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Malignant Progression of Uterine Smooth Muscle Tumor of Uncertain Malignant Potential (STUMP) to Metastatic Leiomyosarcoma: A Six-Year Case Evolution

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Abstract

Uterine smooth muscle tumors of uncertain malignant potential (STUMP) are rare tumors with histologic features of both benign leiomyoma and leiomyosarcoma. Due to this, their clinical behavior is unpredictable, and long-term outcomes of progressing into malignant leiomyosarcoma should be closely investigated. We present the case of a 42-year-old woman diagnosed with STUMP following laparoscopic-assisted myomectomy. Despite total abdominal hysterectomy and negative initial follow-up, she developed metastatic leiomyosarcoma involving the thoracic spine and posterior chest wall within three years and expired due to multiorgan failure six years later. This case underscores the potential malignant behavior of STUMP and raises the question of the need for adjuvant therapy, such as chemotherapy, in selected high-risk patients' post-hysterectomy.

Subject Areas

Gynecology & Obstetrics

Keywords

STUMP, Uterine Tumor, Leiomyosarcoma, Metastasis, Case Report, Gynecologic Oncology

1. Introduction

Smooth muscle tumors of the uterus (STUMP) represent a rarely encountered pa-

thology throughout medical and surgical practice nowadays [1]. STUMPs are not definitively benign or malignant on histologic evaluation due to their undetermined malignant potential [2]. As a result, their clinical course is unpredictable, ranging from indolent behavior to recurrence and, although rare, malignant transformation [3]. Histopathological features such as nuclear atypia, mitotic activity, and coagulative tumor cell necrosis are used to categorize smooth muscle tumors; however, STUMP cases often fall into a gray zone where these features are equivocal [4] [5].

Immunohistochemical markers including Ki-67, p53, estrogen receptor (ER), and progesterone receptor (PR) have been investigated for their prognostic value, but no single marker can reliably predict recurrence or malignant progression [6] [7]. Recent molecular studies reveal that STUMP may share genomic alterations with leiomyosarcoma, including mutations in TP53, ATRX, and MED12, raising the possibility that certain STUMP cases represent precursor lesions of overt malignancy [8] [9]. Despite these findings and advances, management remains controversial [3] [4]. Current guidelines recommend hysterectomy as the primary treatment, with adjuvant therapy generally reserved for recurrent or metastatic disease [10] [11]. Because of the uncertain risk of late relapse, long-term surveillance is universally advised [3] [10].

The objective of this case report is to describe the rare progression of STUMP to fatal metastatic leiomyosarcoma over a six-year period, highlighting the clinical, pathological, and therapeutic decision points. This case highlights the urgent need for refined prognostic markers and evidence-based surveillance strategies.

2. Case Presentation

2.1. Patient History

A 42-year-old woman presented in December 2016 with menorrhagia and with a palpable abdominal mass. She had small uterine myomas for 10+ years and claimed to have heavy amounts of menstruation with blood clots. Sonar findings revealed gradual increase in the size of the mass to around 5 cm.

2.2. Initial Surgery

In January 2017, she underwent laparoscopic-assisted myomectomy, revealing a specimen of multiple myomatous fragments measuring 108 gm totally and up to $4 \times 3 \times 2$ centimeters in size. Pathological examination revealed a smooth muscle tumor of uncertain malignant potential (STUMP), with features of bizarre nuclei, focal infarct-type necrosis, and moderate mitotic activity (2-10/10 HPF). The Ki-67 index was 5% - 10%.

2.3. Follow-Up Surgery

In March 2017, after extensive evaluation obtaining a CT scan which raised suspicion for residual STUMP (**Figure 1**), a total abdominal hysterectomy was performed to prevent recurrence or potential malignant transformation of residual tumor. Pathology showed residual STUMP and two classical leiomyomas. Immunohistochemistry

revealed low Ki-67 (<3%), H-caldesmon, and no evidence of tumor emboli.

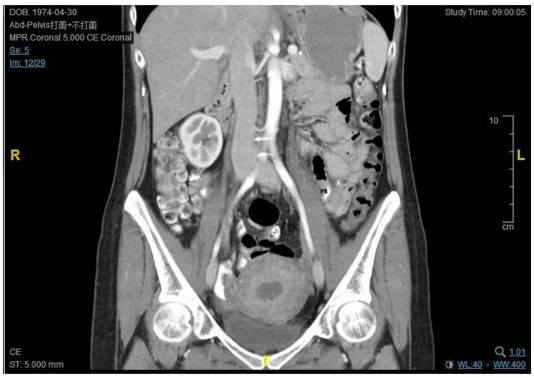

Figure 1. Coronal contrast-enhanced CT scan obtained post-myomectomy demonstrating some heterogenous signal intensity within the uterine myometrium, raising suspicion for residual STUMP.

2.4. Metastatic Progression

In October 2020, the patient initially presented with back pain, and CT-guided biopsy of the T12 vertebra confirmed metastatic leiomyosarcoma. Immunohistochemistry was positive for SMA, desmin, ER, and H-caldesmon, supporting smooth muscle differentiation and indicating a link between the metastatic leiomyosarcoma to the original STUMP.

2.5. Treatment

She subsequently received multiple systemic therapies, including cyclophosphamide, dacarbazine, gemcitabine, hormonal agents (goserelin, tamoxifen), and targeted therapy (lenvatinib), in addition to palliative radiotherapy to the spine and pelvis. Detailed dosing regimens and treatment courses are summarized in the Treatment Table (See **Table 1**). Further progression was confirmed by a CT scan of the abdomen and pelvis in August 2022 with metastatic disease in the posterior chest wall (**Figure 2**). She succumbed to multi-organ failure in July 2023.

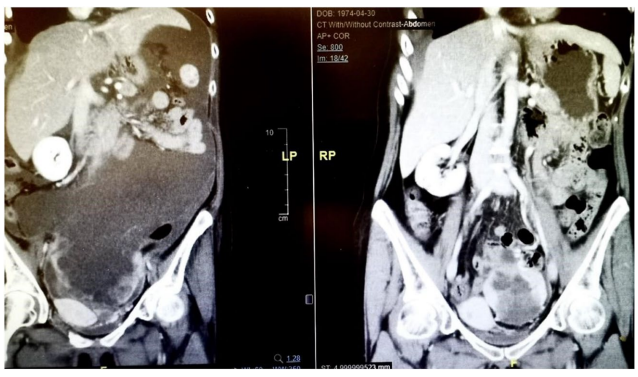

Figure 2. Left panel: Coronal CT image depicting marked ascites within the abdominal cavity. Right panel: Coronal CT image revealing multiple heterogenous soft tissue masses involving the pelvic region and extending to the vertebrae, consistent with metastatic spread of STUMP-derived leiomyosarcoma.

Table 1. Treatment table.

Date	Event	Detailed Notes	Type of Therapy
December 2016	Initial presentation with menorrhagia & palpable mass	Initial diagnosis of uterine myomas	Diagnostic
January 2017	Laparoscopic-assisted myomectomy	Pathology: STUMP	Surgical
March 2017	Total abdominal hysterectomy→ residual STUMP	Residual STUMP and two classical leiomyomas	Surgical
October 22-December16, 2020	Cyclophosphamide (Endoxan)	Standard dosage	Chemotherapy-Alkylating agent
January 20-Feburary 3, 2021	Palliative radiotherapy	Spine (T11 - T12), 3600 cGy in 15 fractions	Radiotherapy-Palliative
June 20, 2022	CT scan evaluation	Interval progression: pulmonary, pleural, bone, peritoneal metastases	Radiologic response
August 17, 2022	Dacarbazine (DTIC)-First cycle	140 mg/m^2 IV daily ×5, every 3 - 4 weeks	Chemotherapy-Alkylating agent
August 2022	Gemcitabine-initiated	300 mg/m^2 IV on D1 & D8 every 3 weeks	Chemotherapy - Antimetabolite
August 25, 2022	Zoladex (Goserelin) & Tamoxifen-initiated	Hormonal therapy	Hormonal therapy
September 6, 2022	Lenvatinib-initiated	Standard dosage	Targeted therapy Tyrosine kinase inhibitor
August 8-September 22, 2022	Palliative radiotherapy	Recurrent pelvic tumor,2500 cGy in 10 fractions (interrupted/rescheduled)	Radiotherapy-Palliative
June 2, 2023	DTIC re-challenge	Continued disease progression	Chemotherapy-Alkylating agent
February 13, 2023	Gemcitabine re-challenge	Continued disease progression.	Chemotherapy - Antimetabolite
February 2023	Post-gemcitabine re-challenge	Disease progression	Radiologic response
June 2023	Post-DTIC re-challenge	Ongoing disease progression	Radiologic response
July 2023	Patient passed away	N/A	N/A

3. Discussion

3.1. Surveillance vs Adjuvant Therapy

In this case, adjuvant therapy was not initiated post-hysterectomy, which aligns with current views emphasizing surveillance in STUMP patients due to their generally indolent behavior and lack of concrete evidence supporting adjuvant benefit [10]-[12]. In uterine STUMP cohorts, adjuvant radiotherapy has shown no proven efficacy, and no standardized chemotherapy protocols exist [13] [14].

3.2. Unpredictable Behavior & Need for Risk Stratification

Furthermore, comprehensive meta-analyses in analogous soft tissue sarcoma contexts demonstrate minimal improvement in survival outcomes with adjuvant

chemotherapy, underscoring the importance of tailoring treatments to individual risk profiles [13]. This case further demonstrates the unpredictable nature of STUMP and its potential in progressing into metastatic leiomyosarcoma [5]. Although initially, the tumor lacked overt malignancy features, including tumor cell necrosis and high mitotic index, patient developed systemic metastasis three years post-surgery [5]. This underscores that even though STUMPs classify with low-grade malignancy, a prolonged survival rate and delayed recurrence, patients with STUMPs must receive closer surveillance because of the risk of metastases even years after initial diagnosis [5]. There has not been a consensus on the optimal post-operative management of STUMP [5]. While some suggest total observation, others recommend long-term surveillance through clinical evaluation and imaging techniques [5]. Given the fatal progression presented here, clinical trials investigating adjuvant chemotherapy or targeted therapy in high-risk STUMP patients are urgently needed [4].

4. Conclusion

This case reveals the rare but serious potential of STUMP to progress into metastatic leiomyosarcoma, even when early histological features suggest low malignant potential [3]. The delayed presentation of systemic metastasis emphasizes the importance of long-term clinical and radiologic surveillance, especially in patients with high-risk histopathological features [6]. In the absence of clear management guidelines, a multidisciplinary approach and consideration of adjuvant therapy may be necessary in selected cases [4] [5]. Further research and specified studies are vital to define reliable prognostic markers and establish well-researched treatment protocols aimed at preventing metastasis and improving long-term outcomes in patients with STUMP [4].

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Consent

Written informed consent for publication was obtained from the patient's brother, acting as the legal next of kin, due to the patient's demise. All patient data have been anonymized. Institutional review and ethical standards were adhered to in accordance with local regulatory guidelines.

Conflicts of Interest

No author has any potential conflict of interest.

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