Brain and lung metastasis of uterine leiomyosarcoma: illustrative case

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BACKGROUND Uterine leiomyosarcoma is a rare, extremely aggressive tumor with a high rate of metastasis. Five-year survival for individuals with metastatic disease is only 10%–15%. Metastases to the brain are exceptionally rare and are associated with poor survival.

OBSERVATIONS The authors report a case of uterine leiomyosarcoma that metastasized to the brain in a 51-year-old woman. A single lesion on magnetic resonance imaging was discovered in the right posterior temporo-occipital region 44 months after resection of the primary uterine tumor. The patient underwent a right occipital craniotomy with gross-total resection of the tumor and is receiving adjuvant stereotactic radiosurgery and chemotherapy with gemcitabine and docetaxel. At 8 months postresection, the patient remains alive and asymptomatic with no sign of recurrence. A literature review of prior reported cases was conducted to analyze patterns of approach to patient treatment and survival.

LESSONS The authors found an apparent survival benefit in patients receiving adjuvant radiation therapy. 

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KEYWORDS leiomyosarcoma; uterine; brain metastasis; lung metastasis

Uterine leiomyosarcoma is a rare, highly malignant tumor of uterine smooth muscle cells that has an estimated incidence rate of 0.36–0.8 per 100,000 women. It accounts for 1%–2% of all uterine malignancies and exhibits aggressive hematological spread with a high rate of recurrence. Common sites of metastasis include the lungs, peritoneal cavity, liver, and pelvic and paraaortic lymph nodes. Lung metastasis is often associated with other distant metastases. Intracranial metastases are exceptionally rare, with an estimated incidence of 0.058–0.128 per 100,000 women. The standard treatment for metastatic disease includes resection and adjuvant chemotherapy. Despite maximum treatment, the prognosis for patients with metastatic disease is very poor, with an estimated 5-year survival of 11.9% (95% confidence interval [CI] 10.0%–14.2%). The main goal of care remains palliative. Here, we report the case of a patient with uterine leiomyosarcoma metastases to the lungs and right temporo-occipital lobe who underwent gross-total resection and remained asymptomatic at 6 months with no recurrence in the brain and stable lung lesions. We conclude this paper with a view of cases of metastatic uterine leiomyosarcoma to the brain in the last 3 decades and discuss recent trends in management and prognosis.

Illustrative Case

A 47-year-old woman initially presented to the gynecological service with presumed uterine leiomyomas. She subsequently underwent a total abdominal hysterectomy and bilateral salpingectomy. Surgical pathology of the uterus revealed high-grade uterine leiomyosarcoma with positive local lymphovascular CD31 and CD34 staining. Computed tomography (CT) scanning of the chest, abdomen, and pelvis revealed no metastatic disease at the time. The patient did not undergo any further treatment and adhered to the recommended follow-up with gynecological oncology every 6 months.

The patient continued to be asymptomatic for 4 years; then, she presented to the emergency department with persistent headaches, blurry vision, nausea, and vomiting. CT scanning of the head revealed a 4.4-cm mass in the right temporo-occipital region with surrounding vasogenic edema and associated mass effect.
Neurological examination revealed a left homonymous hemianopia and no other focal neurological deficits. CT scanning of the chest, abdomen, and pelvis revealed significant bilateral pulmonary metastasis. Magnetic resonance imaging (MRI) of the brain showed a 4.1 × 3.4 × 3.3-cm, well-defined, homogeneously and avidly enhancing mass in the right posterior temporo-occipital region with local mass effect (Fig. 1). The patient subsequently underwent a right temporo-occipital craniotomy for tumor resection. The tumor was found to have a well-defined capsule and was removed en bloc with no complications. Postoperative MRI of the brain confirmed gross-total resection of the tumor with resolving mass effect and T2-weighted hyperintense parenchymal changes (Fig. 2). The patient had an unremarkable postoperative course, with marked improvement in her visual field deficit and no adverse neurological sequelae; she was discharged home on postoperative day 3.

Hematoxylin and eosin staining of the resected brain lesion demonstrated dense atypical cells actively undergoing mitosis with a high nuclear/cytoplasmic ratio (Fig. 3A and B). Immunostaining for smooth muscle myosin heavy chain showed diffuse and strongly positive reactivity (Fig. 3C). Histological diagnosis confirmed the tumor to be metastatic leiomyosarcoma.

Adjuvant stereotactic radiosurgery was performed using a dynamic conformal arc technique with a dose of 24.75 Gy to the resection cavity 7 weeks after resection. The lung metastases were not resected. The patient is currently undergoing systemic palliative chemotherapy consisting of gemcitabine and docetaxel.

Discussion

Observations

Uterine leiomyosarcoma (uLMS) is a highly aggressive tumor of uterine smooth muscle cells that carries a poor prognosis when stage matched to other uterine malignancies.2 The 5-year survival of International Federation of Gynecology and Obstetrics (FIGO) stage I uLMS is approximately 50%,5,7 and the recurrence rate is 53%–71%.8,9 The lungs are a common site of early metastasis in uLMS.4 Regional and distant metastases, corresponding to FIGO stages III and IV, have a 24.6% and 13.1% 5-year survival rate, respectively.6 An extremely rare site of metastasis is the brain, occurring in 0.058–0.128 cases per 100,000 women.3

Adjuvant Therapy

According to the National Comprehensive Cancer Network guidelines, the treatment for uLMS metastasis is resection and adjuvant chemotherapy with doxorubicin or docetaxel and gemcitabine.10 Resection has been shown to be an effective treatment for uLMS brain metastasis. A retrospective study of sarcoma brain metastases in 246 patients, among whom leiomyosarcoma accounted for 18.7% of cases, found that resection was associated with improved overall survival in patients with metastatic disease, with a hazard ratio (HR) of 0.40 (95% CI 0.22–0.72; p = 0.003).11

FIG. 1. Preoperative axial precontrast T1-weighted (left) and axial T2-weighted (right) MRI of the brain demonstrating a well-circumscribed, avidly contrast-enhancing right temporo-occipital extra-axial lesion with mass effect on surrounding brain and vasogenic edema. There was no evidence of other intracranial metastases.

FIG. 2. Postoperative axial precontrast T1-weighted (left) and axial T2-weighted (right) MRI of the brain demonstrating gross-total resection of a right temporo-occipital extra-axial lesion. Mass effect on surrounding brain and vasogenic edema are still present. There was no evidence of other intracranial metastases.

FIG. 3. Hematoxylin & eosin staining under low power (original magnification ×10, A) demonstrates tumor cells and necrosis, whereas high power (original magnification ×40, B) shows mitoses and a high nuclear/cytoplasmic ratio. Immunostaining for smooth muscle myosin heavy chain (SMMHC) showed diffuse and strongly positive reactivity (C).
In addition to surgical management, the use of adjuvant chemotherapy is supported by the largest observational cohort study to date on 7455 patients with leiomyosarcoma by Seagle et al.5 These authors found that adjuvant chemotherapy provided a significant survival benefit to patients with metastatic uLMS (p < 0.001) but not to patients with stage I uLMS (p = 0.18). Chemotherapy agents different from those in guideline-recommended therapies are being explored. Inoue et al.6 reported a single case of uLMS to the brain with no recurrence at 18 months using pazopanib. This is further supported by a randomized, double-blind, placebo-controlled trial of

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<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Age (yrs)</th>
<th>Location of Brain Metastasis</th>
<th>Lung Metastasis</th>
<th>Treatment of Brain Metastasis</th>
<th>Extent of Resection</th>
<th>Time From Primary Tumor to Metastasis (mos)</th>
<th>Survival After Diagnosis of Metastasis (mos)</th>
<th>Cause of Death</th>
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— = not reported/applicable; CNS = central nervous system; RS = radiosurgery; SRS = stereotactic radiosurgery; WBRT = whole-brain radiation therapy.
paopanib in patients with recurrent sarcoma, 43% of whom had leiomyosarcoma, that found a median progression-free survival benefit relative to placebo (4.6 [95% CI 3.7–4.8] months versus 1.6 [95% CI 0.9–1.8] months). 

In addition to resection and adjuvant chemotherapy, stereotactic radiosurgery and whole-brain radiation are common approaches to the treatment of uLMS. However, the use of radiological approaches is complicated by the fact that sarcomas are considered more radioresistant. Despite this, patients with sarcoma metastases undergoing stereotactic radiosurgery had significant local control of the disease, with a 38% 1-year overall survival. In the case series by Chaigneau et al., whole-brain radiation (HR = 0.51; 95% CI 0.35–0.76; p = 0.003) and stereotactic radiosurgery (HR = 0.41; 95% CI 0.19–0.90; p = 0.008) were also found to be associated with improved overall survival.

Survival

We conducted a review of the literature on uLMS brain metastases and found 18 reported cases between 1989 and 2022. The results are shown in Table 1. The mean age at the time of brain metastasis was 49.4 ± 11.1 years (range: 26–66 years). Of the 19 cases, 18 reported the time from primary tumor diagnosis to brain metastasis, with a mean of 44 ± 31.9 months (range: 3–116 months) and a median of 35.5 months (interquartile range [IQR]: 33 months to 66 years). Of the 19 cases, 18 reported the time from primary tumor diagnosis to brain metastasis, with a mean of 44 ± 31.9 months (range: 3–116 months) and a median of 35.5 months (interquartile range [IQR]: 58 months). In all but 1 case, there were concurrent lung and brain metastases. Survival from the time of the diagnosis of brain metastases was reported in 14 cases; the mean survival was 10.1 ± 13.9 months (range: 0.2–99.5 months) and a median of 35.5 months (interquartile range [IQR]: 33 months–57 months). The mean survival time for the 6 patients who had received whole-brain radiation after resection and the 4 patients who had undergone no further treatment after resection. The mean survival time for the 6 patients receiving whole-brain radiation after resection was 9.5 ± 10.1 months and the median was 5 months (IQR: 8.25 months). We separately analyzed the survival time of patients who received whole-brain radiation and surgery alone.

Lessons

Uterine leiomyosarcoma is an aggressive neoplasm with a high rate of recurrence and metastasis, rarely to the brain. Metastatic brain disease is managed with resection of the tumor focus and the variable use of adjuvant chemotherapy and radiation. Patients with brain metastasis continue to experience poor survival even after aggressive treatment. Based on the literature review and the case presented here, resection with adjuvant treatment of stereotactic radiation and chemotherapy with gemcitabine and docetaxel may offer additional survival benefit. However, further research is needed before a clear, significant effect can be established, although these efforts may be hindered by the rarity of these cases and the difficulty of achieving an adequate effect size.

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References


Disclosures
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