

Incidentally Detected Uterine Sarcomas in Patients Operated with Myoma Uteri in a Tertiary Center: Retrospective Cohort Study

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ABSTRACT Objective: To estimate the incidence and report the details of histological, clinical, surgical, and demographic features of incidental uterine sarcomas in patients operated with symptomatic myoma uteri. **Material and Methods:** We designed a retrospective cohort study at Adnan Menderes University Gynecologic Oncology Department that includes totally 896 patients with symptomatic myoma uteri who were operated as a hysterectomy or myomectomy. Following the definition of inclusion and exclusion criterias, incidental uterine sarcoma cases were detailed as histological subtype, tumor diameter, morcellation or fragmentation status in surgery, adjuvant treatment, recurrences, and survival. All cases were reported as a table without specific statistical analyzes. **Results:** A total of 775 hysterectomy and 121 myomectomy cases were analyzed. Fourteen sarcoma cases were reported. Two sarcoma cases were excluded due to adnexal sarcoma in final pathology. Ten cases were reported in final pathology incidentally. 7/10 cases were reported as leiomyosarcoma while low grade endometrial stromal sarcoma were reported in 2 cases. While all recurrences were seen in leiomyosarcoma group (5 cases), two of them died with disease-related complications. **Conclusion:** Studies have shown that uterine sarcomas are malignancies that are extremely rare and cannot be predicted preoperatively. Due to its low incidence and uncertain tumor behavior, in low-risk patients, myomectomy with mechanical or power morcellation is a safe surgical option when it is performed without abdominal spillage which can be common in laparoscopic surgery.

Keywords: Incidental findings; leiomyoma; hysterectomy; sarcoma

Hysterectomy and myomectomy are the most common major gynecologic surgeries performed in the world. Symptomatic uterine myomas represent the indications 30-40% of all benign hysterectomies.¹ Surgical approach to myomas includes both, hysterectomy and myomectomy, which can be performed in various technics, by laparotomy, laparoscopy, vaginal surgery, or hysteroscopy. Over the years, surgical approach in hysterectomy and myomectomy shifted from open laparotomy to minimally invasive surgery which has lower complication rates and faster recovery.² Morcellation is crucial for extraction of large myomas or uterus in minimally in-

vasive surgery. Dissemination of benign or malignant disease is major risk of this approach.³ Uterine sarcomas originating from endometrial connective tissue or myometrial tissue are rare malignancies and have a poor overall survival.⁴ Due to the inability to differentiate fibroids from uterine sarcomas with preoperative imaging methods, unexpected uterine sarcoma was detected in 1 of 352 surgeries performed with the indication of myoma uteri. In November 2014, the U.S. Food and Drug Administration (FDA) issued a warning against the use of morcellation in the majority of women undergoing hysterectomy for leiomyomas.⁵ In the literature, varying incidences of

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unexpected uterine sarcoma was reported by different studies. With this study, we aimed to estimate the incidence of unexpected uterine sarcoma (overall and by type of sarcoma) among women who underwent myomectomy or hysterectomy for myoma uteri and other benign indications.

MATERIAL AND METHODS

This retrospective descriptive study was performed using data from patients with unexpected uterine sarcoma who were operated for benign gynecologic indications at the Adnan Menderes University Hospital, Department of Gynecology between March 2010 and December 2020. This study was approved by Clinical Research Ethics Committee of Adnan Menderes University with a date of November 16, 2023 and protocol number of 2023/185. The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki. Participants who do not provide permission to use their medical records for study were excluded.

Since sarcomas are rare malignancies, the data of all sarcoma cases (medical history, preoperative diagnostic biopsies, surgical details, adjuvant treatments) were recorded (Table 1). Primary aim of the study was to determine incidental sarcoma cases which were operated with the diagnosis of myoma uteri. Patients who underwent surgery with the clinical diagnosis of myoma uteri were included the study. Endometrial biopsy was performed in post-

menopausal uterine bleeding, spotting or endometrial thickness >5 mm and premenopausal abnormal uterine bleeding and/or endometrial cancer risk factors were described in guidelines. Patients with suspicious or positive (prealign or malign) endometrial or cervical biopsy or suspicious imaging findings before surgery were excluded. Surgical procedure details such as hysterectomy, myomectomy, powermorcellation, or fragmented removal of myoma or uterus were obtained from medical records. After surgery, final pathologic reports were categorized into histopathology subgroups based on the 2014 World Health Organization classification of uterine mesenchymal malignancies as leiomyosarcoma (LMS), low grade endometrial stromal sarcoma (LG-ESS), high grade ESS, or undifferentiated sarcoma. Carcinosarcoma cases were excluded.

Final staging of tumors were done with evaluation of postoperative imaging and pathology reports together. Follow up information including adjuvant treatments, site and time of recurrences, death, latest medical examination were obtained from hospital medical data and phone call with patients or close relatives.

STATISTICAL ANALYZES

Statistical methods were not used in the present study, and the details of sarcoma cases were presented as a table (Table 1).

TABLE 1: Patients and tumor characteristics.

Case	Diagnosis	Age*	Largest tumor diameter (mm)	Menopausal status	Surgical approach	Morcellation fragmentation	Adjuvant treatment	Recurrence	Vital status
1	LMS	57	130	Post	TAH+BSO	Yes	None	Yes	23 months
2	LG-ESS	48	112	Pre	TAH+BSO	No	None	No	18 months
3	LMS	62	65	Post	TAH+BSO	No	CT	Yes	26 months
4	LMS	58	60	Post	TAH+BSO	No	None	Yes	Ex
5	LG-ESS	26	57	Pre	Myomectomy	No	None	No	60 months
6	LMS	49	80	Pre	TAH+BSO	No	RT	No	28 months
7	LMS	53	140	Post	TAH+BSO	No	RT	Yes	13 months
8	LMS	48	135	Pre	TAH+BSO	No	CT+RT	No	77 months
9	LMS	59	75	Post	TAH+BSO	No	None	No	85 months
10	LMS	62	120	Post	TAH+BSO	No	RT	Yes	Ex

*Age at diagnosis; LMS: Leiomyosarcoma; LG-ESS: Low grade endometrial stromal sarcoma; TAH+BSO: Total abdominal hysterectomy and bilateral salpingoophorectomy; CT: Chemotherapy; RT: Radiotherapy.

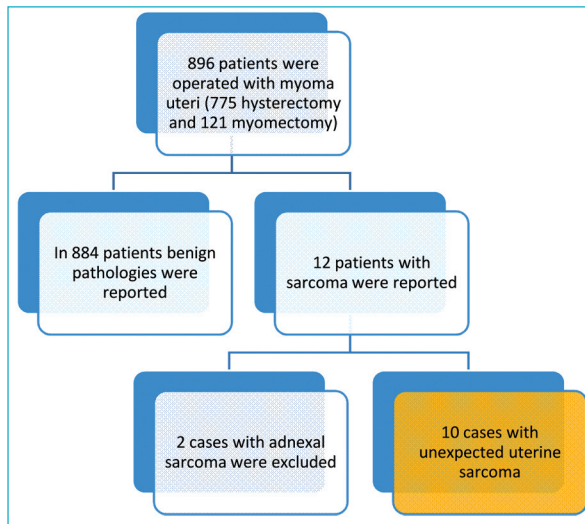


FIGURE 1: Patient selection criteria.

RESULTS

Between March 2010 and December 2020, as described in the Figure 1, 896 patients were operated for symptomatic myoma uteri. Hysterectomy and myomectomy procedures were performed in 775 and 121 patients, respectively. In hysterectomy group, 300 patients were premenopausal while all patients (n=121) in myomectomy group were premenopausal. Totally 12 sarcoma cases were reported. Two cases with adnexal sarcoma in final pathology were excluded. Hysterectomy and myomectomy were performed with the prediagnosis of myoma uteri or benign pelvic mass. Totally, 10 cases were reported as a sarcoma of uterus incidentally. 4/10 cases were premenopausal, while 6/10 cases were postmenopausal. 8/10 cases were reported as LMS, while LG-ESS were reported in 2 cases. Hysterectomy was performed in 9/10 cases while myomectomy was performed in 1 case (case 5) with LG-ESS. All recurrences were seen in LMS group. In LMS group, recurrence was seen in 5/8 patients and two of them (cases 4 and 10) died 7 and 9 months after the recurrences, respectively. Two patients (2/5) in non-recurrence group and 3 patients (3/5) in recurrence group received adjuvant treatment (radiotherapy and/or chemotherapy).

DISCUSSION

Unexpected uterine sarcoma is a rare but important reality for patients with benign uterine pathologies.

It can be difficult to distinguish unexpected malignancies from benign pathologies with preoperative or intraoperative assessment.⁶ The definitive diagnostic imaging or chemical methods to distinguish sarcomas from fibroids has not been discovered yet. Compared to the epithelial tumors, reliability of frozen section analyzes is controversial in mesenchymal malignancies.⁷

In this study, the incidence of unexpected uterine sarcoma among all women undergoing hysterectomy and myomectomy for myoma uteri is 1.11% or 10 in 896. In Multinu et al.'s study; 1 in 256 (0.39 %) unexpected uterine sarcoma was reported in uterine fibroid group. The incidences varied between 0.08% (1 in 1124) and 0.2% (1 in 454) in different studies among women undergoing hysterectomy for all benign indications.⁸⁻¹⁰ A possible reason of higher incidence rate in our study was the relatively low number of patients.

In our study, all women with uterine sarcoma were older than 45 years except 1 case (Case 5). When only premenopausal patients were analyzed, unexpected uterine sarcoma incidence was 0.9% or 4 in 421. In Multinu et al.'s study, the incidence was found to be 0.11% (1 in 881).⁸ Brohl et al. reported similar results that the risk of unexpected uterine sarcoma increases with age.¹¹ With this lower malignancy incidences, myomectomy can be a safe option for younger patients who want fertility sparing procedures.

Although ESS is the characteristic histologic type (especially in China) in some studies, LMS is still the main histologic type of uterine sarcoma in the literature and FDA reports.¹²⁻¹⁴ Consistent with the literature, LMS was detected as the main histologic type in our study (8/10 cases). Considering sarcomas diagnosed by preoperative endometrial biopsy, ESS which is closely related to the endometrium, can be detected as the major histologic type.

Few studies have reported the relation between sarcoma incidence and uterine weight. Since the data were absent about uterine weight, we couldn't estimate the relation between the incidence of sarcoma and uterine weight. While previous studies demonstrated that sarcoma could be reported also in a small uterus, Multinu et al. reported that higher uter-

ine weight was associated with an increase in sarcoma incidence.^{8,9,15} Uterine weight stratification was made in sarcoma subtypes and benign conditions in their study.

In this study, all hysterectomies were performed as open laparotomy and laparoscopic surgery without fragmentation or morcellation, while myomectomies were performed with open surgery. We avoid uterine morcellation due to the FDA reports.⁵ Minimally invasive procedures with morcellation have less morbidity, short hospital stay and lower post-operative pain but have the theoretical risk of poorer outcomes with uncontained mechanical or power morcellation as noticed by the FDA in 2014.¹⁶ Recent literature published by Pritts, described lower incidence of LMS as 1 in 1,428 cases when including both prospective and retrospective studies and a Danish nationwide cohort study reported the incidence as 1 in 865 patients.^{17,18} Although the possibility of unexpected sarcoma is a potential risk of cancer dissemination, minimally invasive surgery is still a good option in patients with low malignancy potential and if it was performed with a controlled morcellation techniques.

The limitations of our study can be listed as follows: Lack of survival data due to insufficient number of patients, the small number of sarcoma cases, the inability of comparison between the open surgery and minimally invasive procedures due to the small number of minimally invasive surgeries, and the lack of uterine weight data that could be associated with the distinction between malignant and benign mesenchymal diseases.

CONCLUSION

As a result, our study and previous studies have shown that uterine sarcomas are malignancies that are extremely rare and can not be predicted preoperatively. Although its incidence is quite low, surgery should be performed with caution due to its uncertain but possibly high malignant potential. In low-risk patients, myomectomy with mechanical or power morcellation is a safe surgical option when it is performed without abdominal spillage which can be common in laparoscopic surgery.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Alper Seyhan; **Design:** Alper Seyhan; **Control/Supervision:** Reyhan Baş; **Data Collection and/or Processing:** Alper Seyhan, Reyhan Baş; **Analysis and/or Interpretation:** Alper Seyhan; **Literature Review:** Reyhan Baş; **Writing the Article:** Alper Seyhan; **Critical Review:** Alper Seyhan; **References and Fundings:** Reyhan Baş; **Materials:** Alper Seyhan.

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