Case Report

Undifferentiated uterine sarcoma metastatic to the brain

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Abstract

Background: Undifferentiated uterine sarcoma (UUS) is a rare tumor with an aggressive growth pattern. They occur in women from 40 to 60 years and are generally characterized by poor prognosis, a high rate of local recurrence, and distant metastases. UUS accounts for 0.2% of all gynecological malignancies. Possible treatments include surgery, radiotherapy, and chemotherapy.

Case Description: A 65-year-old female with postmenopausal bleeding was found to have a uterine mass for which she underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. The pathologic evaluation was consistent with undifferentiated endometrial sarcoma. She began experiencing headaches with associated visual disturbances. Magnetic resonance imaging (MRI) of the brain showed a homogenous enhancing occipital dural-based mass measuring 1.6 x 1.8 x 1.7 cm. Due to the rarity of metastatic uterine sarcoma to the brain, this was believed to represent a meningioma and subsequently observed. Interval MRI scan revealed a significant increase in size of the right occipital mass to 2.3 cm with increased edema and mass effect. She underwent right occipital image guided craniotomy for resection of the mass. Histopathology confirmed UUS metastases.

Conclusion: Randomized trials analyzing these treatment options are limited due to the rarity of this disease; therefore, a standard therapy is not established. Based on a review of the literature, this is only the fourth case reported of UUS metastatic to the brain.

Key Words: Brain metastases, endometrial stromal sarcoma, uterine sarcoma, undifferentiated uterine sarcoma

INTRODUCTION

Uterine sarcomas are rare tumors of mesodermal origin accounting for 2-6% of uterine malignancies.[1] The incidence of uterine sarcomas is estimated between 0.5 and 3.3 cases per 100,000 females per year.[7] In general, they are the most malignant tumors of the uterus with a great tendency for local recurrence and aggressive hematologic dissemination, associated with a poor prognosis.

The three most common histologic variants are endometrial stromal sarcoma (ESS), malignant mixed mullerian tumor or carcinosarcomas, and leiomyosarcoma.[5] ESS is a rare gynecologic malignancy accounting for 0.2-1% of uterine malignancies and 6-25% of uterine sarcomas.[5] They are generally characterized by poor prognosis, a high rate of
local recurrence, and distant metastases. The most common sites of distant metastasis are lung, liver, and peritoneal cavity. Metastasis at time of recurrence to lymph nodes, heart, skin, bone, and brain are rare. A comprehensive literature review identified only three cases of metastatic undifferentiated uterine sarcoma (UUS) to the brain. Fifteen cases of uterine leiomyosarcoma metastatic to the brain were identified, one case metastatic to the cavernous sinus, and one case metastatic to the skull. Based on a review of the literature, this is only the fourth case reported of UUS with recurrent metastases to the brain.

**CASE REPORT**

A 65-year-old gravida 3, para 3-0-0-3, female presented with postmenopausal bleeding in July 2008. The patient sought medical attention from her gynecologist who performed a D and C, which revealed high-grade sarcoma of the uterus. Subsequent computed tomography (CT) scan of the chest, abdomen, and pelvis noted 9.5 × 6 cm irregular low density mass in the uterus with no extrauterine disease. She underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy. The tumor measured 10 × 8 cm and demonstrated extensive necrosis. The margins were negative although the posterior wall of the myometrium was extensively involved. The final pathologic evaluation was consistent with undifferentiated endometrial sarcoma. She subsequently underwent pelvic radiation receiving 45 Gy in 25 fractions.

One year follow up imaging revealed multiple lung metastases for which she underwent a needle biopsy, consistent with metastatic undifferentiated uterine endometrial sarcoma. She completed six doses of a single chemotherapy agent, Adriamycin, with good radiographic response on interval CT and positron emission tomography (PET) scan. Three months later she began complaining of headaches and visual complaints. Magnetic resonance imaging (MRI) of the brain showed a homogenous enhancing occipital dural-based mass measuring 1.6 × 1.8 × 1.7 cm with a small amount of surrounding edema [Figure 1]. Due to the rarity of uterine sarcoma metastasizing to the brain, this was believed to represent a meningioma. Interval MRI scan revealed a significant increase in size of the right occipital mass to 2.3 cm with increased edema and mass effect. She underwent right occipital image guided craniotomy for resection of the mass. Postoperative imaging revealed complete resection of the dural-based mass [Figure 2]. Histopathology confirmed UUS metastases [Figures 3 and 4]. The patient was discharged on postoperative day one and started on taxol and carboplatin chemotherapy, as well as Gamma Knife stereotactic radiosurgery to the tumor bed.
DISCUSSION

Uterine sarcomas are uncommon neoplasms, compromising only 1% of all gynecological malignancies, with an aggressive clinical course and poor prognosis. ESSs are a rare entity of uterine malignancy, only accounting for 0.2-1% of uterine malignancies. ESS is classified into two histological subtypes: Low-grade ESS (LGESS) and high-grade ESS (HGESS). LGESS is characterized by fewer than 10 mitosis per 10 high-power fields, lack of atypia, and often expresses estrogen and progesterone receptors. HGESS exhibits greater than 10 mitosis per 10 high-power fields, often lacks recognizable stromal differentiation, and commonly contains necrosis.

UUSs are high grade epithelioid or spindle cell sarcomas that are grouped together with HGESS. UUSs are characterized by aggressive behavior, with a tendency of frequent and early recurrences with 5-year survival rates of 25-55%.

UUSs usually present with abdominal pain or pelvic pain in the postmenopausal women. Although these tumors are usually confined to the uterus at the time of diagnosis, there is a high incidence of recurrence with distal metastasis. An autopsy study of 73 patients with uterine sarcoma (12% of which were stromal sarcoma) looked at sites of metastasis. For the 8 patients with ESS, which was not divided into HGESS and LGESS, the most frequent sites of metastasis were lung (12), intraperitoneal (10), bone (3), heart (1), and brain (2).

Brain metastasis from sarcoma are rare events, with 1-8% of patients with sarcoma from various histology develop intraparenchymal brain metastasis. There are 15 cases of leiomyosarcoma metastatic to the brain, one case of leiomyosarcoma metastatic to the sphenoid sinus, and one reported uterine sarcoma metastatic to the skull.

Figure 4: Vimentin immuno caption: Strong cytoplasmic positivity for vimentin indicative of mesenchymal differentiation; pan-cytokeratin and GFAP immunohistochemical stains were negative (×100)

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The case reported here is only the fourth case of UUS metastatic to the brain.

While there are only a few cases of UUS metastatic to the brain, there are multiple other cases described of histological variants of uterine sarcoma. Fleming et al. found two cases of brain metastasis in 22 patients with uterine sarcoma, one with leiomyosarcoma and the other with mixed mesodermal carcinoma. Salazar et al. found two cases of brain metastases, both from mixed mesodermal sarcoma, in 75 patients. Goff et al. reviewed 31 uterine sarcoma patients and found a single brain metastases in a patient with ESS.

The treatment of choice for UUSs is total abdominal hysterectomy and bilateral salpingo-oophorectomy. The use of adjuvant chemotherapy and radiation therapy has limited impact on outcome. However, radiation is typically recommended for stage I and II UUSs as it appears to improve local control without significant impact on survival. The high incidence of metastasis of uterine sarcoma makes adjuvant chemotherapy an appealing option; although currently there is little evidence in the literature supporting the use of adjuvant chemotherapy due to the rarity of uterine sarcoma.

Due to the rarity of UUSs and paucity of literature, treatment of uterine sarcoma brain metastasis is sparse. The patient described here presented with a single brain metastasis. Considering the Patchell et al. work, patients who receive treatment with surgical resection plus radiotherapy have fewer recurrences of cancer to the brain, have a better quality of life than those patients treated with radiation therapy alone, and live longer. Espat et al. looked at patients with soft tissue sarcoma and brain metastasis and concluded that surgical resection was associated with an improved median postmetastasis survival (9.6 vs. 2.7 months for unresected patients, \( P < 0.01 \)). Bindel et al. showed a median 11.8 months survival postresection of 21 patients with brain metastasis from sarcoma. Also, patients undergoing complete resection survived 14 vs. 6.2 months in patients undergoing incomplete resection. In all types of brain metastasis, surgical resection can give better results than radiotherapy alone when the lesion is accessible and causing mass affect.

CONCLUSION

This is only the fourth case in the literature of UUS metastatic to the brain and the first to be described. It demonstrates a unique site of metastasis for UUSs, the treatment challenges, and need for better adjuvant therapy. While aggressive surgical treatment of brain metastasis can improve neurological symptoms, the overall prognosis remains poor.
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