

Brain Metastasis of Papillary Ovarian Adenocarcinoma

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ABSTRACT

Brain metastasis from epithelial ovarian cancer is a rare diagnostic entity with a reported incidence of 1-2%. Serous epithelial ovarian cancer is usually associated with a poor prognosis and is the most common malignancy metastasizing to the brain. The median time from primary diagnosis to development of cerebral lesions is directly correlated with the initial tumour grade and stage. The median survival after diagnosis of brain metastases is 6 months. It is suggested that brain imaging studies should be included in the follow up of patients after treatment for ovarian carcinoma. We report a case of brain metastasis of ovarian adenocarcinoma 2 years post-surgery and six cycles of chemotherapy.

Key words: brain, metastases, ovarian, adenocarcinoma

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INTRODUCTION

A 46-year-old female was brought to the emergency department due to loss of consciousness. The patient had a history of right-sided weakness associated with headache 1½ months prior. Her headache was intermittent in nature and located at the frontal region. There were 2-3 episodes of generalized seizures and 3-4 episodes of projectile vomiting for the last 20 days. Two years prior, the patient had been diagnosed with high grade serous epithelial ovarian carcinoma stage III having CA-125 levels of 800 IU/ml. The patient underwent total abdominal hysterectomy, bilateral salphingo-oophorectomy and omentectomy. The final histopathology report showed high grade serous epithelial ovarian carcinoma. Post-surgery, the patient underwent 6 cycles of chemotherapy and was on regular follow up. The follow up was uneventful for 1½ years. Her last serum CA-125 level was 10.6 IU/ml before being lost to follow up.

Following this, non-contrast computed tomography (CT) scan of the brain was advised which showed a ring enhancing lesion at the left frontal region measuring 3.5 x 3.2 cm. The lesion was at the grey-white mater junction with necrotic areas surrounded by hypodense areas. There was midline shift of 1.1 cm to the left with no evidence of infarction or intracranial bleeding. Radiologically, a probable diagnosis of metastasis was made. Magnetic resonance imaging (MRI) showed left frontal space-occupying lesion. Serum CA-125 levels were elevated (110.8 IU/ml). Left frontoparietal craniotomy was performed. A biopsy sample was submitted with a clinical impression of abscess. Gross examination showed multiple grey brown to grey white, soft, friable tissue fragments measuring 5 x 4 x 2 cm in total. Microscopic examination revealed pleomorphic cells with prominent nucleoli arranged in papillary architecture and clusters invading normal brain parenchyma. There were areas of hemorrhage and necrosis. On immunohistochemical staining, these tumour cells were positive for cytokeratin, epithelial membrane antigen (EMA), and CA-125, and negative for glial fibrillary acidic protein (GFAP). A final diagnosis of metastatic deposits from papillary adenocarcinoma of ovary was made.



DISCUSSION

Brain metastases from epithelial ovarian carcinoma is a rare diagnostic entity with a reported incidence of 1-2% and is associated with poor prognosis.¹ Epithelial ovarian carcinoma most commonly progresses to intraperitoneal dissemination, followed by metastasis to the pleural cavity, liver, and lung.² Brain metastases are more common with primary tumours of the lung, breast, renal, colorectal

carcinomas and melanoma. A study done by Piura and Piura suggested that out of all gynaecological cancers, the incidence of brain metastasis of ovarian malignancy is 1.2% which is twice the incidence associated with cervical or endometrial cancer.³ The most common histologic subtype of ovarian carcinoma associated with brain metastasis is the serous type, followed by mixed epithelial, endometrioid adenocarcinoma, mucinous, undifferentiated, and clear cell type.⁴

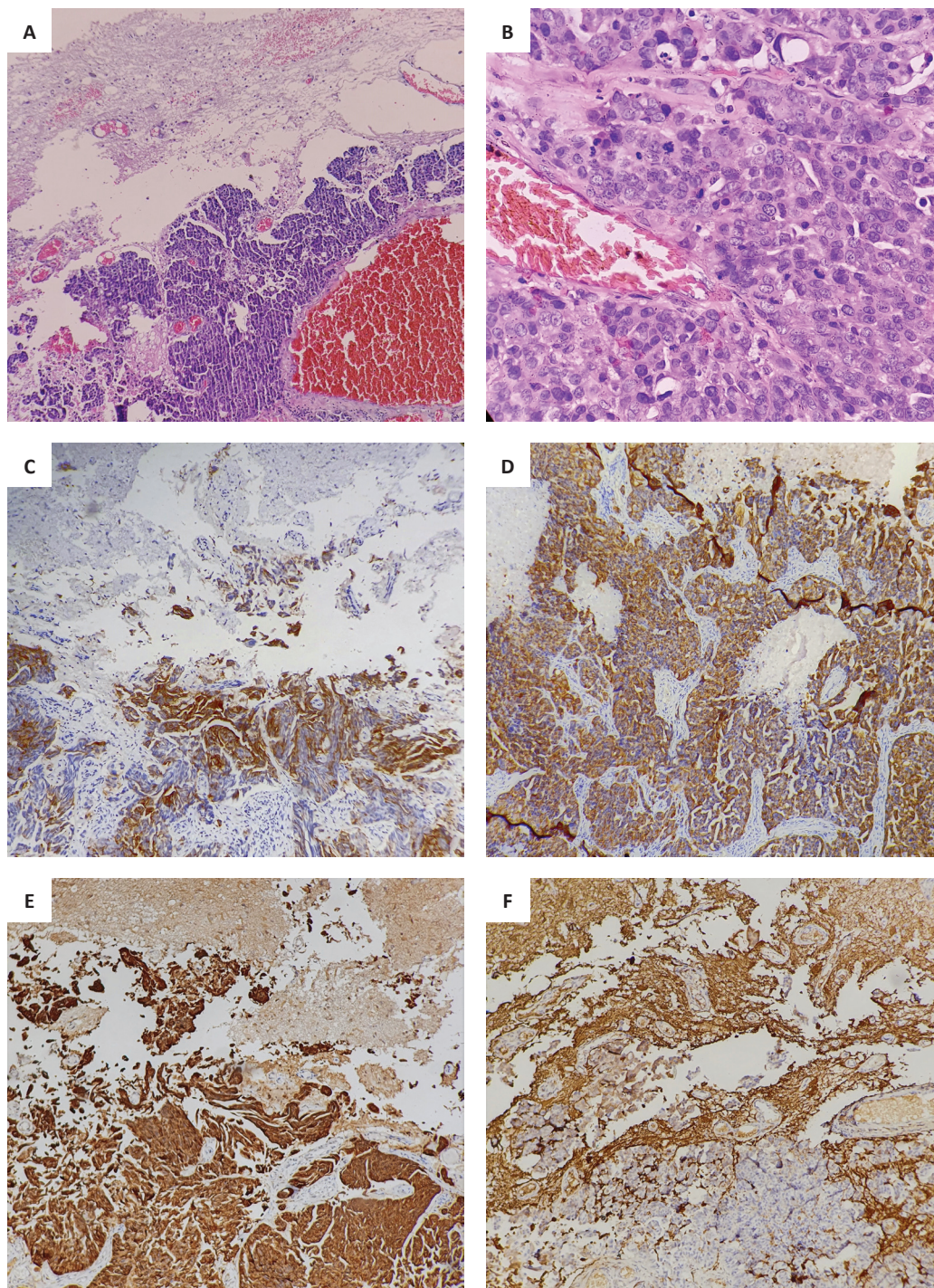


Figure 1. (A) Infiltration of papillary adenocarcinoma of ovary into brain parenchyma (H&E, 100x); (B) High power view of papillary adenocarcinoma of ovary (H&E, 400x); (C) CA-125 positivity in metastasis of ovarian carcinoma (IHC, 100x); (D) Cytokeratin positivity in metastatic of ovarian carcinoma (IHC, 100x); (E) EMA positivity in metastatic of ovarian carcinoma (IHC, 100x); (F) GFAP positivity in normal brain parenchyma and negativity in metastatic of ovarian carcinoma (IHC, 100x).

Some studies have demonstrated the correlation between germline mutations of BRCA1 (BRCA-1) mutations and incidence of brain metastases in ovarian carcinoma. BRCA-1 and BRCA-2 gene mutations, which are detected in 10% of ovarian carcinoma, are associated with aggressive behaviour and metastatic disease.⁴

In the brain, the cerebrum is the most common site for metastases, followed by the cerebellum, and leptomeninges.³ The frontal lobe is the most commonly involved area.⁴ Symptoms of brain metastases include headaches, nausea, vomiting, confusion, dizziness, decreased mental status, general or extremity weakness, urinary incontinence, gait disturbance, ataxia, visual disturbance including diplopia, photophobia, speech impairment, syncope, and seizures. Contrast enhanced MRI brain and CT scan together, are the most accurate imaging modality. Metastasis on CT scan appears as a heterogeneous, contrast enhancing lesion.

The multimodal treatment approach includes surgical resection of the brain metastases, whole brain radiotherapy, and chemotherapy. In the case of single brain metastasis, surgery should be considered if the site is approachable and the tumour is producing mass effects. In the case of multiple metastases, multimodality treatment approach is advised.³ The reported median time from primary diagnosis to development of cerebral lesions ranged from 11 to 46 months and directly correlated with the initial tumour grade and stage.^{1,4} Patients with poorly differentiated ovarian carcinoma (grade 3) had a median time interval of 1.5 years between diagnosis and brain metastasis. Patients with well- to moderately differentiated ovarian carcinoma (grades 1 and 2) had a median time interval of 4.73 years. The median survival after diagnosis of brain metastases is 6 months, however, multimodal treatment approach improves the outcome of the patient.¹ A combination of surgery, radiotherapy and chemotherapy has a median survival time of 20 months; 17 months for surgery and radiotherapy; 9.1 months for radiotherapy and chemotherapy; 4.5 months for radiotherapy only; 7.5 months for chemotherapy only; and 18 months for stereotactic radiosurgery (SRS) or gamma-knife radiosurgery (GKRS). Out of all these, SRS and GKRS yielded better survival results.¹

Serum CA-125 is done as a part of routine follow-up for ovarian cancer patients, however, it cannot be relied upon to detect CNS relapse. It is advisable to include brain imaging studies in the follow up of patients after treatment for ovarian carcinoma.^{1,2}

The patient started chemotherapy but was lost to follow up after 1 month. There was no other information available regarding further treatment.

CONCLUSION

Ovarian cancers rarely metastasize to the brain and is associated with poor prognosis. A careful clinical examination and proper therapeutic approach, including chemotherapy and radiotherapy, may lead to prolonged survival.

ETHICAL CONSIDERATION

Patient consent was obtained before submission of the manuscript.

STATEMENT OF AUTHORSHIP

All authors certified fulfilment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

The authors declared no conflict of interest.

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