanged from baseline and both 6 and 12 months before. The patient underwent a left stereotactic frontal craniotomy with resection of an intradural, intra-axial mass 4 days after admission. The patient tolerated the procedure well and was transferred to the neurology ICU for postoperative

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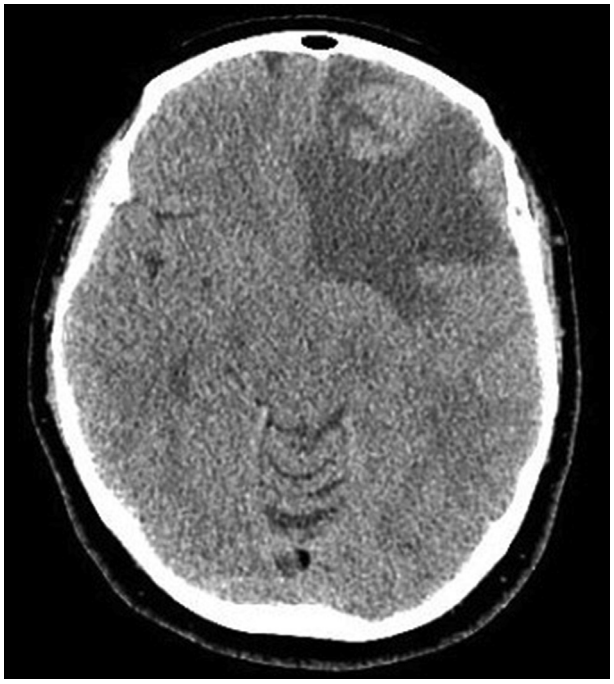
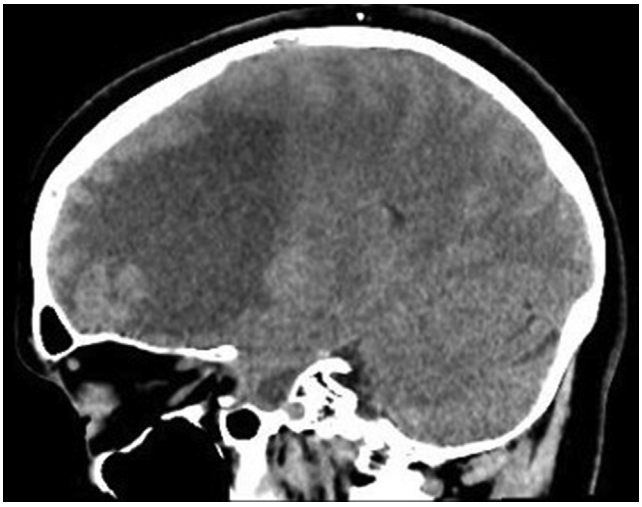
https://doi.org/10.1016/j.gore.2020.100540
Received 10 November 2019; Received in revised form 14 January 2020; Accepted 27 January 2020
Available online 30 January 2020



Scheme 1a. CT image demonstrating 2.4 × 2.4 cm singular lesion with surrounding edema in left frontal lobe in coronal view.

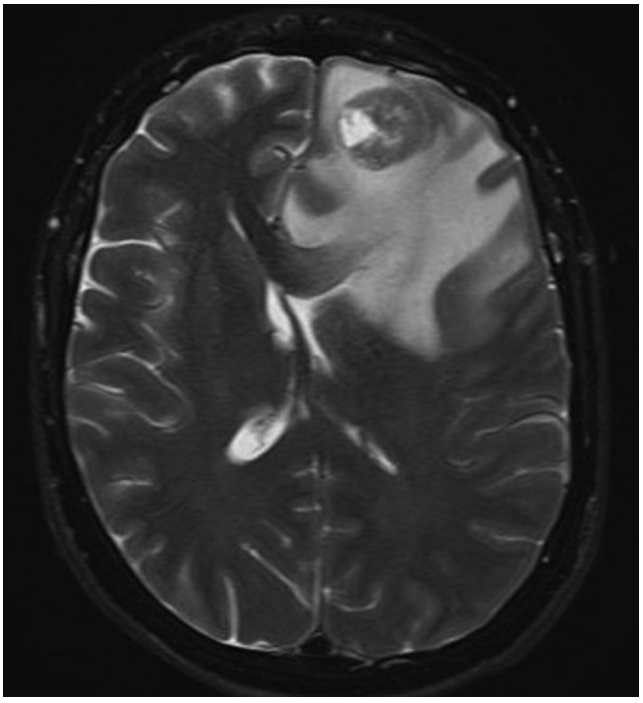


Scheme 1b. CT image demonstrating 2.4 × 2.4 cm singular lesion with surrounding edema in left frontal lobe in sagittal view.

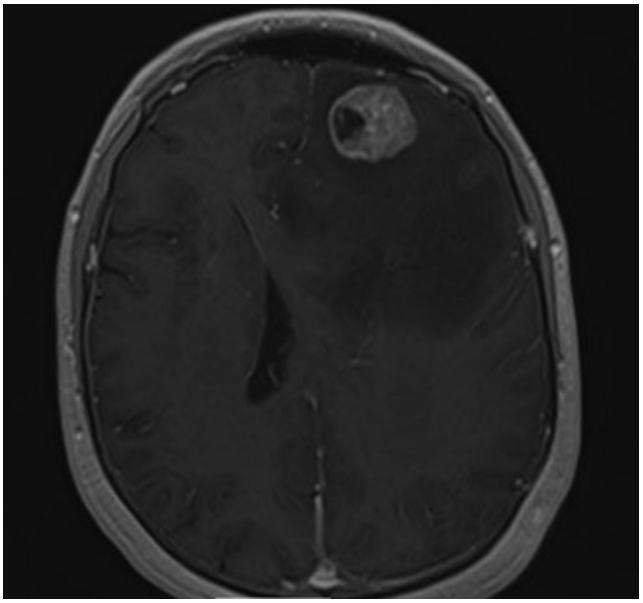
management.

Her postoperative course was complicated by an episode of questionable loss of consciousness. A repeat brain MRI demonstrated edema. No acute intracranial process was noted. An echocardiogram was performed and was significant for a large size (1.8 × 1.5 cm), nonmobile, echogenic mass attached to the right atrial wall. Prophylactic anticoagulation was started. A lower extremity duplex study was negative. A repeat chest CT scan was positive for a left lower lobe branch small pulmonary artery embolism. There was no evidence of right heart strain. Daily head CTs were performed and on postoperative day 5, increased hemorrhage was noted and IV anticoagulation was halted. A transesophageal echocardiogram was obtained and demonstrated a large 4.6 × 2.1 cm echogenic broad-based mass adherent to the right atrial wall. This was most consistent with a thrombus however malignancy was still unable to be ruled out.

The final pathology of the left frontal mass was significant for



Scheme 2. T2-weighted MRI demonstrating heterogeneously enhancing circumscribed 2.5 cm mass within the left anterior frontal region with extensive vasogenic edema, mass-effect and midline shift in coronal view.

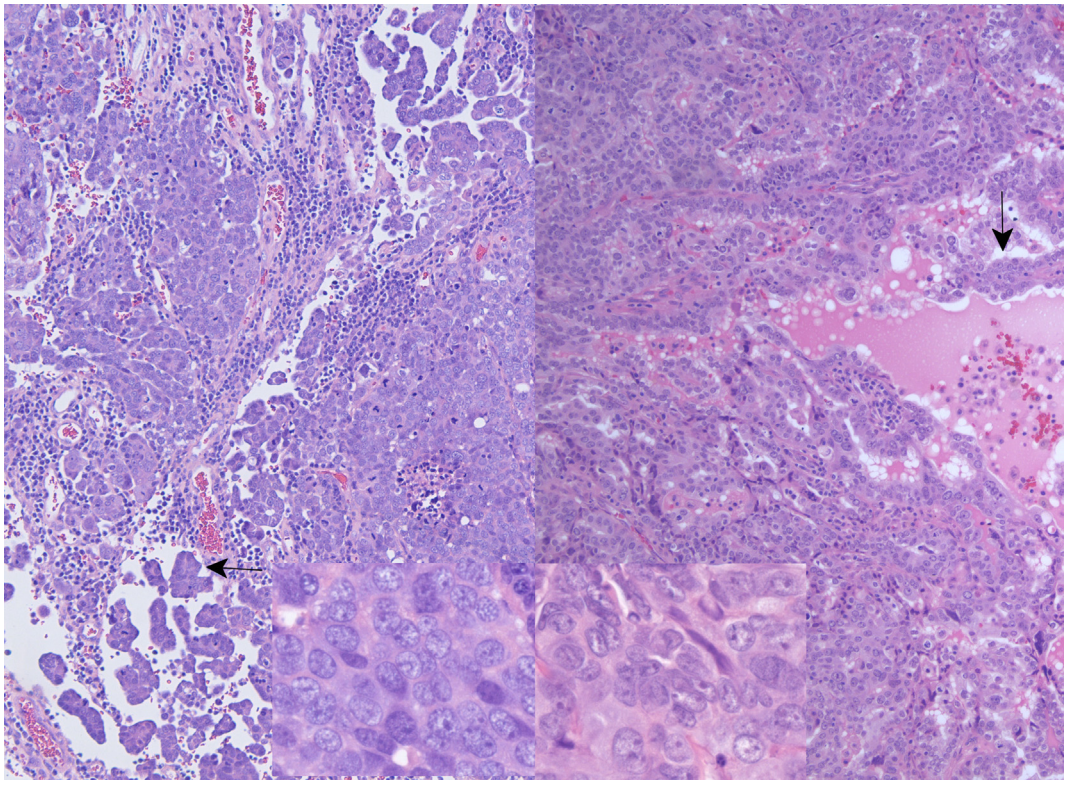


Scheme 3. T1-weighted MRI demonstrating heterogeneously enhancing circumscribed 2.5 cm mass within the left anterior frontal region with extensive vasogenic edema, mass-effect and midline shift in coronal view.

metastatic poorly differentiated adenocarcinoma. This lesion was similar to some of the poorly differentiated foci of the ovarian carcinoma. The patient remained stable and was discharged 14 days after initial presentation. Further management included brain radiation therapy with four cycles of Carbo/Taxol adjuvant chemotherapy.

3. Discussion

Endometrioid ovarian cancer makes up only 10% of epithelial ovarian cancer (Torre et al., 2018). This subtype is often diagnosed at



Scheme 4. Histologic comparison of ovarian primary tumor (right) and brain metastasis (left), medium magnification. Arrows highlight papillary epithelial tufts present. Insets (high magnification) demonstrate similar nuclear features in the tumors.

stage I (59%) (Torre et al., 2018), as seen in our patient. This patient had developed one of the rarer epithelial ovarian cancers, endometrioid subtype, but was diagnosed as stage IA (defined as limited to one ovary or fallopian tube) which is more common in this subtype (59%) (Torre et al., 2018; Javadi et al., 2016). Treatment for stage I ovarian cancer includes surgery to remove adnexa on the side of the tumor, resection of the contralateral adnexa, hysterectomy, resection of greater omentum, retroperitoneal lymph node dissection and peritoneal biopsy (Hirose et al., 2018). Given that this patient's tumor was poorly differentiated (grade 3(Javadi et al., 2016), despite stage Ia, she received 6 cycles of Carbo/Taxol. The survival rate of women with stage I epithelial ovarian cancer is 92% (versus 17–28% in advanced stages) (Doubeni et al., 2016), with recurrence of 20–25% in stage I (Ushijima, 2010). Histological grade of the tumor is the most important prognostic indicator in disease-free survival (Javadi et al., 2016).

Brain metastases is rare in ovarian cancer with the incidence estimated to be between 0.29 and 5% with evidence of other sites of metastasis prior to this time (Ushijima, 2010; Pectasides, 2006). These patients usually have more advanced stage of disease (Pectasides, 2006). This patient was unique because the early stage of her cancer and no other confirmed metastatic sites. A retrospective study done by Kolomainen et al. found that the stage of the disease had little effect on the time to brain metastasis (Kolomainen et al., 2002). Brain metastasis often occurs late in the course of the disease and patients will present with CNS symptoms only (Kolomainen et al., 2002). Our patient presented 18 months after initial diagnosis and her only significant symptoms were headache, fatigue and drowsiness. To the authors' knowledge, there has only been one similar case report that described a patient who presented with symptoms of increased intracranial pressure and was found to have a brain lesion with ovarian origin (Matsunami et al., 1999). On laparoscopic examination, there was no evidence of locally invasive disease and the carcinoma would have otherwise been categorized as stage IA (Matsunami et al., 1999).

Single site brain metastases are less common than multiple brain metastases, potentially ranging from 35% to 46% of cases and are most commonly seen in the cerebral hemisphere (Pectasides, 2006). In a review by Pectasides et al., there was no difference in the development of brain metastasis between the histological subtypes of ovarian cancer (Pectasides, 2006).

There has been some discussion on the impact of platinum-based chemotherapy on the blood brain barrier, allowing for brain metastasis, however, it appears to be controversial and requires further study (Pectasides, 2006; Pietzner et al., 2009). Our patient had completed her chemotherapy regimen prior and it could have contributed to the development of brain metastasis. Although further study could be warranted, it would be difficult to study the effects of chemotherapy on brain metastasis in this subset of patients since diagnosing early stages of ovarian cancer is uncommon, many may not have received chemotherapy treatment, and the incidence of brain metastasis is low.

Patients with brain metastasis benefit from aggressive combined treatment with external whole brain radiation and surgery with or without chemotherapy compared to those who were treated using single treatment modalities, especially in patients that have no evidence of disease at other sites (Anupol et al., 2002; Cohen et al., 2004). Corticosteroids are used in the treatment of brain metastasis however, their use is purely palliative and has no survival benefit (Pietzner et al., 2009). Positive prognostic factors for patients that have brain metastasis include younger age at diagnosis of both the primary tumor and the brain metastasis, lower grade of primary tumor and higher functional status (Pakneshan et al., 2014). In this case, the patient was diagnosed at a later age and her brain functionality is still intact, leading to the increased likelihood that she will have a positive prognosis despite this newly developed brain metastasis.

4. Conclusion

The risk of metastatic brain lesions from ovarian cancer is positively correlated with advanced stage disease. Time to metastasis has no such

association and typically occurs more than one year after diagnosis. Other proposed associations include genetic mutations and chemotherapeutic drugs. The risk of a single metastatic brain lesion after diagnosis of stage Ia, grade 3 ovarian cancer is minimal, especially when the patient does not have a history of any known risk factors. However, when a patient with a history of ovarian cancer presents with constant headache, there should be consideration for metastasis, regardless of the stage of the disease. Imaging can aid to direct further intervention. While the overall prognosis of this patient is good, further surveillance will be essential.

Author contribution

Sophia Halassy: Manuscript drafting and editing, Katrina Au: Review of literature, Nishan Chobanian: Editing

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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