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Case Report

Cerebellar Metastasis of Low-Grade Serous Carcinoma of the Ovary

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Abstract

Introduction: Ovarian carcinoma is pathologically classified into serous, mucinous, clear cell and endometrioid types, with serous carcinoma accounting for approximately 30% of cases. Serous carcinoma is further subdivided into High-Grade Serous Carcinoma (HGSC), Low-Grade Serous Carcinoma (LGSC) and borderline serous carcinoma. Brain metastasis from ovarian carcinoma is rare and most reported cases originate from HGSC. Brain metastasis from LGSC is extremely uncommon.

Case Description: We report the case of an 81-year-old woman in whom an ovarian tumor was detected on abdominal Computed Tomography (CT) six years earlier. The tumor was completely resected and histopathological examination confirmed LGSC. The patient was subsequently followed without adjuvant chemotherapy. Six years later, she developed ataxia of the left upper limb. Brain Magnetic Resonance Imaging (MRI) revealed a tumor in the left cerebellar hemisphere accompanied by extensive surrounding edema. Brain metastasis from ovarian carcinoma was suspected and the tumor was surgically removed under microscopic visualization. Histopathological examination of the resected specimen revealed features consistent with LGSC, identical to those of the primary ovarian tumor.

Outcome: The postoperative course was uneventful and no neurological deficits were observed. Following local radiation therapy, systemic chemotherapy was initiated. No tumor recurrence has been detected during the six months since surgery.

Discussion: Serous ovarian carcinoma typically spreads through direct invasion of adjacent tissues and rarely exhibits hematogenous metastasis. When distant metastasis occurs, it is often associated with malignant transformation into HGSC. Brain metastasis from serous ovarian carcinoma is rare and to the best of our knowledge, no previous reports have described brain metastasis originating from LGSC. In the present case, histopathological analysis demonstrated that the metastatic brain lesion retained the characteristics of LGSC, suggesting a possible novel metastatic pathway.

Conclusion: LGSC of the ovary may metastasize to the brain, although such cases are extremely rare.

Keywords: Cerebellar Metastasis; Low-Grade Serous Carcinoma; Ovary; Brain Metastasis

Introduction

Brain metastases most commonly originate from the lung, followed by the colon, breast and urinary system. In contrast, metastases from gynecological malignancies are relatively uncommon [1,14]. Tumors arising from the female genital tract characteristically exhibit a tendency for direct invasion into adjacent structures, such as the Douglas pouch and the greater omentum, rather than distant hematogenous dissemination [2,9]. Ovarian carcinoma is pathologically classified into four major subtypes: serous, mucinous, clear cell and endometrioid carcinoma [1]. Among these, serous carcinoma is further divided into High-Grade Serous Carcinoma (HGSC), Low-Grade Serous Carcinoma (LGSC) and borderline serous carcinoma [3,6]. Most reported cases of brain metastasis from ovarian carcinoma have been associated with HGSC or borderline serous carcinoma

[3,4,8]. In gynecologic oncology, the standard treatment for HGSC generally consists of cytoreductive surgery followed by chemotherapy. In contrast, LGSC is relatively resistant to chemotherapy and surgical resection remains the primary treatment modality [6]. In the present case, the patient developed left upper limb ataxia six years after surgical treatment for ovarian LGSC and neuroimaging revealed a cerebellar tumor. The tumor was completely resected and histopathological examination demonstrated LGSC identical to the primary ovarian lesion. To our knowledge, brain metastasis originating from ovarian LGSC has not previously been reported. This case may therefore provide insight into a potential novel mechanism of metastasis.

Case Report

An 81-year-old woman presented with mild ataxia of the left upper limb and was referred to our department from the Department of Obstetrics and Gynecology. Positron Emission Tomography-Computed Tomography (PET-CT) demonstrated increased uptake in the left cerebellar hemisphere without evidence of intraperitoneal lesions. Brain CT revealed an isodense round mass in the left cerebellar hemisphere (Fig. 1). Six years earlier, an ovarian tumor had been incidentally detected on abdominal CT. The patient subsequently underwent surgical resection at the Department of Obstetrics and Gynecology and the tumor was completely removed.

Histopathological examination of the ovarian tumor revealed a monotonous proliferation of cuboidal cells with amphophilic to lightly eosinophilic cytoplasm. Micropapillary architecture composed of cuboidal cells with mild to moderate nuclear atypia and low mitotic activity was also observed, findings characteristic of LGSC (Fig. 2). Immunohistochemical staining showed positivity for p53, Estrogen Receptor (ER) and Wilms Tumor-1 (WT-1), with an MIB-1 labeling index of approximately 10% (Fig. 2). The patient was subsequently followed on an outpatient basis without evidence of recurrence.

The cerebellar tumor measured 35 mm in maximum diameter and was associated with extensive surrounding edema. Magnetic Resonance Imaging (MRI) demonstrated an isointense lesion on T1-weighted images with ring enhancement following gadolinium administration and hyperintensity on T2-weighted images (Fig. 3). Repeat abdominal CT revealed no evidence of recurrence in the ovary or other abdominal organs.

Based on these findings, solitary brain metastasis from ovarian carcinoma was suspected and surgical resection was planned. Under general anesthesia, a left suboccipital craniectomy was performed. After opening the dura mater, the tumor was identified and completely removed under microscopic visualization. No neurological deterioration occurred postoperatively. Histopathological examination of the resected cerebellar tumor demonstrated features consistent with LGSC, identical to those observed in the primary ovarian lesion (Fig. 4). Immunohistochemical staining revealed the same profile as that of the primary tumor, including positivity for p53, ER and WT-1, with an MIB-1 labeling index of approximately 10% (Fig. 4).

The patient's neurological symptoms improved after surgery and postoperative MRI confirmed complete tumor removal (Fig. 5). Stereotactic radiosurgery was subsequently performed for the resection cavity. The patient is currently undergoing systemic chemotherapy under the care of the Department of Obstetrics and Gynecology and no tumor recurrence has been detected during the six months since surgery.

Figure1

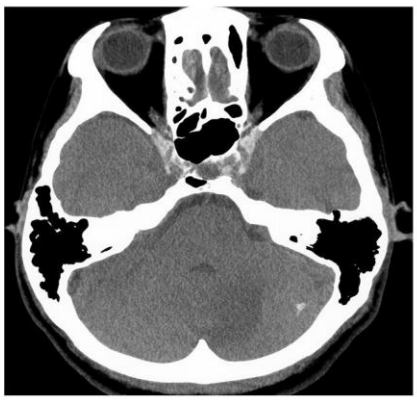

Figure 1: Plain brain CT on axial section showed an iso-density mass lesion with intratumoral calcification at the right cerebellar hemisphere.

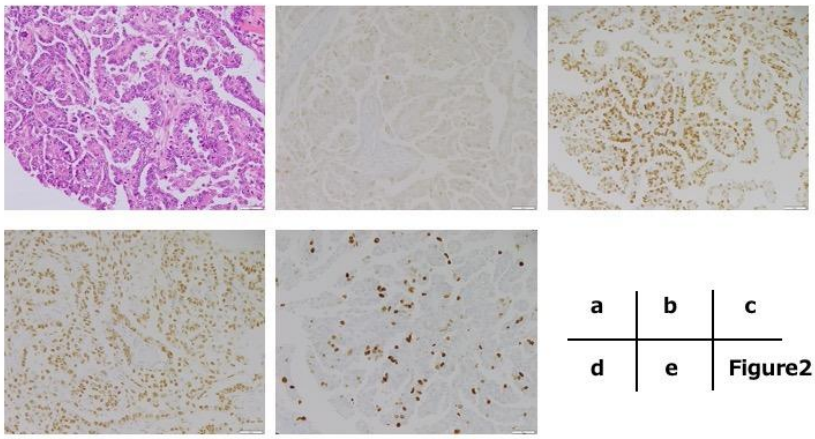

Figure 2: Pathological examination of the surgical specimen of the ovarian tumor revealed monotonous population of cuboidal cell with an amphophilic and lightly eosinophilic cytoplasm, leading to a diagnosis of LGSC (Hematoxylin and Eosin staining, a). Immunohistochemical staining showed the positive findings for p53 (b), estrogen receptor (c) and Wilmus Tumor-1 (d), while the MIB-1 labeling index was about 10% (e, magnification each x 20).

Figure3

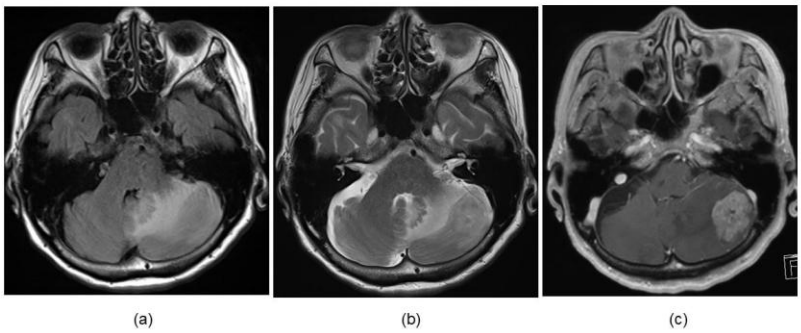

Figure 3: Magnetic resonance imaging of the head on the axial section displayed the round tumor located at the right cerebellar hemisphere as iso-intensity on T1-weighted image (a) and hyper-intensity on T2-weighted image indicating extensive surrounding edema (b) with diffuse and heterogenous enhancement after gadolinium administration.

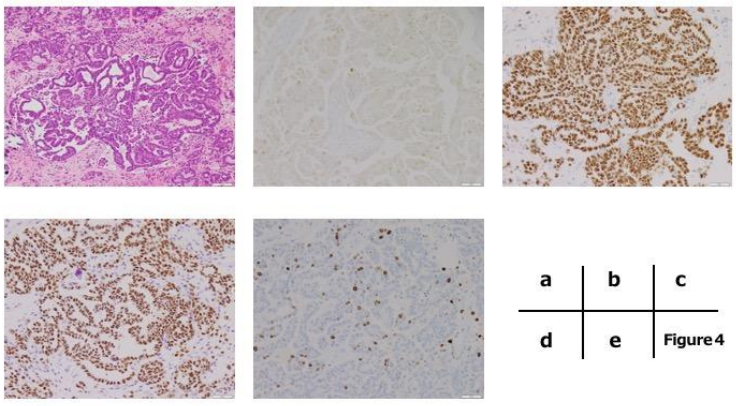

Figure 4: Pathological examination of the surgical specimen of the right cerebellar hemisphere revealed features consistent with LGSC, identical to the primary ovarian lesion (Hematoxylin and Eosin staining, a). Immunohistochemical staining also showed the positive findings for p53 (b), estrogen receptor (c) and Wilmus Tumor-1 (d) and MIB-1 staining revealed 10% positive result (e), which was same findings as the primary lesion (magnification x 20).

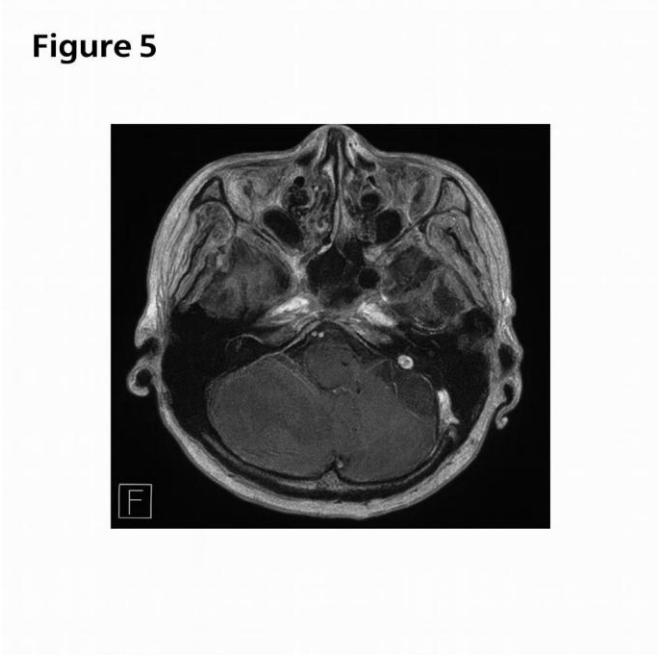

Figure 5: Magnetic resonance imaging of the head on the axial section with gadolinium-enhancement showed complete removal of the tumor.

Discussion

We report an extremely rare case of cerebellar metastasis from ovarian LGSC occurring six years after the initial surgical resection of the primary tumor. The patient had been followed without adjuvant chemotherapy and no evidence of peritoneal recurrence was observed at the time of diagnosis of the brain lesion. Histopathological examination confirmed that the cerebellar tumor retained the histological characteristics of LGSC.

To the best of our knowledge, brain metastasis from ovarian LGSC without evidence of abdominal recurrence has not previously been reported [16].

Serous ovarian carcinoma generally spreads through peritoneal dissemination and direct invasion into adjacent structures and rarely metastasizes hematogenously [9]. When distant metastasis does occur, it is often associated with malignant transformation into HGSC or other high-grade histological variants [7]. In the present case, however, the metastatic lesion retained the histological features of LGSC, suggesting the possibility of a previously unrecognized metastatic pathway.

Approximately 30% of ovarian carcinomas are serous carcinomas, which are further classified into LGSC, HGSC and borderline serous carcinoma. Among these subtypes, HGSC is the most common, whereas LGSC accounts for only 5-10% of serous ovarian carcinomas [6].

HGSC is frequently diagnosed at an advanced stage and generally responds well to chemotherapy, although the overall prognosis remains poor [11]. One important molecular distinction between HGSC and LGSC is the presence of TP53 mutations, which are commonly observed in HGSC but rarely detected in LGSC. These mutations are associated with increased production of vascular endothelial growth factor, promoting angiogenesis and vascular permeability, which may facilitate hematogenous dissemination, including brain metastasis [3,4,8,9,15].

In contrast, the mechanisms underlying hematogenous metastasis in LGSC remain poorly understood. Several factors may contribute to the occurrence of brain metastasis in LGSC. First, LGSC typically exhibits slow progression, with a reported 10-year survival rate of approximately 55% even in patients with FIGO stage II-IV disease, allowing a prolonged period during which distant metastasis may occur. Second, malignant transformation may potentially develop during the long clinical course of the disease [7,15].

In the present case, however, the metastatic cerebellar lesion remained histologically consistent with LGSC without evidence of malignant transformation. Furthermore, the interval between the initial treatment and the detection of brain metastasis was six years, which is not particularly long compared with previously reported cases of ovarian carcinoma metastasis. The precise mechanism by which LGSC metastasized to the brain in this patient therefore remains unclear. Nevertheless, this case suggests that distant metastasis may occur even in LGSC and highlights the importance of careful long-term follow-up after surgical treatment.

Conclusion

We describe an extremely rare case of cerebellar metastasis from low-grade serous carcinoma of the ovary. The metastatic lesion retained the histological features of LGSC without evidence of malignant transformation, suggesting the possibility of a previously unrecognized metastatic pathway. Even in patients with completely resected LGSC, careful long-term follow-up should be considered.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Acknowledgement

None

Data Availability Statement

Not applicable.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Informed Consent Statement

Informed consent was taken for this study.

Authors' Contributions

All authors contributed equally to this paper.

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