Case Report

Brain metastasis from early stage endometrial carcinoma 13 years after primary treatment: a case report and review of the literature

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Abstract: Brain metastases from endometrial adenocarcinoma are quite rare. Here, we report a case of a 64-year-old woman who presented with a history of left limb weakness of 45 days’ duration. Her medical history was significant for the endometrial carcinoma diagnosed 13 years earlier, for which she had undergone a total hysterectomy. The patient received a craniotomy and was finally diagnosed with brain metastasis from endometrial adenocarcinoma. We performed a MEDLINE search of the pertinent literature, searching for information focusing on the diagnosis, mechanism, treatment, and prognosis of this rare tumor type.

Keywords: Brain metastasis, endometrial carcinoma, whole-brain radiotherapy

Introduction

Endometrial adenocarcinoma is the most common invasive gynecological tumor among women [1, 2], yet brain metastases from this disease are rare with an estimated incidence of less than 0.3% and generally portend a poor prognosis and limited life expectancy [3]. Studies show that patients develop brain metastasis an average of 19 months after primary treatment, and 97 percent of relapses are detected within 5 years [4, 5]. Here we report one case of endometrial carcinoma which developed brain metastases 13 years after a hysterectomy but was disease free at all other locations.

Case report

A 64-year-old woman presented with a history of left limb weakness of 45 days’ duration. No other symptoms, such as headache, dizziness, or amnesia were presented. A neurological examination showed that the muscle strength of the left limbs were grade 4. The medical history was significant for endometrial carcinoma diagnosed 13 years earlier, for which she had undergone a total hysterectomy. The histologic finding was a FIGO grade 2, stage Ia endometrioid adenocarcinoma. No adjuvant radiation therapy or chemotherapy was given after the surgery. After admission to our ward, the patient received a series of examinations. The MRI revealed a 33*31*28 mm mass in the right parietal region. The tumor was isointense on T1-weighted images (Figure 1A, 1B) and hypointense on T2-weighted images (Figure 1C) and showed mulberry enhancement with obvious brain edema (Figure 1D-F). A preoperative chest X-ray was normal and the serum CA-125 was 40.6 U/ml. 2-[F-18]-fluoro-2-deoxy-D-glucose positron emission tomography showed no intense FDG uptake except in the right parietal region. On the basis of these findings, the patient was suspected of suffering from a metastatic tumor, and a craniotomy was performed.

At surgery, a solid mass of greyish-red appearance was found in the parietal lobe, with a rich blood supply. The boundary of the tumor was
clear, and all the tumor tissues were removed under the microscope. The further course was uneventful, and postoperative imaging showed the preceding mass being totally removed.

A histologic examination revealed that the tumor was composed of hyperchromatic nuclei cells with finely stippled chromatin, inconspicuous nucleoli, and high nuclear to cytoplasmic ratios (Figure 2A, 2B). Immunohistochemically, the tumor cells were positive for CK (AE1/AE3), CK7, ER, PR, P16 and PAX-8 and non-immunoreactive for CK20, Napsin A, CDX2, WT1, and vimentin. The tumor tissues also showed focal positively for P53, and the Ki-67 index was 30% (+) (Figure 2C-F). Thus, the diagnosis of brain metastasis from endometrial carcinoma was established. The patient’s symptoms improved. Although there was a slight, fine motor disturbance in the left upper limb, no other neurological signs or symptoms occurred after the operation. At 12-months follow-up, the patient remained well with no clinical or neuroradiological evidence of recurrence (Figure 3).

Discussion

Adenocarcinoma of the endometrium is the most common invasive malignancy of the female genital tract [6]. The disease usually spreads into the surrounding tissue by direct infiltration and disseminates through the lymphatic pathways. Distant hematogenous metastases are less common, and the most frequent sites are the lungs, liver, and bone [6]. The spread of disease to the brain is a rare event with an estimated incidence of less than 0.3%, and which generally portends a poor prognosis [3]. The median survival for endometrial carcinoma patients after the diagnosis of brain metastasis varies from 3 to 6 months [1, 6], and the median interval between the completion of primary treatment and the diagnosis of brain metastasis was only 2 months [5]. It is reported that almost two thirds of patients relapse within 2 years, and there are very few incidences of recurrence beyond 5 years post-surgery [4]. Researchers have identified the factors that are associated with brain metasta-
Figure 2. Histologic examination revealed the tumor was composed of hyperchromatic nuclei cells with finely stippled chromatin, inconspicuous nucleoli, and high nuclear to cytoplasmic ratios (A) (hematoxylin and eosin, 200×), (B) (400×). Immunohistochemically, the tumor cells were positive for CK (C), ER (D), PAX-8 (E), and PR (F).
is that a small volume of the disease present, but it goes undiagnosed in the lungs and is subsequently cleared by an endogenous immune response or, more likely, extrinsically administered cytotoxic chemotherapy [3].

The treatment of brain metastasis resulting from endometrial carcinoma consists of surgical resection, whole-brain radiotherapy (WBRT), chemotherapy, stereotactic radiosurgery, or combinations of these therapeutic modalities [11]. Surgery is the mainstay of treatment in patients with brain involvement regardless of tumor origin, especially for a single lesion [11]. Often, surgical resection followed by WBRT is the best option for a single BM in a patient with solitary and resectable lesions with good overall health and performance status [5, 6, 12]. Patients treated with a combination of surgery and radiotherapy experienced a longer median survival than patients who are treated with either surgery or radiotherapy alone (15 months VS 2 months) [12]. Our case received a tumor resection, followed by WBRT with a total dose of 30 Gy (3 Gy per fraction for 10 fractions). The patient showed no evidence of tumor recurrence 12 months after treatment. For patients with multiple brain lesions, Ratner et al. found that the prognosis of brain metastasis resulting from endometrial carcinoma may be much better using a combination of gamma knife radiosurgery and WBRT than in the patients who received gamma knife radiosurgery or WBRT alone [13]. Chemotherapy is not the choice for patients with isolated brain metastasis in EC because the transition of chemotherapeutic drugs from the brain-blood barrier is limited [14]. However, Nakagawa et al. asserted that the damage of this barrier could facilitate the transition of the chemotherapeutics drugs after the early period of the craniotomy, suggesting it is an option for combined therapy [15]. Kimyon et al. conducted a meta-analysis and found that chemotherapy was not associated with improved post-brain involvement survival [11]. Therefore, further clinical research is still needed to determine the role of chemotherapy in patients with BM resulting from endometrial carcinoma.

In conclusion, brain metastases from endometrial carcinoma are rare and usually occur in widely disseminated disease. However, our cases should alert clinicians to keep in mind that low tumor grade, with no presence of lymphovascular space invasion can also be correlated with the future development of brain metastases, even many years after primary tumor resection. Whether routine brain imaging should be undertaken in a subset of patients with identifiable risk factors is an unanswered question in the literature due to the low incidence. Patients with BM from endometrial carcinoma many years after primary treatment have a better prognosis than those who developed BM early on after a hysterectomy. Timely
surgical resection followed by WBRT is the best choice for patients, especially for those whose tumors can be completely removed.

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Disclosure of conflict of interest

None.

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