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JMIG The Journal of Minimally Invasive Gynecology

Original Article

The Role of Endometrial Biopsy in the Preoperative Detection of Uterine Leiomyosarcoma

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ABSTRACT **Study Objective:** To assess the sensitivity of preoperative endometrial biopsy in detection of uterine leiomyosarcoma (ULMS).

Study Design: Retrospective analysis of a prospectively collected database (Canadian Task Force III).

Setting: Two academic tertiary referral centers.

Patients: All cases of ULMS treated at participating institutions between January 2005 and August 2012 were identified following IRB approval.

Interventions: Abstracted data included demographics, preoperative evaluation, presenting symptom, surgical management, pathology and clinical outcomes. Chi-square tests were used for statistical analysis.

Measurements and Main Results: 329 cases were identified, of which 152 cases had complete pathologic data available for review. Sixty-eight (45%) of 152 patients had endometrial sampling prior to surgery. Patients with postmenopausal bleeding were significantly more likely to be biopsied preoperatively (51.6% vs 9.5%, p = <.0001). Of those sampled, 43 (63%) underwent endometrial pipelle biopsies and 25 (37%) had dilation and curettage. Endometrial sampling was significantly more likely to detect a concern for malignancy in patients who presented with postmenopausal bleeding (72.7% vs 32.3%, p = 0.002), however it was less likely to detect malignancy in patients with abnormal premenopausal bleeding (31.8% vs 64.3%, p = .02), compared to other presenting symptoms. Overall, 51.5% of patients with ULMS on final pathology had pre-operative endometrial biopsies in which leiomyosarcoma or atypical spindle cell proliferation were diagnosed, whereas 35.5% of the pre-operative biopsies identified ULMS specifically.

Conclusions: The sensitivity of an endometrial biopsy to detect ULMS is low, illustrating the difficulty of diagnosing ULMS preoperatively. As expected, the probability that an endometrial biopsy will detect ULMS or a related worrisome pathological finding is higher for patients with post-menopausal bleeding. Thus, benign endometrial biopsy results, particularly in pre-menopausal patients, should be interpreted with caution if there is suspicion for leiomyosarcoma. However, a positive or suspicious result can play an important role in the subsequent management of patients with ULMS, even if the absolute numbers of affected patients are small. Journal of Minimally Invasive Gynecology (2016) 23, 567–572 © 2016 AAGL. All rights reserved.

Keywords: Uterine leiomyoma; Uterine leiomyosarcoma; Endometrial biopsy

Distinguishing uterine leiomyoma from its malignant counterpart uterine leiomyosarcoma (ULMS) is very difficult clinically and radiographically, yet critical for appropriate referrals and subsequent management. Uterine leiomyoma is the most common pelvic tumor among women, with an estimated lifetime risk of 70% in white women and 80% in black women [1]. In contrast, ULMS is rare, although its exact incidence is a matter of debate

The authors declare that they have no conflict of interest.
Previously presented as a poster presentation at the Society for Gynecologic Oncology's 46th annual meeting, March 28-31, 2015 (poster 407).
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Submitted December 22, 2015. Accepted for publication January 27, 2016.
Available at www.sciencedirect.com and www.jmig.org

1553-4650/$ - see front matter © 2016 AAGL. All rights reserved.
http://dx.doi.org/10.1016/j.jmig.2016.01.022

[2–4]. Furthermore, unlike benign leiomyoma, ULMS is an aggressive malignancy with 5-year overall survival of less than 50% [2].

Minimally invasive surgical techniques, especially hysterectomy and myomectomy facilitated by morcellation, have come under great scrutiny owing to concerns about inadvertent morcellation of ULMS. Patients with inadvertently morcellated ULMS through any method of extraction, including both power and hand morcellation techniques, appear to be at increased risk for disseminated peritoneal disease and to have worse 5-year disease-free and overall survival compared with women whose tumors were removed intact [5–7]. In 2014, the Food and Drug Administration released statements formally cautioning against the use of laparoscopic power morcellation for hysterectomy or myomectomy for uterine myomas owing to the low, but serious risk of inadvertent morcellation of malignancy [3,4]. Since that time, much attention has been turned to preoperative differentiation of benign and malignant uterine masses [8–11].

Endometrial sampling, which is used almost uniformly for the preoperative diagnosis of endometrial neoplasms, has not been well studied in ULMS. Literature reports of sensitivity of preoperative sampling in ULMS range from 38% to 67%, although previous studies were limited owing to small sample size (8–16 patients) [12–14]. The present study was conducted to determine the sensitivity of preoperative endometrial sampling in a larger cohort of patients with ULMS, and assess whether sensitivity differs based on selected patient characteristics and presenting symptoms.

Materials and Methods

Following Institutional Review Board approval, cases of ULMS treated at the 2 participating institutions between January 2005 and August 2012 were identified from the pathology archives. Cases were excluded from the study for incomplete clinical or pathological data. Data from the preoperative evaluation, including the presence or absence of preoperative endometrial biopsy and sampling method used, were collected. Preoperative endometrial sampling was performed by either Pipelle biopsy or traditional uterine curettage in all cases. The decision to perform Pipelle biopsy or uterine curettage was at the discretion of the evaluating physician.

Diagnosis of ULMS as determined by pathological hysterectomy (66 cases) or myomectomy (2 cases) was confirmed by a dedicated gynecologic pathologist at each participating institution. However, many of the preoperative biopsies were performed at outside institutions (32 of 68; 47%) and were unavailable for pathological review; in those cases, the pathology reports from the referring institution were used. A biopsy was considered positive if the pathologist diagnosed ULMS or pathological findings were specifically described as "atypical spindle cell proliferation" or "atypical smooth muscle neoplasm," which are considered suspicious for, but not fully diagnostic of, malignancy. In addition, 2 cases reported alternate malignancy and were considered positive as well. Atypical cells or other findings not explicitly described as suspicious for malignancy were considered benign.

Patient records were reviewed for demographic and clinical data. Each patient's presenting symptom was obtained from the initial physician's consultation note. Symptoms were grouped into the following categories: abnormal premenopausal bleeding, postmenopausal bleeding, pelvic pain, abdominal fullness or bloating, incidental finding, and presentation suspicious for malignancy. The incidental finding category included patients in whom imaging performed for a nongynecologic indication revealed uterine tumors. Patients who presented with initial symptoms that were indicative of or concerning for malignancy, including acute hemorrhage requiring emergent surgical intervention, massive ascites, evidence of metastatic disease, and recurrent mass postmyomectomy, were classified ax "presentation suspicious for malignancy." Presenting symptoms were not considered mutually exclusive, so patients with multiple symptoms were included in each relevant analysis.

The overall sensitivity of endometrial biopsy for detecting a concern for malignancy was calculated, as was the sensitivity to specifically detect ULMS. Subanalyses were performed to evaluate sensitivity by type of preoperative endometrial biopsy (Pipelle vs curettage) and presenting symptom.

Sensitivities were compared using the χ^2 test. All statistical analyses were performed with SAS 9.3 (SAS Institute, Cary, NC).

Results

A total of 329 cases of ULMS were identified between January 2005 and August 2012. Of these cases, 152 had adequate clinical and pathological data available for further analysis. Four patients had limited information regarding presenting symptoms and thus were excluded from the subanalysis of presenting symptoms. Demographic characteristics, tumor characteristics, and type of surgery at time of diagnosis are summarized in Table 1. There were no differences in sociodemographic parameters when between the patients who underwent preoperative endometrial biopsy and those who did not.

In the full cohort of 148 patients with presenting symptoms available for analysis, abnormal premenopausal bleeding was the most common presenting symptom (n = 45; 30.4%), followed by postmenopausal bleeding (n = 41; 27.7%), pain (n = 29; 19.6%) and bulk symptoms (n = 25; 16.9%). Eleven patients (7.4%) were incidentally found to have a uterine tumor, and 9 patients (6.1%) presented with an emergent surgical issue or high suspicion for malignancy. Sixty-eight of 152 patients (45%) underwent endometrial sampling prior to surgery. When stratified by presenting symptom (Table 2), patients with postmenopausal bleeding were significantly more likely to undergo

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