



Long-Term Survival of a Patient with Uterine Leiomyosarcoma Treated With Repeated Metastasectomies: A Case Report

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Abstract

Uterine leiomyosarcomas are uncommon malignancies characterized by early recurrence and metastasis. The authors report the case of a female patient, who has undergone total extirpation of the uterus for leiomyosarcoma, followed by further ten metastasectomies performed in two body cavities. The patient died 23 years after her initial surgery.

According to the available literature, neither postoperative adjuvant chemotherapy, nor irradiation has proven successful for the treatment of leiomyosarcoma. In particular, neither of these procedures can halt the propagation and the metastatic spread of the tumor, as well as both fail to improve survival. Lately, repeated surgical resections and metastasectomies have proven the most effective therapeutic interventions, as these might improve survival. It appears that the location of metastases (i.e. pulmonary vs. extrapulmonary) is unimportant-what matters is to remove them.

Keywords: Uterine leiomyosarcoma; Multiple resections; Oophorectomy; Pulmonary metastasis; Survival

Introduction

Leiomyosarcoma of the uterus is a particularly rare tumor accounting for only one percent of uterine malignancies. Its annual incidence is reported at 0.64 case per 100,000 women [1]. Its etiology is currently unknown, and appears to be unrelated to pregnancy or childbirth. Most patients are diagnosed in the fifth decade of life. In the vast majority of cases, the tumor involves the uterine fundus and/or the cervix [2,3]. Leiomyosarcomas tend to be subclinical. Often, clinical manifestations occur only when the tumor exerts pressure on adjacent blood vessels and nerves, or dislocates neighboring organs. The leading symptoms include bleeding, hemorrhagic diathesis, and more or less severe lower abdominal pain. Leiomyosarcomas are usually diagnosed 'by chance' – that is, during the histological evaluation of the surgical specimens of removed uterine fibroids.

The prognosis of uterine leiomyosarcoma is poor – 5-year survival is 50 to 65 percent after the complete resection of Stage I and II tumors [2-4]. In 30 to 35% of cases, malignancy has already spread beyond the uterus by the time of diagnosis [5]. Nearly 80% of the recurrences occur outside the pelvis [3,6]. In more than 70% of patients with a leiomyosarcoma confined to the uterus, and in all cases with an extrauterine tumor, surgical resection is followed by recurrence within 8 to 16 months on average [2,3,6].

Case Presentation

1. In 1986, at the age of 41 years, the female patient underwent surgery for a pelvic mass of 4 cm diameter. The lesion was contiguous with the uterine portion of the cervix, and filled the uterovesical pouch. Total uterine extirpation was performed by the abdominal route. The final histopathological diagnosis was leiomyosarcoma and therefore, the patient was re-laparotomized and the uterine appendages removed. Subsequently, the patient underwent pelvic telecobalt radiation therapy.

2. A symptom-free period of nine years followed and then, in 1995, chest imaging detected an asymptomatic metastasis of 2 cm diameter in the third segment of the right lung. Atypical resection of the right upper pulmonary lobe was performed (Figure 1).

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Figure 1: Lung metastasis identified in the right upper pulmonary lobe (arrow) on the chest x-ray film.



Figure 2: Surgical specimen: the three removed lesions.

3. In 1997, a metastatic lymph node of 3 cm diameter was removed from the left para-aortic region. The patient was symptom-free; doxorubicin chemotherapy was administered after the operation.

4. In 1998, follow-up evaluation detected a retroperitoneal lymph node metastasis, which was then removed.

5. In 1999, round shadows (of 7 to 8 mm diameter each) were observed in the second, sixth, and tenth segments of the left lung. Two additional, one-centimeter large masses were described in the sixth and tenth segments of the right lung. Bilateral pulmonary metastasectomy was performed through transverse sternotomy, and altogether seven metastases were removed.

6. In 2000, a CT-scan depicted a pelvic soft-tissue mass of 25 mm diameter, located above the aortic bifurcation and in front of the inferior vena cava. Follow-up CT-scans confirmed the propagation of the lesion and by 2002, it had grown to a size of 40 mm and therefore, it was excised through the retroperitoneal approach.

7. In 2005, MRI revealed a 5.5 × 3.5 cm large mass, located below the level of the aortic bifurcation, among the intestines. Two additional masses of 3.4 × 2.3 cm and 3 × 2 cm size were identified in the left para-iliac region. Again, all these lesions were removed surgically (Figure 2).

8. Still in 2005, a pelvic lesion of 10 × 7 cm size was detected left to the urinary bladder; it caused an indentation of the wall of the

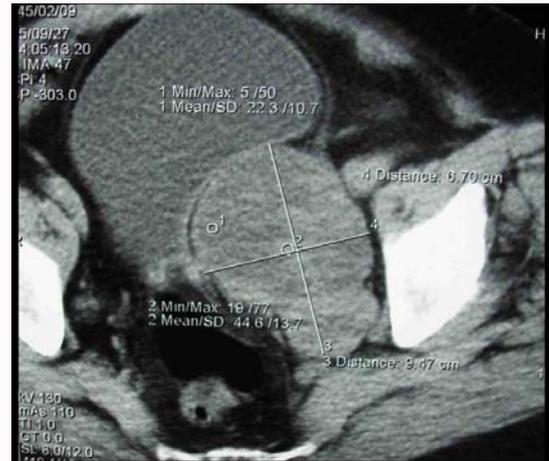


Figure 3: The tumor causes indentation of the wall of the urinary bladder.

latter. The lesion, located on the pelvic surface of the sacrum, was extirpated (Figure 3).

9. In 2006, the PET/CT-scan showed a 51-mm mass in the left half of the pelvis, next to the acetabulum, along with another 58-mm lesion. A third lesion of 28 mm size and exhibiting minimal FDG-enhancement was detected in the corresponding location on the right side. According to the literature, leiomyosarcoma is an intensely FDG-avid malignancy. Therefore, the negligible FDG-enhancement seen in this case might have reflected the well-differentiated/slowly progressive nature of the tumor. All these lesions were removed.

10. In 2007, CT imaging performed on the asymptomatic patient showed three metastases, which were then removed. One subcutaneous lesion of 5×5×5 cm size was located in the right subcostal region. Another, 15 × 15 × 15 cm large mass was detected at the bifurcation of the left common iliac artery. Finally, a third tumor of 4 × 4 × 4 cm dimension was identified under the junction of the left iliac vein and the inferior vena cava.

11. The last operation was performed in January 2009 for a lesion discovered by chance during the follow-up evaluation of the asymptomatic patient. On this occasion, a mass of 4 × 3 × 3 cm size, located at the thoracic-diaphragmatic border, was removed from the splenic region.

In May 2009, a follow-up CT-scan confirmed multiple pulmonary metastases; however, further surgical intervention was no longer possible. In December 2009, the patient died from acute renal failure at the age of 64 years. It can thus be concluded that follow-up treatment comprised multiple excisions of small, easy-to-remove lesions, which were detected at the follow-up visits scheduled every year at the outset, and every six months after 2005. The patient recovered without serious complications after these operations; abdominal wall reconstruction for hernia was necessary on two occasions.

The presence of metastatic leiomyosarcoma has been confirmed pathologically in all surgical specimens obtained during the above operations. The histological appearance of the tumor tissue was suggestive of low malignancy; mitotic cells were seen in moderate numbers, without any tissue necrosis.

Immunohistochemistry staining was positive for vimentin and for smooth muscle actin after the ninth, as well as for vimentin and

desmin after the last operation. Histopathology evaluation did not detect vascular invasion in any of the surgical specimens obtained during the ten procedures performed for metastatic spread.

Discussion

Uterine leiomyosarcoma is a rare disorder and hence, only meager information is available in the literature to develop an appropriate management strategy.

The current (NCCN 2015) guidelines recommend hysterectomy with bilateral salpingo-oophorectomy for leiomyosarcoma confined to the uterus, as confirmed by preoperative diagnostic evaluation. The surgical management of advanced disease or of extrauterine organ involvement should be individualized. Surgery is the treatment of choice for resectable disease (e.g. local propagation, metastatic spread, or symptomatic disease). Leitao et al. [7] found that while prolonging progression-free survival, surgical cytoreduction has no impact on overall survival. According to two additional studies, preservation of the ovaries does not influence patient survival either [2,3]. On the other hand, there is evidence that oophorectomy might have a negative effect on survival [8]. A recent study of 1396 female patients established that oophorectomy alone does not influence survival [9].

The need for para-aortic lymph node dissection is controversial. In leiomyosarcoma, the incidence of lymph node metastases is 6.6 to 9.1%, and these lesions are usually accompanied by metastases to additional extrauterine locations [3,6,9,10]. As lymphadenectomy does not improve patient survival [9,11], this intervention is not recommended in the absence of lymphadenopathy or extrauterine metastases.

Leiomyosarcoma recurs in 45 to 73% of cases; the initial recurrence occurs within 18 months on average [8]. In many instances, patient survival is long despite the presence of metastases, whereas recurrence is aggressive in others. Overall, recurrence is influenced by the extent of primary spread, tumor grade, and tumor rupture [8].

Several studies have identified doxorubicin and iphosphamide as the most effective chemotherapeutic agents [12-14]. Add-on cisplatin [15], or paclitaxel [16] prolongs both progression-free and overall survival. However, the latest guidelines recommend watchful waiting in early (Stage I/II) leiomyosarcoma of the uterine corpus, whereas adjuvant chemotherapy (gemcitabine + docetaxel followed by doxorubicin) is recommended for advanced (III to IV) stages of the disease [17]. Some patients might respond to endocrine therapy [18].

The retrospective analysis of the SEER database found that adjuvant radiotherapy does not prolong patient survival [19]. Another study of 3000 patients established that although it reduced the recurrence rate, radiotherapy had no impact on survival [20]. Therefore, this modality may be considered, in the first place, as definitive or palliative therapy for advanced stages, or as an individual treatment option.

Because of the limited oncological treatment modalities available for patients with metastases, data on the outcomes of surgical treatment are relatively abundant. The removal of pulmonary leiomyosarcoma metastases prolongs survival [21,22,23]. In their series of 21 patients treated with lung resection, McCORMACK & MARTINI reported 27% 5-year survival [21]. Levenback et al. [22] studied a heterogenous population of 45 patients with uterine sarcoma and found 43% 5-year, and 35% 10-year survival following the removal of isolated pulmonary metastases. According to Leitao

[7], this intervention achieved a 71% 2-year survival rate. This is a remarkable result, considering that these patients usually receive only chemotherapy and survive for 7 to 15 months on average. In particular, survival was 60 months in patients who underwent thoracotomy later than 60 months after hysterectomy, whereas those thoracotomized within 60 months survived only for 31 to 32 months. The comparison in terms of the presence of intra- vs. extrathoracic metastasis did not reveal any significant difference in patient survival [24]. BILLIGSLEY found longer survival in non-surgical patients, compared with – at least in part – resectable pulmonary metastases. According to this comparison, survival was much better when the pulmonary metastases could be removed completely [25].

Survival is dependent on several factors. GIUNTOLI *et al.* [8] followed-up 208 patients with leiomyosarcoma for 24 years. They found that survival was longer (4.9 years on average), when the tumor was discovered in an earlier stage, at a younger age (<51 years), and at a size less than 5 cm upon detection. According to their multivariate analysis, only the type of surgery (i.e. complete vs. partial removal of the lesion; the occurrence vs. the lack of tumor rupture before or during surgery) influenced survival [8]. As shown by the univariate analysis undertaken by LEITO *et al.* [24], longer time (>12 months) to the first recurrence, and complete tumor removal were associated with longer survival. Possibly, early recurrence indicates persistent rather than recurrent disease. PAUTIER analyzed data on 78 leiomyosarcomas identified amongst 157 uterine sarcoma cases, and found that only staging information correlated with tumor recurrence and patient survival [26]. SAGAE emphasized that complete tumor removal is the most important prognostic factor [27].

Conclusion

The surgical treatment of leiomyosarcoma should consist of hysterectomy with bilateral salpingo-oophorectomy. As shown by literature data, adjuvant therapy is not necessarily effective in reducing the propagation and metastatic spread of the tumor, or in prolonging patient survival. Therefore, surgical removal remains the mainstay of therapy. The lesion must always be removed, regardless of its location (i.e. pulmonary or extrapulmonary). This conclusion is exemplified by the case described in the foregoing. In the lack of an effective, non-invasive, and curative treatment modality, surgical resection should be offered to all patients with recurrent, resectable leiomyosarcoma, as the repeated removal of recurrent tumors may improve survival.

References

1. Harlow BL, Weis NS, Lofton S. The epidemiology of sarcomas of the uterus. *J. Natl Cancer Inst.* 1986; 76: 399-402.
2. Berchuck A, Rubin SC, Hoskins WJ, Saigo PE, Pierce VK, Lewis JL Jr. Treatment of uterine leiomyosarcoma. *Obstet Gynecol.* 1988; 71: 845-850.
3. Gadducci A, Landoni F, Sartori E, Zola P, Maggino T, Lissoni A, et al. Uterine leiomyosarcoma: analysis of treatment failures and survival. *Gynecol Oncol.* 1996; 62: 25-32.
4. Mayerhoffer K, Obermair A, Windbichler G, Petru E, Kaider A, Hefler L, et al. Leiomyosarcoma of uterus: a clinicopathologic multicenter study of 71 cases. *Gynecol Oncol.* 1999; 74: 196-201.
5. Zivanovic O, Leitao MM, Iasonos A, Jacks LM, Zhou Q, Abu-Rustum NR, et al. Stage-specific outcomes of patients with Uterine leiomyosarcoma: A comparison of the international federation of gynecology and obstetrics and american joint committee on cancer staging systems. *J Clin Oncol.* 2009; 27: 2066-2072.

6. Goff BA, Rice LW, Fleischhacker D, Muntz HG, Falkenberry SS, Nikrui N, et al. Uterine leiomyosarcoma and endometrial stromal sarcoma: lymph node metastases and site of recurrence. *Gynecol Oncol.* 1993; 50: 105-109.
7. Leitao MM Jr, Zivanovic O, Chi DS, Hensley ML, O'Ceirbhail R, Soslow RA, et al. Surgical cytoreduction in patients with metastatic uterine leiomyosarcoma at the time of initial diagnosis. *Gynecologic Oncology.* 2012; 125: 409-413.
8. Giuntoli RL 2nd, Metzinger DS, DiMarco CS, Cha SS, Sloan JA, Keeney GL, et al. Retrospective review of 208 patients with leiomyosarcoma of the uterus: prognostic indicators, surgical management, and adjuvant therapy. *Gynecol Oncol.* 2003; 89: 460-469.
9. Kapp DS, Shin JY, Chan JK. Prognostic factors and survival in 1396 patients with uterine leiomyosarcomas: emphasis on impact of lymphadenectomy and oophorectomy. *Cancer.* 2008; 112: 820-830.
10. Major FL, Blessing JA, Silverberg SG, Morrow CP, Creaman WT, Currie JL, et al. Prognostic factors in early-stage uterine sarcoma: a Gynecologic Oncology Group study. *Cancer.* 1993; 71: 1702-1709.
11. Ayhan A, Aksan G, Gultekin M, Esin S, Himmetoglu C, Dursun P, et al. Prognosticators and the role of lymphadenectomy in uterine leiomyosarcomas. *Arch Gynecol Obstet.* 2009; 280: 79-85.
12. Omura GA, Major FJ, Blessing JA, Sedlacek TV, Thigpen JT, Creasman WT, et al. A randomized study of adriamycin with and without dimethyl triazenoimidazole carboxamide in advanced uterine sarcomas. *Cancer.* 1983; 52: 626-632.
13. Omura GA, Blessing JA, Major F, Lifshitz S, Ehrlich CE, Mangan C, et al. A randomized clinical trial of adjuvant adriamycin in uterine sarcomas: a Gynecologic Oncology Group Study. *J Clin Oncol.* 1985; 3: 1240-1245.
14. Sutton GP, Blessing JA, Barrett RJ, McGehee R. Phase II trial of ifosfamide and mesna in leiomyosarcoma of the uterus: a Gynecologic Oncology Group study. *Am J Obstet Gynecol.* 1992; 166: 556-559.
15. Sutton G, Brunetto VL, Kilgore L, Soper JT, McGehee R, Olt G, et al. A phase III trial of ifosfamide with or without cisplatin in carcinosarcoma of the uterus: a Gynecologic Oncology Group Study. *Gynecol Oncol.* 2000; 79: 147-153.
16. Homesley HD, Filiaci V, Markman M, Bitterman P, Eaton L, Kilgore LC, et al. Phase III trial of ifosfamide with or without paclitaxel in advanced uterine carcinosarcoma: a Gynecologic Oncology Group Study. *J Clin Oncol.* 2007; 25: 526-531.
17. Hensley ML, Ishill N, Soslow R, Larkin J, Abu-Rustum N, Sabbatini P, et al. Adjuvant gemcitabine plus docetaxel for completely resected stages I-IV high grade uterine leiomyosarcoma: Results of a prospective study. *Gynecologic Oncology.* 2009; 112: 563-567.
18. Hardman MP, Roman JJ, Burnett AF, Santin AD. Metastatic uterine leiomyosarcoma regression using an aromatase inhibitor. *Obstet Gynecol.* 2007; 110: 518-520.
19. Wright JD, Seshan VE, Shah M, Schiff PB, Burke WM, Cohen CJ, et al. The role of radiation in improving survival for early-stage carcinosarcoma and leiomyosarcoma. *Am J Obstet Gynecol.* 2008; 199: 536.
20. Sampath S, Schultheiss TE, Ryu JK, Wong JYC. The Role of Adjuvant Radiation in Uterine Sarcomas. *Int J Radiat Oncol Biol Phys.* 2010; 76: 728-734.
21. McCormack PM, Martini N. The changing role of surgery for pulmonary metastasis. *Ann Thorac Surg.* 1979; 28: 139-145.
22. Levenback C, Rubin SC, McCormack PM, Hoskins WJ, Atkinson EN, Lewis JL Jr. Resection of pulmonary metastases from uterine sarcomas. *Gynecol Oncol.* 1992; 45: 202-205.
23. Benoit L, Arnould L, Cheynel N, Goul S, Collin F, Fraisse J, et al. The role of surgery and treatment trends in uterine sarcoma. *Eur J Surg Oncol.* 2005; 31: 434-442.
24. Leitao MM, Brennan MF, Hensley M, Sonoda Y, Hummer A, Bhaskaran D, et al. Surgical resection of pulmonary and extrapulmonary recurrences of uterine leiomyosarcoma. *Gynecol oncol.* 2002; 87: 287-294.
25. Billingsley KG, Burt ME, Jara E, Ginsberg RJ, Woodruff JM, Leung DH, et al. Pulmonary metastases from soft tissue sarcoma: analysis of patterns of disease and postmetastasis survival. *Ann Surg.* 1999; 229: 602-612.
26. Pautier P, Genestie C, Rey A, Morice P, Roche B, Lhomme C, et al. Analysis of clinicopathologic prognostic factors for 157 uterine sarcomas and evaluation of a grading score validated for soft tissue sarcoma. *Cancer.* 2000; 88: 1425-1431.
27. Sagae S, Yamashita K, Ishioka S, Nishioka Y, Terasawa K, Mori M, et al. Preoperative diagnosis and treatment result in 106 patients with uterine sarcoma in Hokkaido, Japan. *Oncology.* 2004; 67: 33-39.