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Short Communication

Uterine Leiomyosarcoma: A Rare Cancer Much as Complicated to Prevent, Diagnose and Treat

Tinelli A*

International Translational Medicine and Biomodelling Research Group, Department of Applied Mathematics, Moscow Institute of Physics and Technology (State University) Moscow Region, Russia

***Corresponding author:** Dr. Andrea Tinelli, Division of Experimental Endoscopic Surgery, Imaging, Technology and Minimally Invasive Therapy, Department of Obstetrics and Gynecology, Vito Fazzi Hospital, Lecce, Italy, Email: andreatinelli@gmail.com; andrea.tinelli@unisalento.it

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Abstract

The uterine leiomyosarcoma (LMS) is a rare cancer arising from the smooth myometrial cells. The LMS is clinically aggressive malignancy, accounting for 2% to 6% of uterine malignancies and a very low annual incidence. The incidence of LMS increases in postmenopausal women, although it is not a disease that can be pre-operatively diagnosed with sufficient certainty and accuracy. In fact, often the diagnosis is unexpected, out of the surgical specimen, after histological examination of the uterus. As therapy, an optimal cytoreduction is associated with improved overall survival of affected women. Moreover, the FDA launched an alert discouraging the use of "power" or electromechanical morcellation for hysterectomy and myomectomy in most women with uterine myoma, for the risk of dissemination of occult uterine cancer, included LMSs. This alert has greatly complicated the use of minimally invasive surgery, which is greatly limited in its daily use in benign disease and has once again pushed the use of traditional surgery.

Keywords: Uterine fibroids; Uterine leiomyosarcoma; Myoma; Gynecological cancers; Morcellators

The leiomyosarcoma (LMS) is a very rare uncommon uterine cancer, has an incidence ranging from 0.5 to 3.3 per 100,000 women per year, with a further incidence of sarcomas in women with myomas at rapid growth of 0.27%, representing 1-1.3% of all uterine malignancies and about 5% of uterine sarcomas [1]. Generally, LMS arises within the myometrium, from the smooth muscle cells, clinically aggressive smooth muscle malignancy. The histological diagnosis of leiomyosarcoma is based on prominent cellular atypia, abundant mitoses (≥ 10 per 10 high power fields), and areas of coagulative necrosis.

Indisputable scientific data strongly suggest that uterine LMSs are solitary lesions and are not commonly found in association with uterine leiomyomas. If there is malignant transformation of uterine leiomyomas, is a rare event [2].

The hypothesis that a uterine LMS derived from a myoma or are the result of malignant transformation of benign leiomyomas is never demonstrated [3].

LMS is a so aggressive tumor associated with a high risk of recurrence and death, regardless of a stage at presentation: 2% -6% of uterine malignancies have poor prognosis and annual incidence is 1.7 per women [4].

Uterine LMS is usually detected during the fifth or sixth decades of life. Malignant alteration occurs mainly in postmenopausal women and is rarely asymptomatic. The main presenting symptoms of uterine LMSs are abnormal vaginal bleeding, pain in the lower abdomen and a pelvic or abdominal mass [5].

In the past, if sudden growth of fibroids was observed, especially after menopause, malignancy should be suspected and these tumors should be surgically removed. Anyway, recent evidences indicate that in premenopausal women, "rapid uterine growth" almost never indicates presence of uterine LMS [6].

Parker and colleagues examined 1,332 women who had undergone a hysterectomy for uterine leiomyoma as the sole indication for surgery. Only 1 patient out of 371 women operated on for a "'myoma fast-growing" had proved to be a LMS. When the surgeons had judged that the leiomyoma was at "rapid growth", defined as an increase of uterine volume as a womb of 6 weeks of pregnancy in one year of observation, none of the 198 patients who had this diagnosis showed to a uterine LMS at histological examination. Two of these women had instead endometrial stromal sarcoma. A patient of 30 years in the group of patients candidates for hysterectomy showed a normal uterus 22 months before; to gynecological presurgical, had a very large size of the uterus, such as a uterus of 16 weeks. After surgery, histological examination showed a LMS. None of the 198 patients who had the criteria of "*rapidly growing myoma*" had a LMS, a mixed mesodermal tumor, or endometrial stromal sarcoma. None of the 17 postmenopausal women admitted for rapid uterine growth proved to be a LMS [7].

Preoperatively, diagnose of uterine LMS is very difficult, even if diagnostic imaging and endometrial sample have been performed preoperatively. There is no scientifically validated screening instruments that diagnose a LMS, the diagnosis of LMS is purely histological and sometimes mixed with areas of benign myoma. In fact, to perform a diagnosis of LMS is not easy, even on extemporaneous histological examination. Frozen section is not always decisive intra operatively [8].

In some investigations the potential utility of LDH-3 isoenzyme and MRI T2 weighted image were tested as promising diagnostic tool for uterine leiomyosarcoma, although there is still a high false positive and low specificity.

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In most medical centers, the frozen sections are not the histological technique for the final diagnosis. From one to three slides of a so-called "fibroid" can be routinely assessed when examining the frozen sections. It is more common than pathologist could think wrong or could miss the diagnosis of uterine LMS in the frozen section [9].

Genetic differences between fibroids and LMSs indicate that LMSs do not result from malignant degeneration of fibroids and comparative genomic hybridization did not find specific anomalies shared by fibroids and LMSs [10].

So, the diagnosis of LMS is established by a pathologist or after surgical removal of a presumed benign uterine mass. In most cases the diagnosis of LMS is made following hysterectomy. The overall incidence of uterine LMS in surgical cases is less than 0.5%, even if this risk is increased with age, so that in women older than 60 years is 1.7% [4].

In that fibroid growth is not predictable, women with fibroids who are mildly or moderately symptomatic, may choose to defer treatment. As women approach menopause and there is limited time to develop new symptoms, "watchful waiting" may be considered. There is no evidence that not having treatment for fibroids results in harm, except for women with severe anemia from fibroid-related heavy menstrual bleeding or hydronephrosis due to obstruction of the ureter(s) from an enlarged fibroid uterus. After one year of "watchful waiting", 77% of women with uterine size 8 weeks or greater had no significant changes in the self-reported amount of bleeding, pain or degree of bothersome symptoms [11].

Even if surgical treatment is the first treatment, recurrence is up to 70% in stage 1 and 2. Commonly, place of recurrence are lungs or upper abdomen: liver, abdomen, pelvis and pelvic or par aortic lymph nodes are other site of metastases [12].

In women with confined disease to pelvis (stage 2) or the abdomen (stage 3), surgical cytoreduction is also performed [13]. An optimal cytoreduction is associated with improved overall survival [14]. In women with metasis extending beyond the peritoneal cavity there is no benefit to surgery [15]. Pelvic lymphadenectomy is mandatory in women with enlarged pelvic nodes and extra uterine disease [14].

From what it is reported in the literature, it understandable how much the disease is rare and not easily diagnosable and treatable.

Moreover, while the U.S. Food and Drug Administration (FDA) approved the first electromechnical morcellation device in 1995, it recently issued a statement discouraging the use of "power" or electromechanical morcellation for hysterectomy and myomectomy in most women with uterine myoma. The FDA cited safety concerns, specifically the potential for dissemination of occult uterine cancer that may occur with the morcellator technology [16]. The FDA's recommendations must be taken very seriously, as patient safety and avoiding preventable harm are of paramount importance.

However, the studies analyzed by the FDA in formulating this recommendation were not stratified by risk factors for LMS and were not necessarily performed in the setting of reproductive-age women with presumed benign leiomyomata [17].

A recent study published on JAMA, demonstrated that uterine cancers occurred in 27 per 10000 women undergoing morcellation (0.27%), and other malignancies and precancerous abnormalities were also detected [18].

Although morcellators have been in use since 1993, few studies have described the prevalence of unexpected pathology at the time of hysterectomy. Further, in addition to the risk-benefit ratio of morcellator technology, it must also be considered the implications of alternative surgical options for women if morcellator use is suspended nationwide. In any case, it is proved the utility of the "inside-bag" power morcellation approach adapted by many MIS Centres subsequent to FDA ban, even if this practice should only be considered as experimental due to similar risk of cancer spread in case the bag is accidentally broken inside the abdomen. In addition, various alternatives were also proposed to safely extract the uterine specimen via minilaparotomy or vaginal cuff.

The AAGL agrees that morcellation is generally contraindicated in the presence of documented or highly suspected malignancy. Meticulous adherence to preoperative screening guidelines, including endometrial biopsy and cervical cytology, to exclude coexisting uterine or cervical malignancy or premalignancy is imperative. Certain types of uterine cancers, such as leiomyosarcomas, are more difficult to detect preoperatively, though 38-68% of leiomyosarcomas can be detected in this manner. The AAGL's position is that surgeons should improve but not abandon power morcellation, and that power morcellation with appropriate informed consent should remain available to appropriately screened, low risk women.

The alternatives for women with large uteri or uterine myomas would, in some cases, involve the minimally invasive surgery (MIS) abandoning or the ability to morcellate and potentially deny the clear benefits of this approach.

In considering these scenarios, laparotomy as an alternative carries its own set of clearly defined risks, some of which are serious and life threatening, more than MIS.

Concluding, established that the LMS is a very rare condition and not be diagnosed with sufficient certainty, because of its complex biology [19], as well as to design a proper treatment, it remains to determine how to deal with the problem of relative tranquillity of a younger patient with a uterine mass [20].

Research aimed at optimizing MIS approaches in the greatest number of women and the development of diagnostic tools to identify more accurately those women who may be potentially harmed by morcellation, so as for unexpected LMSs, are urgently needed.

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