

A Clinicopathologic Study of Uterine Smooth Muscle Tumours of Uncertain Malignant Potential (STUMP)

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Abstract

Introduction: The clinical management of Smooth Muscle Tumours of Uncertain Malignant Potential (STUMPs) remains controversial because little is known about the natural history of these tumours and pathological classifications do not correlate well with clinical outcomes and therefore cannot direct management. The objective of this study was to review a single institution's experience with STUMP and recommend a rational clinical approach to the management of patients with this histological diagnosis. **Materials and Methods:** A systematic review of all diagnoses of STUMP and leiomyosarcoma from the gynaecologic oncology and pathology databases between January 1970 and February 2006. **Results:** A total of 18 diagnoses of STUMP and 72 diagnoses of leiomyosarcoma were made during the study period. None of these 72 cases of leiomyosarcoma had a prior diagnosis of STUMP. There were no recurrences in the 18 cases of STUMP with all 18 cases being registered as disease-free after 5 years. **Conclusions:** We recommend that patients with a diagnosis of STUMP be expectantly managed given the low likelihood of leiomyosarcomatous transformation, the lack of any evidence that adjuvant treatments result in better long-term outcomes and that recurrences are amenable to surgical resection with good outcomes.

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Introduction

Smooth Muscle Tumours of Undetermined Malignant Potential or STUMPs are interesting tumours from both the standpoint of histological diagnosis and classification as well as clinical management mainly because, as a group, its natural history is poorly understood. Prognostic criteria of how STUMP tumours will behave have been studied and proposed based on histological features, surface marker expression and mitotic counts. The predictive value of these proposed prognostic factors remains nebulous at best because each factor has been studied in series limited by size. This problem is compounded by the relative rarity of STUMP diagnoses, even in women presenting with abnormal uterine bleeding.¹ It is because the malignant potential of STUMP tumours remains uncertain that clinicians may be tempted to err on the side of caution and be aggressive both with primary cytoreductive surgery and with adjuvant treatment.

We present a review of a tertiary referral women's

hospital's experience with STUMP tumours and how this experience has resulted in the rationale of expectant management for STUMP tumours and finally explains why this represents both a rational and reasonable approach to clinical management.

Materials and Methods

A retrospective chart review of the oncology database and the histopathological databank of a single tertiary referral gynaecologic cancer centre was performed. Cases from the period between January 1970 and February 2006 were reviewed. Eighteen patients with a histological diagnosis of a uterine smooth muscle tumour of uncertain malignant potential were found in the above period of study.

A retrospective review of all registered cases of leiomyosarcoma during the same period between January 1970 and February 2006 was also performed. Case histories were reviewed in detail for documentation of a history of

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STUMP, cellular leiomyomata and borderline leiomyomata or smooth muscle tumours.

Results

The average age at diagnosis was 44.6 years and 83% of patients (15/18) were premenopausal. The clinical presentation and indication for initial surgery were stratified as follows (Table 1): 50% (9/18) presented with a pelvic mass, 33.3% (6/18) presented with findings consistent with uterine fibroids which remained the preoperative diagnosis and 16.7% (3/18) presented with menorrhagia.

Surgical management was stratified as follows (Table 2): 27.7% (5/18) underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAHBSO), 11.1% (2/18) underwent total abdominal hysterectomy with ovarian conservation (TH), 11.1% (2/18) underwent

total laparoscopic hysterectomy and bilateral salpingo-oophorectomy (TLHBSO), 33.3% (6/18) underwent open myomectomy, 11.1% (2/18) underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, pelvic lymphadenectomy and omentectomy, and 5.6% (1/18) underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy, splenectomy and omental biopsy. Only 16.7% (3/18) underwent formal assessment of the intraperitoneal cavity, where in all cases, no gross evidence of intra-abdominal disease consistent with metastasis was noted. In all 3 cases where there was formal exploration of the intraperitoneal space, there was a frozen section diagnosis of a spindle cell tumour of uncertain malignant potential.

All 18 tumours were given the histopathological diagnosis of STUMP. The mitotic counts of these 18 tumours ranged from 0 to 42 mitoses per 10 high-power fields with an average of 6 mitoses per 10 high-power fields.

In all 18 cases, clinical histories, operative and histopathological findings were formally presented at the multi-disciplinary Tumour Board. Close clinical surveillance and observation were uniformly recommended for management in all 18 cases. In all 18 cases of STUMP, the 5-year overall and disease-free survival was recorded to be 100%. A review of all 18 cases with a sub-set analysis of patients who were at least 10 years post-diagnosis was performed to evaluate long-term outcomes in our cohort of STUMP patients. The results are summarised in Table 3. Two recurrences were noted with similar clinical courses. These were noted to be slow-growing masses which were clinically observed over a period of 6 to 12 months with a decision to proceed with surgical resection. The histologies of these recurrent tumours were noted to be consistent with the primary histological diagnoses when comparisons were made on review. These outcomes are consistent with the experience reported by other single-institution series where neither the mode nor approach of initial surgery seemed to impact negatively on outcome.

There were a total of 72 cases of leiomyosarcoma between January 1970 and February 2006. None of these 72 cases had a previous diagnosis of STUMP, cellular leiomyomata and borderline leiomyomata or smooth muscle tumours.

Table 1. Indications for Surgery in Reported Cases

Surgery	Number of Cases	Percent of Total
Pelvic mass	9	50% (9/18)
Uterine fibroids	6	33.3% (6/18)
Menorrhagia	3	16.7% (3/18)

Table 2. Mode of Surgery in Reported Cases

Surgery	Number of Cases	Percent of Total
THBSO	5	27.7% (5/18)
TH	2	11.1% (2/18)
TLHBSO	2	11.1% (2/18)
Open Myomectomy	6	33.3% (6/18)
THBSO, PLND, omentectomy	2	11.1% (2/18)
THBSO, PLND, omentectomy, splenectomy	1	5.6% (1/18)

THBSO = Total hysterectomy, bilateral salpingo-oophorectomy

TH = Total hysterectomy with ovarian conservation

TLHBSO = Total laparoscopic hysterectomy, bilateral salpingo-oophorectomy

PLND = Pelvic lymphadenectomy

Table 3. Summary of Outcomes at 10 years

Surgery	Number of Cases	Number and % of each surgical subset	Outcome
THBSO	5	1 (20%)	Recurrent 3 cm tumour at the vaginal cuff, likely incervical remnant. 7 years after initial surgery.
TH	2	0	No recurrence
TLHBSO	2		No recurrence
Open Myomectomy	6	1 (16.7%)	Recurrent 5 cm tumour noted to be slow-growing and serially observed till repeat surgery.
THBSO, PLND, omentectomy	2	0	No recurrence

Discussion

Smooth muscle tumours of the uterus remain a relatively uncommon diagnosis. This encompasses a large group of neoplasms representing the entire spectrum from benign to malignant.² Statistically, a patient presenting with a uterus enlarged by globular corporeal tumours is likely to have a final diagnosis of benign uterine leiomyoma. There are no firm guidelines on the clinical management of a patient with a globular or rapidly enlarging uterus largely due to the rarity of frankly malignant smooth muscle tumours such as leiomyosarcomas in patients presenting with rapidly enlarging uteri.³ Furthermore, the majority of leiomyosarcomas arise *de novo* and not from the malignant transformation of benign leiomyomata. Cytogenetic testing may be helpful in a small subset of smooth muscle tumours where a deletion in chromosome 1 has been shown to result in specific morphological changes and clinical features akin to leiomyosarcoma.⁴

However, the histologic distinction between malignant and benign smooth muscle tumours remains challenging. Bell et al⁵ provided one of the largest series of problematic uterine smooth muscle tumours. Three criteria were examined: coagulative tumour cell necrosis (CTCN), degree and extent of atypia and mitotic index (MI). Of these, CTCN and extensive severe atypia seemed to correlate with malignant behaviour.

The prognosis and management of uterine smooth muscle tumours are not uniform, and may be controversial in some settings. This is especially so with a histopathologic diagnosis of STUMP. Numerous small series have investigated the use of marker expression profiles to aid in the triage of smooth muscle tumours. A significant difference in staining intensity for Ki-67 between leiomyosarcoma and STUMP has been reported.⁶ Other investigators have suggested that STUMPs that express p16 and p53 may have a greater propensity to recur.⁷

Given the “borderline” nature of this histopathologic diagnosis, clinical management can be problematic for the following reasons. Firstly, the preoperative diagnosis in cases of STUMP is usually that of uterine leiomyomata; based on low pre-test probability for malignancy, the operative procedure planned may not be comprehensive in ensuring there is no residual disease or establishing the full extent of disease spread. Secondly, even in the uncommon instance where a preoperative diagnosis of STUMP is made, risk-benefit considerations are complicated. Decision-making on the radicality of surgical management is complicated by the lack of consistent data to support offering either a conservative or limited approach versus one that is more consistent with complete staging and debulking. Finally, management of the patient with a postoperative histological diagnosis of STUMP is also complicated by difficulty in

counselling patients with regards to the likely clinical course and recommending adjuvant therapy, if any.

The body of evidence with regards to the diagnosis of STUMP, its natural history, clinical course and optimal management remains sparse and controversial. Patients with tumours of uncertain malignant potential have varied and uncertain clinical courses. In one series, 27% of patients with STUMP had recurrences. Seventy-five percent (3 of the 4 who had recurrences) of these patients with recurrences experienced long-term survival; only 1 case followed an aggressive course and succumbed to her disease despite favourable histology.⁸ Other case reports and series highlight the possibility that despite the uncertain nature of uterine STUMPs, they can exhibit metastatic activity, recur as STUMPs or undergo malignant transformation to leiomyosarcomas.^{9,10} Conversely, Guntupalli et al¹⁰ in their series of 41 patients with STUMP reported no difference in long-term outcomes between patients who had myomectomy versus complete hysterectomy. This conclusion seems to be consistent with findings from other small series where surgical approach (laparoscopic, hysteroscopic or laparotomy) and the modality of surgical treatment (myomectomy, resectoscopic resection or hysterectomy) did not seem to affect long-term outcomes which were generally reported to be favourable.

However, there is limited data suggesting that tumours with up to 20 mitoses per 10 high-power fields and with no CTCN or diffuse severe cellular atypia and which only have focal mild atypia, have a negligible recurrence risk and almost always behave as benign leiomyomas.

In the Bell schema, Group 1 is represented by “leiomyomas with increased mitotic index” for those with >5 MI. The other atypical group in the Bell schema are tumours without CTCN, or diffuse moderate to severe atypia and low MI. These were termed “leiomyomas with a low risk of recurrence (Bell group 2b). These tumours were generally felt to be benign. Some would define STUMP as:

- (i) a minimally atypical smooth muscle neoplasm with a low mitotic index but with uncertainty about the histologic type (standard vs myxoid or standard vs epithelioid);
- (ii) a combination of standard smooth muscle differentiation, marked diffuse severe atypia, low mitotic index and uncertainty about whether coagulative tumour cell necrosis is present;
- (iii) moderate to severe atypia plus uncertain mitotic index because possible mitotic figures may be degenerating nuclei mimicking mitotic figures.¹¹⁻¹³

The multi-disciplinary tumour group at our institution, by consensus, has adopted a conservative approach to the management of smooth muscle tumours of uncertain malignant potential (STUMPs), by uniformly

recommending expectant management in the form of “close clinical observation” in all patients diagnosed with STUMP.

This recommendation is made based on the fact that expectant management is also the recommended regimen in other tumours of uncertain malignant potential.

Finally, the baseline “defaulter” or “no show” rate amongst our patient population remains low and compliance with scheduled care and prescribed treatment plans remains high.

Based on the above data, it does not seem unreasonable to adopt a conservative approach in the management of patients with STUMP. The small sample size and the relatively short observational period reported in this study are its main limitations.

Conclusion

In conclusion, the diagnosis of smooth muscle tumours of uncertain malignant potential (STUMP) carries with it an uncertain prognosis, although data from our series and other clinical case series seem to suggest that the recurrence risk is low and that clinical outcomes are generally favourable, a conclusion that seems to be supported by recent clinicopathologic data.⁷ When disease recurs, it is likely to be loco-regional in nature and amenable to resection. As such, recommending clinical observation or expectant management does not seem to be unreasonable, especially when consideration has to be given to the use of surgical resection as a primary modality for the treatment of recurrence which adjuvant radiation therapy or chemotherapy might make difficult. This is especially important given the dearth of evidence that adjuvant treatment improves outcomes and that adjuvant radiation or chemotherapy may actually limit treatment options for recurrent disease. Questions for future study might include whether complete surgical “re-staging” after histological diagnosis aids treatment and therefore outcome, and what adjuvant therapy if any is appropriate. The question of the value of cytogenetics and immunohistochemistry in diagnosis, characterisation and clinical stratification should be looked at with cost-benefit analyses; studies of this nature

could guide the clinical management of patients with a preoperative diagnosis of “uterine fibroids” and the long-term management of patients with a diagnosis of STUMP.

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