

UTERINE SARCOMAS: A REPORT OF 10 CASES AND REVIEW OF LITERATURE

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ABSTRACT

Background: Uterine sarcomas (US) are rare and aggressive malignant tumors. Due to their non-specific signs and symptoms, they are commonly diagnosed in advanced stage, the treatment includes a complete surgery and no standard recommendation is available for adjuvant therapy. **Methods:** This was a retrospective study of patients diagnosed and treated at our center for a histologically confirmed uterine sarcoma from January 2008 to January 2012. **Results:** We identified 10 patients with US during this period, 6 of them were leiomyosarcomas, 3 cases of endometrial stromal sarcoma and 1 case of high grade polymorphic sarcoma. The median age at presentation was 54.7 years, vaginal bleeding and the presence of pelvic mass were the two main symptoms, all patients underwent total hysterectomy with bilateral salpingo-oophorectomy, 3 patients received adjuvant radiotherapy, 2 of them relapsed at 4 months and 2 years, they received palliative mono-chemotherapy by adriamycin (60mg/m²). At the end of our follow-up, only one patient survived without evidence of recurrence 5 years after diagnosis. **Conclusion:** Uterine sarcoma is a rare subtype of uterine cancers with a poor prognosis, Tumor stage is the most important prognostic factor, therefore, early diagnostic workup and optimal therapy management are essential.

KEYWORDS: Uterine sarcomas, Surgery, Adjuvant treatments, Prognosis.**INTRODUCTION**

Uterine sarcomas are rare tumors with a poor prognosis, representing 3 to 7% of malignant tumors of the uterus.^[1,2] They include three histological subtypes: leiomyosarcomas, endometrial stromal sarcomas and adenosarcomas. Since 2009, carcinosarcomas are no longer considered as a subtype of uterine sarcomas, but as metaplastic carcinomas by the FIGO International Federation of Gynecology and Obstetrics.

Surgery is the cornerstone of uterine sarcoma management. The role of adjuvant therapies is not completely clear. A better knowledge of prognostic factors may lead to a more precise treatment selection.

We report in this article, ten cases of uterine sarcomas treated in the obstetrics and gynecology unit M1 at the Maternity Souissi-Rabat from 2008 to 2012.

METHODS

This is a retrospective study, in which 10 cases of uterine sarcomas were collected at the Gynecology and

Obstetrics department M1 at Maternity Souissi-Rabat between 1st January 2008 and 31 December 2012.

The aim of our study was to analyze the epidemiological, clinical and paraclinical data of uterine sarcomas and discuss the diagnostic and therapeutic difficulties from our series and a review of the literature.

RESULTS**1. Epidemiological characteristics**

Over a five-year period (from 01/01/2008 to 12/31/2012), 107 cases of endometrial cancer were collected at the obstetrics and gynecology department M1 at the Maternity Souissi -Rabat, of which 10 uterine sarcomas (9%).

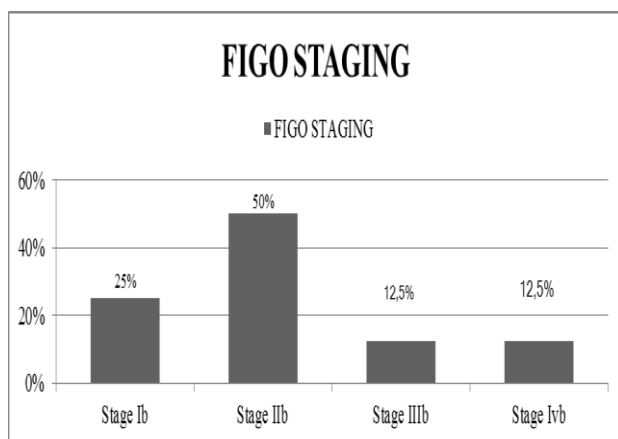
The average age of the patients was 54.7 years (36-72 years), 80% of the patients were multiparous, 4 patients had used oral contraceptives and 6 patients were postmenopausal at the time of diagnosis (none of them were using hormone replacement therapy).

2. Clinical study

The interval between the onset of first symptoms and the histological diagnosis was 30 weeks (range 4-52 weeks). The two main symptoms in our series were vaginal bleeding and the rapid increase of pelvic mass (70 and 60% respectively).

Histological distribution was as follows: 6 cases of LMS, 3 cases of ESS and 1 case of high grade polymorphic sarcoma.

According to the FIGO 2009 classification, 50% of our patients were classified as Stage IIB (see Fig1).



3. Treatment

All patients underwent a Total hysterectomy with bilateral salpingo-oophorectomy

2 patients died postoperatively, five were lost to follow-up after surgery and 3 patients received adjuvant radiotherapy (50 Gy in 25 sessions, 2 Gy per session), 2 of them experienced a relapse at 4 months and 2 years, they received palliative mono-chemotherapy by adriamycin (60mg/m²). They died at 1 year and 2 years of the initial diagnosis.

At the end of our follow-up, only one patient survived without evidence of recurrence 5 years after diagnosis (Uterine LMS satge IIB)

DISCUSSION

Uterine sarcomas are rare tumors that account for less than 3% of malignant female genital tract tumors and between 3 and 7% of malignant tumors of the uterine corpus.^[1,2]

Leiomyosarcoma remains the most frequently found histological type of uterine sarcomas,^[3-8] the other subtypes are endometrial stromal sarcomas (ESS) and undifferentiated sarcomas. Carcinosarcomas are no longer considered as a subtype of uterine sarcoma but as a dedifferentiated or metaplastic form of endometrial carcinoma.

The average age at diagnosis of uterine sarcomas is 64 years (Range 14-100 years).^[9-12] In our case series, the median age at diagnosis was 54.7 years which is below

the data found in the literature, this can be explained by the high prevalence of leiomyosarcomas and endometrial stroma sarcomas in our case series. Indeed, patients with carcinosarcomas and adenosarcomas tend to be much older than patients with other sarcomas.^[13-15]

Prolonged use of tamoxifen, a uterine estrogen receptor agonist, is associated with a three times risk of sarcoma development. Pelvic irradiation, a history of retinoblastoma in childhood, hereditary leiomyomatosis and renal cell carcinoma are other documented risk factors.^[16-18]

Symptoms of uterine sarcomas are not specific, patients often present with vaginal bleeding or discharge (56%), lower abdominal mass (54%) and/or pelvic pain (22%).^[19]

Neither preoperative imaging with ultrasonography, CT, MRI or PET scans is able to differentiate between leiomyomas and uterine sarcomas. Tamai *et al.*,^[20] reported that diffusion-weighted imaging (DWI) could help to discriminate uterine sarcomas from benign fibroids. The ADC values of normal myometrial zone and degenerated fibroids were higher than uterine sarcomas.^[20] Then we can classify patients into two groups: those with low-risk disease that is probably benign, and those with high-risk disease in whom there is a possibility of uterine sarcoma.^[21,22]

Endometrial sampling is considered a standard preoperative diagnostic test in uterine neoplasms. However, it has a low predictive value in diagnosing uterine sarcomas.^[23]

The vast majority of uterine sarcomas are diagnosed after a first intervention (hysterectomy or myomectomy). Total hysterectomy with tumor debulking if present outside the uterus is the gold standard treatment of uterine sarcomas, it is important to avoid uterine morcellation or intraoperative rupture of the mass into the peritoneal cavity.

Ovarian preservation may be considered in premenopausal patients with early-stage leiomyosarcomas. A Surveillance, Epidemiology, and End Results (SEER) study by Kapp *et al.* did not show a survival advantage of bilateral salpingo-oophorectomy in patients under the age of 50 with leiomyosarcoma.^[24] For patients presenting an endometrial stromal sarcoma, it is necessary to perform a bilateral salpingo-oophorectomy since this subtype is often sensitive to hormones and it has been shown that patients retaining their ovaries have a much higher risk of recurrence.^[25]

The role of lymph node dissection remains controversial, only suspicious lymph nodes should be removed.^[26]

A trial by the European Organization for Research and Treatment of Cancer (EORTC) failed to demonstrate a survival advantage of adjuvant RT in patients with stage I and II uterine sarcomas. There was only a significant improvement in local control overall.^[27]

A SEER (Surveillance, Epidemiology, and End Results) analysis also concluded that adjuvant RT had no survival benefit in this population.^[28]

The role of adjuvant chemotherapy is uncertain, it is not standardly administered in patients who underwent hysterectomy for uterine sarcomas confined to the uterus (stages I and II). For advanced and metastatic uterine sarcomas, a doxorubicin based regimen should be prescribed as a first line therapy, the combination of gemcitabine and docetaxel is also effective in uterine LMS, other agents with moderate activity include ifosfamide, liposomal doxorubicin, temozolomide and trabectedin (Table 1).^[29-45]

| | Study | Responders/evaluable patients (N) | Objective response rate (%) |
|---|--|--------------------------------------|--------------------------------|
| Doxorubicine | Omura et al. ^[29] | 7/28 | 25 |
| Ifosfamide | Sutton et al. ^[30] | 6/35 | 17 |
| Doxorubicine- Ifosfamide | Leyvraz et al. ^[31] Sutton et al. ^[32] | 12/25 10/33 | 48 30 |
| Gemcitabine | Look et al. ^[33] | 9/42 | 20 |
| Mitomycine, doxorubicine et cisplatine | Edmonson et al. ^[34] | 8/35 | 23 |
| Doxorubicine liposomale | Sutton et al. ^[35] | 5/32 | 16 |
| Gemcitabine- Docétaxel | Hensley et al. ^[36] Hensley et al. ^[37] Hensley et al. ^[38] | 17/42 13/48 15/42 | 40 27 36 |
| Trabectédine | Grosso et al. ^[39] | 3/22 | 14 |
| Témozolomide | Anderson et al. ^[40] Talbot et al. ^[41] | 2/12 2/11 | 17 18 |
| Doxorubicine trabectedine | Pautier et al. ^[42] | 28/47 | 60 |
| Doxorubicine, cisplatin and ifisfamide | Hadoux et al. ^[43] | 16/33 | 48 |

In our case series, a doxorubicin-based chemotherapy (Adriamycin 75mg) was indicated for two patients who experienced a metastatic relapse.

Hormone therapy is an effective treatment for low-grade ESS since it is considered as a hormone-dependent malignancy. Treatment with aromatase inhibitors and gonadotropin-releasing hormone agonists has shown acceptable long-term outcomes in advanced disease with a favorable toxicity profiles, they can also be an alternative to chemotherapy for uterine LMS expressing steroid receptors with low disease burden.⁽⁴⁶⁻⁴⁷⁾

CONCLUSION

Uterine sarcomas are rare cancers with poor prognosis. Surgery is the cornerstone of uterine sarcomas management, the role of adjuvant therapies remains uncertain and the standard treatment for advanced or recurrent disease is chemotherapy with adriamycin or gemcitabine/docetaxel, Low-grade endometrial stromal sarcomas are indolent, hormone sensitive with favorable prognosis.

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