



## Case report

## Pazopanib-mediated long-term disease stabilization after resection of a uterine leiomyosarcoma metastasis to the brain: A case report

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## ABSTRACT

A 48-year-old woman underwent a total abdominal hysterectomy after preoperative diagnosis of multiple uterine leiomyomas. The histopathological diagnosis was leiomyosarcoma (LMS). After 47 months, multiple lung metastases were detected and resected. The patient was also diagnosed with pelvic bone metastasis and received six cycles of adjuvant chemotherapy with gemcitabine plus docetaxel and local radiation therapy to control the pain. Seventy-seven months from the initial diagnosis, she had a headache and developed left hemiparesis and aphasia. Imaging studies detected a solitary brain metastasis in the right frontal lobe. The patient underwent a craniotomy and resection of the lesion, which was a confirmed metastasis from uterine LMS by histopathology. One month after the craniotomy, the patient experienced lower abdominal pain, and a pelvic metastasis was detected. She was prescribed oral pazopanib (800 mg per day). For twelve months, she remained asymptomatic, but gradually, pelvic pain increased due to pelvic mass growth. After 14 months of pazopanib treatment, pazopanib was discontinued. To date, for 18 months after the brain surgery, she is alive with disease, and the brain metastasis has not recurred.

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## 1. Introduction

Brain metastasis of uterine leiomyosarcoma (LMS) is rare (Wroński et al., 1994 Aug; Honeybul & Ha, 2009 Mar; Yamada et al., 2011 Dec; Rose et al., 1989 Mar 1; Fleming et al., 1984 Oct). Several case reports suggest a resection of brain metastases of uterine LMS could result in longer survival, for which controlling systemic disease is a prerequisite (Wroński et al., 1994 Aug; Honeybul & Ha, 2009 Mar; Yamada et al., 2011 Dec; Gadducci et al., 1996 Jul). However, adjuvant therapies after brain surgery have not been established. Radiotherapy after brain surgery can lower recurrence rates, but long-term toxic side effects of radiation, such as cognitive decline, decrease quality of life, and radiation cannot control systemic disease. Pazopanib is approved for soft tissue sarcomas and penetrates the blood-brain barrier (BBB) (Iwamoto et al., 2010 Aug). Several case reports in other malignancies suggest that pazopanib treatment could elicit survival benefits for patients with brain metastases in addition to controlling systemic disease (Jacobs et al., 2013 Mar 1; Hingorani et al., 2014). We present the first case report of long-term disease stabilization with pazopanib treatment after a resection of solitary brain metastasis from uterine LMS.

## 2. Case report

A 48-year-old multiparous woman underwent a total abdominal hysterectomy for what was thought to be multiple uterine leiomyomas. Final histopathology revealed uterine LMS, and she was referred to our hospital.

Subsequent positron emission tomography/computed tomography (PET/CT) showed no metastatic lesions, and she was followed up without further surgery or adjuvant therapy. Forty-seven months after the initial diagnosis, a biannual follow-up computed tomography (CT) scan revealed multiple lung metastases, and video-assisted thoracic surgery (VATS) was performed. The surgical specimens were confirmed LMS metastases. Shortly after the VATS procedure, the patient developed pelvic pain, and PET/CT imaging suggested a pelvic bone metastasis. She was treated with six cycles of adjuvant chemotherapy with gemcitabine and docetaxel, and local radiation therapy was administered to control the pain. Seventy-seven months after the initial diagnosis, she had a gradually worsening headache, and 2 weeks later, she developed left hemiparesis and aphasia with a Karnofsky performance scale (KPS) score of 40. Magnetic resonance imaging (MRI) revealed a solitary 58 mm × 45 mm lesion in the right frontal lobe with a midline shift (Fig. 1). The patient underwent a craniotomy and complete resection of the lesion, after which she showed no neurological deficit, and her KPS score improved to 90. Immunohistochemical findings of the resected metastatic brain tumor were positive for alpha-smooth muscle

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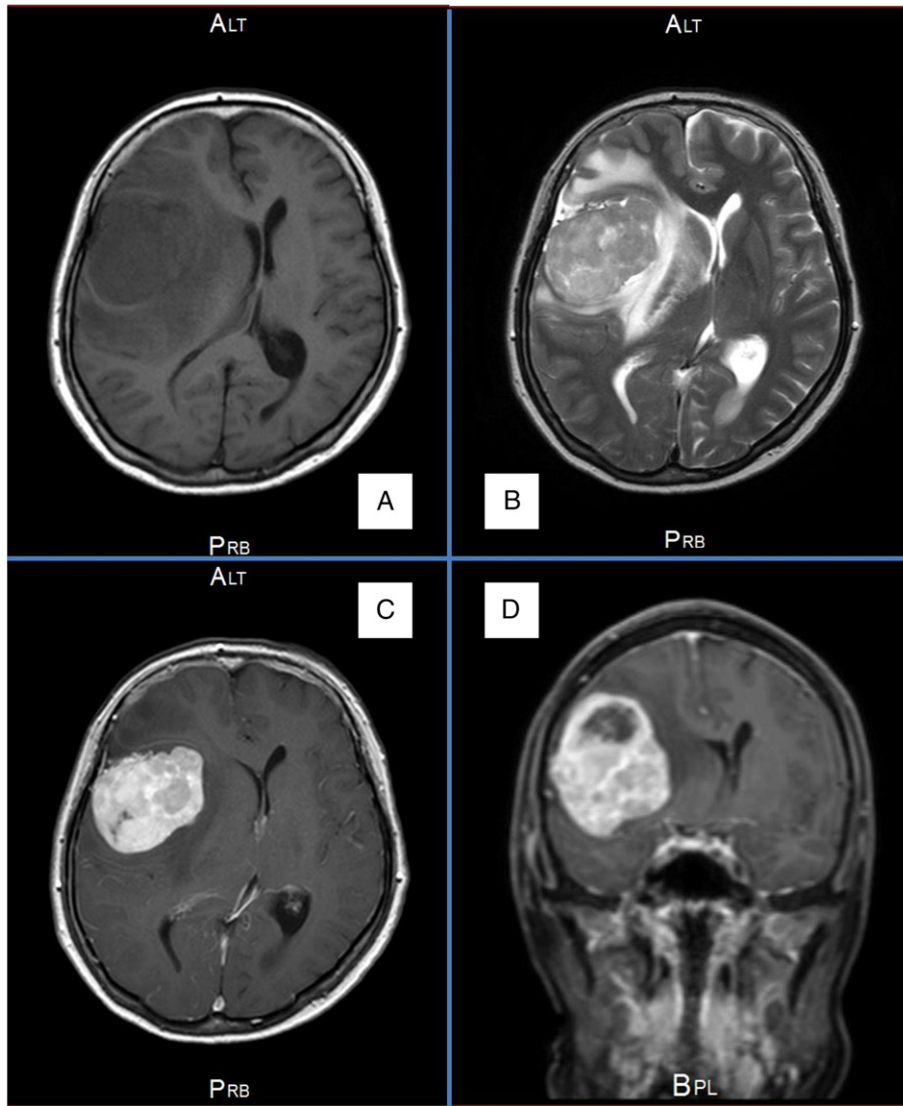


Fig. 1. MRI images of the solitary brain metastatic lesion in the right frontal lobe. A: T1 image, B: T2 image, C and D: Gadolinium-enhanced MRI.

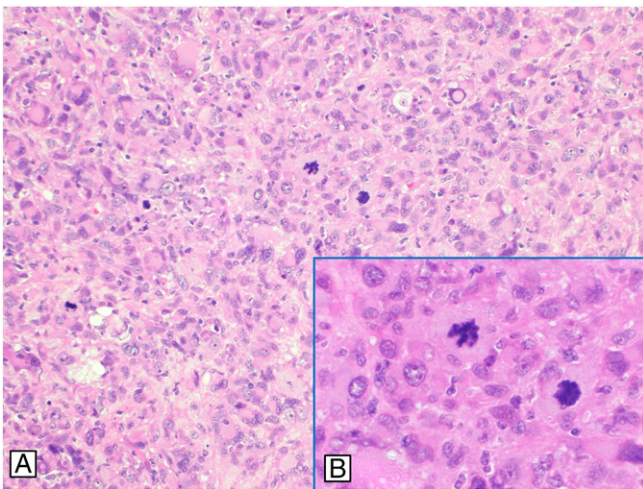


Fig. 2. Microscopic findings of the resected metastatic brain tumor. Marked cellular pleomorphism, nuclear atypia, and mitotic figures are present. A: Hematoxylin and eosin (H&E),  $\times 20$ , B: The inset of A,  $\times 40$ .

actin, vimentin, desmin, and epithelial membrane antigen staining, and LMS metastasis to the brain was confirmed (Figs. 2 and 3). One month after the craniotomy, she experienced lower abdominal pain that required opioids, and a CT scan revealed a pelvic mass that was suggestive of recurrence and was unresectable (Fig. 4). The patient was informed about an increased risk for intracranial hemorrhage by using pazopanib. One month after the brain surgery, she began oral pazopanib (800 mg per day). One month later, she was free of pain, and no opioid was necessary. She experienced mild diarrhea and mild hypertension, both of which were well-controlled.

For 12 months, the patient remained asymptomatic. There was no recurrence of brain metastasis. However, the pelvic lesions gradually enlarged, causing a severe pain. Therefore, 14 months after starting pazopanib, it was discontinued. To date, she remains alive with disease, 18 months after the brain surgery.

### 3. Discussion

Uterine LMS is aggressive in nature, and prognosis of recurrent LMS is very poor. The risk of recurrence after complete resection of uterus-limited LMS, which was estimated to be 70% after 2 years in a retrospective study, is high (Major et al., 1993 Feb 15). The most common sites of uterine LMS metastasis are the lung, pelvis, and vagina (Rose et al., 1989

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