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Difficult Diagnosis and Management in a Rare Case of Solitary Third Ventricle Metastasis in Ovarian Cancer

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Abstract

We report a rare case of a solitary brain metastasis of third ventricle in a 62-year-old patient with a history of ovarian high-grade serous papillary adenocarcinoma (FIGO stage IIIc) treated with surgery plus adjuvant chemotherapy. One year after the end of adjuvant chemotherapy without signs of residual disease during the follow-up program, she was admitted for apathy, severe mental confusion and temporal disorientation. Craniospinal magnetic resonance imaging (MRI) showed a solitary cystic-necrotic mass lesion occupying the third ventricle and the hypothalamus, reaching both the foramina of Monro. Biopsy of lesion confirmed metastasis of ovarian origin. The patient underwent radiotherapy with stereotactic technique (SRT) with partial response of lesion. Three months after SRT, she developed meningeal carcinomatosis. This case highlights difficult management about differential diagnosis of radiological findings and treatment options in atypical brain metastasis from ovarian cancer.

Keywords

Ovarian cancer; Brain metastasis; Third ventricle metastasis; Stereotactic radiotherapy

Background

Brain metastasis from epithelial ovarian cancer are rare, with less than 700 patients documented in the literature [1], and usually found in association with disseminated systemic disease. The reported incidence ranges from 0.29 to 11.6% [1, 2]. The purpose of this case report is to describe clinical features, neuroradiological findings, and therapeutic options of an adult woman with a third ventricle intraventricular metastasis as relapse of ovarian cancer.

Case Presentation

In May 2013, a 62-year-old patient was admitted for apathy, severe mental confusion and temporal disorientation, without motor or sensory deficits. She had a history of ovarian cancer. In January 2012, she was diagnosed with ovarian cancer and treated with total hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy as cytoreductive surgery. Histological Diagnosis

was high-grade serous papillary adenocarcinoma with focal areas of undifferentiated carcinoma (G3, FIGO stage IIIc). After surgery patient was undergone to six cycles of adjuvant chemotherapy with carboplatin-AUC 5 and paclitaxel. In June 2012, clinical suspicious of persistent disease (CA 125 level: 123 UI/ml) led to a second-look laparotomy resulting in para-aortic lymph nodes dissection and peritoneal random biopsies. Histological examination was negative for disease. Three- and six-month follow-up body CT-PET studies did not show signs of recurrence before onset of neurological symptoms.

Magnetic resonance imaging (MRI) of the brain (Figure 1A-D) showed an inhomogeneous, contrast-enhancing cystic-necrotic mass lesion occupying the third ventricle and the hypothalamus, reaching both the foramina of Monro, and thus resulting in biventricular hydrocephalus. Spinal MRI was negative for dissemination. An external ventricular derivation, in order to relief endocranial hypertension, and a biopsy were performed. At histological examination, the ovarian origin of the metastasis was demonstrated by the presence of papillary groups of neoplastic cells showing positivity for cytokeratin 7 and WT1 (Figure 2). Cerebrospinal fluid examination showing malignant WT1-positive cells, consistent with ovarian origin was performed. Abdomen and thorax CT was negative for recurrent malignancy. Serum Ca125 levels were 65 UI/ml.

Since the lesion was not surgically removed, an approach by radiation treatment was chosen. The patient underwent radiotherapy with stereotactic technique (SRT) in July 2013. A delivered total dose was 27 Gy with a prescription to 90% isodose. Stereotactic radiotherapy was performed with 9 beams and delivered in 3 fractions (9 Gy/fr). No neurological toxicity after RT occurred. Despite the positivity for ovarian cells in cerebral fluid examination, this patient, according to our clinical evaluation, was not candidate for craniospinal irradiation considering her clinical performance status and potential toxicity of this latter treatment.

In September 2013, restaging CT-PET was negative for systemic recurrence and craniospinal MRI showed reduction in size of the lesion in the third ventricle. In October 2013, she had sharp headache and brain MRI (Figure1e-h) showed small leptomeningeal and ependymal nodules, suggesting meningeal carcinomatosis. Thus, in November 2013, systemic chemotherapy was started, including a combination of paclitaxel (175 mg/m^2) plus bevacizumab (10 mg/kg) every 28 days. Serum CA125 levels decreased to 25 U/ml. However, in February 2014, general conditions worsened and the patient died.

Discussion

To the very best of our knowledge, this is a very rare case of relapsing disease in ovarian cancer by a third ventricle metastasis. Intraventricular metastases account for 0.9% to 4.6% of cerebral metastases [3], the most common causes in adults being renal, colon, and lung carcinoma.

Neuroradiological findings of a solitary intraventricular metastasis may be indistinguishable from those of an intraventricular meningioma or a choroid plexus neoplasm; however, these are more frequent in the lateral ventricles [3]. A history of primary tumour should raise suspicion for metastases, such as in the patient reported herein.

Meningiomas as well as choroid plexus papillomas are easily excluded at histology, whereas the differential diagnosis with a choroid plexus carcinoma may be challenging. The age of the patient and the history of primary ovarian cancer were helpful diagnostic clues in our patient's history. Furthermore,

neoplastic cells showed the immunohistochemical phenotype characteristic of serous ovarian cancer [4]. Brain metastasis from ovarian cancer are uncommon, however are often fatal. Recently, they have been identified with an increasing incidence, and prolongation of survival associated with platinum-containing chemotherapy has been claimed to be the main reason for this rising incidence [1, 2]. Notably, the control of tumour cell deposits is effective in the abdominal cavity but not in the central nervous system, since chemotherapy molecules have difficulties in crossing the blood-brain barrier. To date, the pathogenesis of hematogenous spread from genital tract to the brain is unknown, however recent studies focused on the role of adhesion molecules, such as neural cell adhesion molecule [5].

The majority of patients with brain metastasis from ovarian cancer had a primary advanced stage, i.e. stage III/IV, serous epithelial carcinoma and a histological grade G3, such as in the patient presented herein. Brain metastasis from ovarian cancer are usually intraaxial, especially in the brain, and are more often multiple [1]. Leptomeningeal involvement is rare [1]. Presenting symptoms of brain metastasis varied according to the site of disease: headache, dizziness, nausea and instability, due to increased intracranial pressure are most common onset symptoms [1, 2].

Neuroradiological diagnosis is made by CT and especially MRI. When spinal MRI is negative, cerebrospinal fluid examination is nevertheless useful to confirm diagnosis and to evaluate the risk of spinal dissemination. Biopsy or surgical removal is needed to obtain histological diagnosis.

Current treatments for brain metastasis include surgical resection, whole brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), SRT, and chemotherapy [6]. Albeit no combination of this treatment has showed prolonging patient survival, SRS or SRT are becoming the more widely used treatments for patients with a single brain metastasis [6, 7]. The rationale of this approach is a shorter treatment for metastatic patient, avoiding the significant neurotoxicity compared to a WBRT, with a non-invasive approach allowing to treat lesions located in eloquent areas respect to surgery.

Metastatic lesions and primary tumour located in third ventricle have a high risk for craniospinal dissemination especially with positive liquor for cancer cells, such as in the patient reported herein.

Learning Point

Although very uncommon, there is the possibility of brain metastasis from ovarian cancer without peritoneal, hepatic and lung involvement. Neuroradiological findings and pathological exam should be always correlated with patient's history considering the wide range of differential diagnosis of intraventricular masses. According to our experience, cerebral fluid examination should be performed in every case with third ventricle mass to evaluate risk of cerebrospinal fluid dissemination. SRT is a feasible and well-tolerated treatment for central brain metastasis but in patient with high risk for meningeal carcinomatosis SRT plus craniospinal irradiation should be considered.

Figures

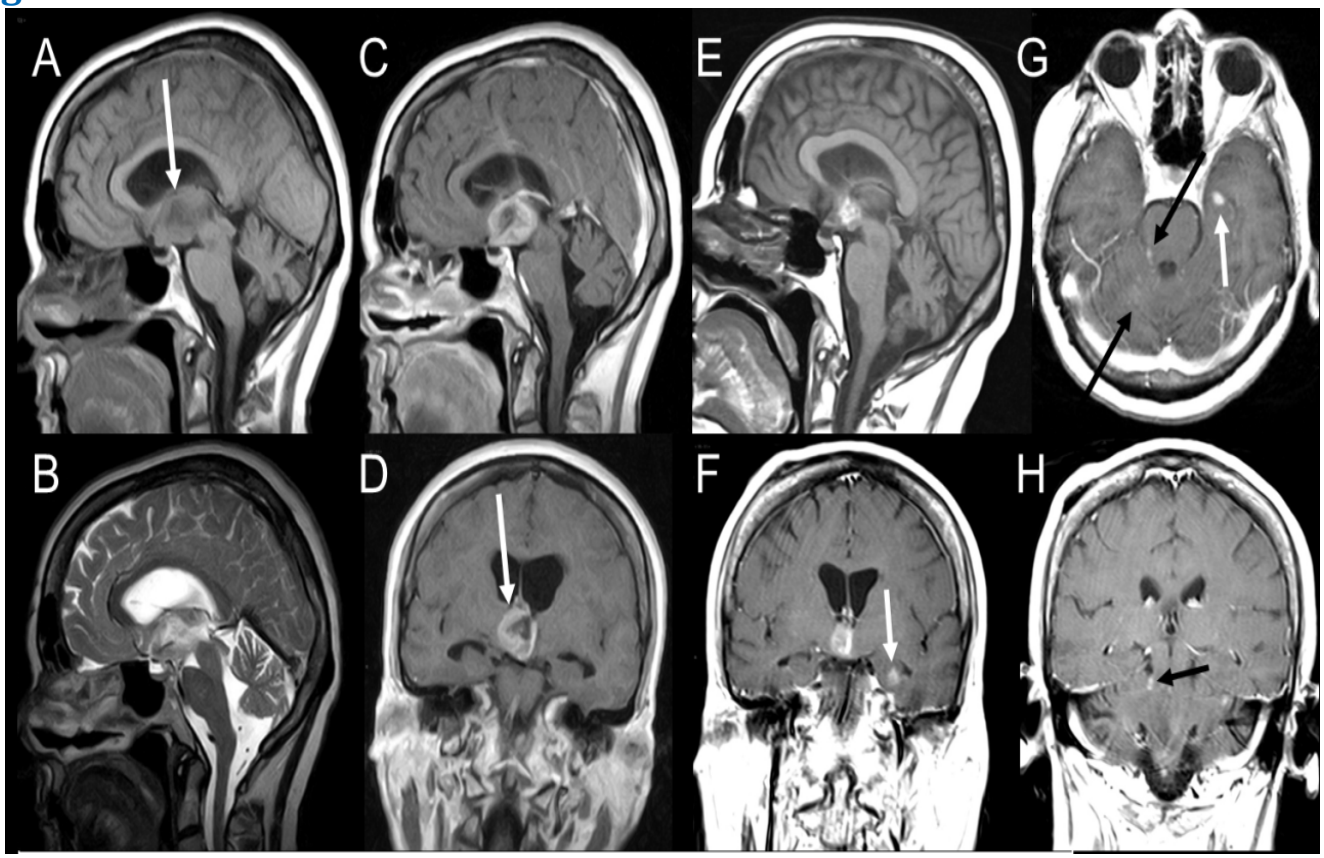

Figure 1: Magnetic resonance (MR) imaging of the brain: diagnosis (A-D) and five-month follow-up (E-H).

At diagnosis, unenhanced T1- (A), T2- (B) and gadolinium-enhanced T1- (C) weighted sagittal and coronal (D) MR images show an inhomogeneous, contrast-enhancing mass lesion (*white arrows*) in the third ventricle. Five months later, unenhanced T1-weighted sagittal (E) and gadolinium-enhanced T1-weighted coronal (F,H) and axial (G) MR images show clear-cut size reduction of the intraventricular metastasis which shows signs of hemorrhagic infarction, as well as the appearance of leptomeningeal nodules in the left temporomesial (*white arrows*) and right ponto-cerebellar (*black arrows*) regions.

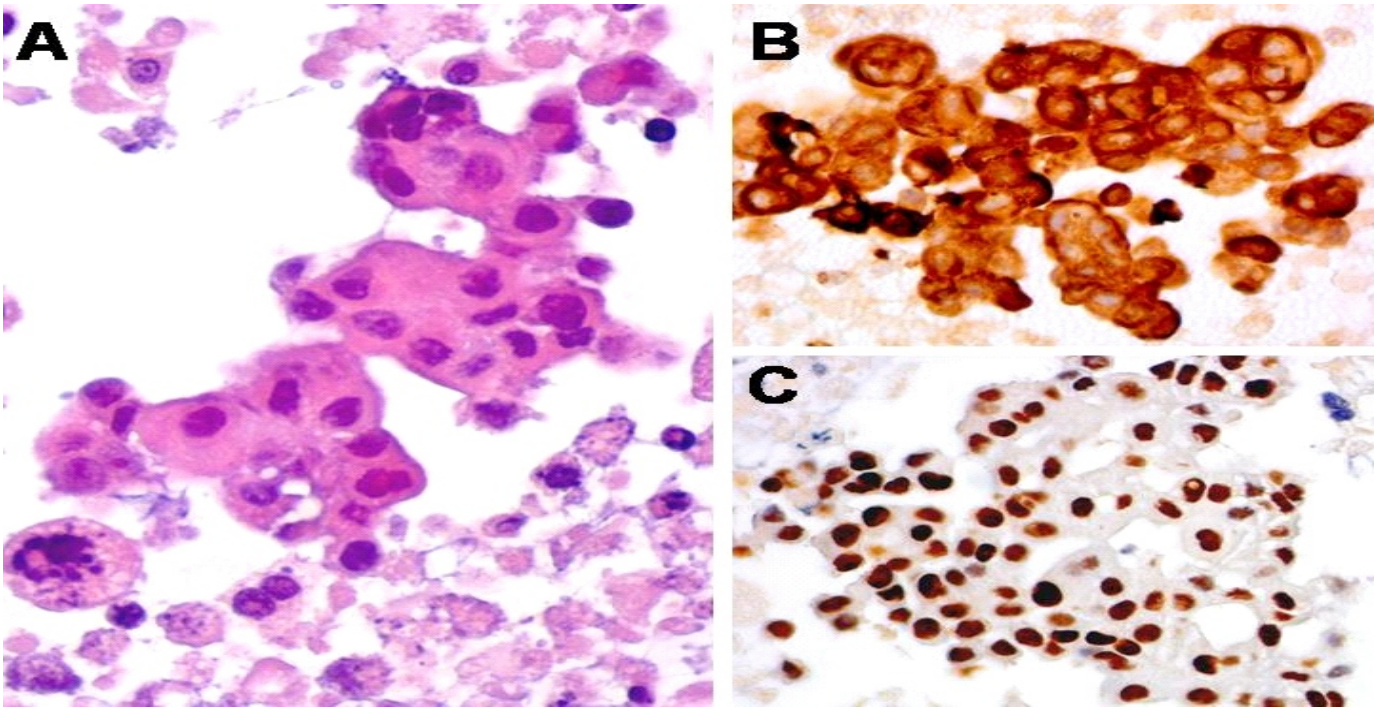

Figure 2: Pathology: haematoxylin and eosin (A) and immunohistochemistry, avidin-biotin method, chromogen: diaminobenzydine (brown stain) (B, C): original magnification: x 400.

Neoplastic cells in papillary groups admixed with necrotic debris (A) are strongly positive for cytokeratin 7 (B).There is also nuclear positivity for WT1 in most neoplastic cells (C).

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