Thai Journal of Obstetrics and Gynaecology
September 2000, Vol. 12, pp. 241-246

GYNAECOLOGY

Uterine Sarcomas in Ramathibodi Hospital (1987-1998)

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ABSTRACT

Objective To study the incidence, clinical characteristics, treatment and outcome of patients with uterine sarcomas in Ramathibodi Hospital.

Design Retrospective cohort study.

Setting Department of Obstetrics and Gynaecology, Faculty of Medicine, Ramathibodi Hospital.

Subjects Twenty-six patients with uterine sarcomas who were diagnosed and treated in Ramathibodi Hospital from January 1987 to December 1998.

Results Twenty-six uterine sarcomas out of 346 uterine malignancies admitted (7.5%) were found during 12 - year period. The mean age was 45.1 years (range 15 - 70 years), with the mean parity of 2.9 (range 0 - 9). Nine patients (34.6 %) were post-menopausal. The most common presenting symptoms was abnormal uterine bleeding (65.4 %). Only 30.8 % of the cases could be diagnosed preoperatively. Fourteen patients had leiomyosarcomas, 5 patients had malignant mixed mesodermal tumors, 4 patients had high-grade endometrial stromal sarcomas and 3 patients had low-grade endometrial stromal sarcomas. The distribution by FIGO staging was as follows: stage I: 73.1 %,none in stage II, stage III: 11.5 %, stage IV: 15.4 %.The treatment was mainly hysterectomy, with either post-operative radiation or chemotherapy in advanced stager of the disease. The median follow-up time was 22 months. The five-year survival rate was 61.7 %.

Conclusions The incidence of uterine sarcoma in Ramathibodi Hospital is 7.5 % of uterine malignancy patients, or 10.7/10,000 gynecologic admissions. The most common histology was leiomyosarcoma (53.9 %). The most frequent presenting symptoms were uterine bleeding and abdominal mass. Treatment modalities were surgery, combined with chemo/radiotherapy in selected cases. The five-year survival rate of the whole group was 61.7 %.

Key words: Uterine sarcoma, Ramathibodi Hospital

Uterine sarcoma is a rare form of neoplasm characterized by rapid clinical progression with poor prognosis. The worldwide incidence rate is between 0.5 - 3.3 cases per 100,000 women per year[1] and comprises between 3 - 5% of uterine tumors.[2,3] The histologic diversity of the disease leads to several systems of classification. The version endorsed by the Gynecologic Oncology Group classified this neoplasm into 5 subgroups as followed: leiomyosarcomas, endometrial stromal sarcomas, mixed homologous

mullerian sarcomas (carcinosarcomas), mixed heterologous mullerian sarcomas (mixed mesodermal sarcomas) and other sarcomas.[2,3]

Due to the rarity of the disease, most reports are retrospective with a limited number of cases, thus optimal management has not been established. The mainstay of treatment is surgery. Although the extent of surgery varies by histologic subtype, the standard procedure is total abdominal hysterectomy and bilateral salpingo-oophorectomy. The roles of adjunctive radiotherapy and chemotherapy have not yet been clearly defined.

Our purpose is to study the incidence, clinical characteristics, treatment and outcome of patients with uterine sarcomas in Ramathibodi Hospital.

Materials and Methods

During the period of January 1987 to December 1998, 26 patients with uterine sarcomas were treated at Ramathibodi Hospital. All medical records and pathological reports were reveiwed. The histopathologic criteria for the diagnosis of leiomyosarcomas (LMS) included tumors with more than 10 mitoses/10 high power fields (HPF) or tumors with 5 - 9 mitoses/ 10 HPF with atypical neoplastic cells. Endometrial stromal sarcomas (ESS) were subclassified into low-grade ESS with less than 10 mitoses/10 HPF and high-grade ESS with 10 mitoses or higher / 10 HPF. The tumors were designated as malignant mixed mesodermal tumor (MMMT, mixed mullerian sarcomas) when they comprised an admixture of both sarcomatous and carcinomatous components.[4]

All patients were staged according to the modified staging of the International Federation of Gynecology and Obstetrics (FIGO) as followed: stage I: tumor limited to the corpus, stage II: tumor extends to the cervix, stage III: regional spread to the pelvis and stage IV: extrapelvic spread.[5]

Most of the patients were scheduled for post-operative follow-up every 1 - 3 months for 2 years and every 6 months afterward. Patients lost to follow-up were interviewed by phone or post and called for examination if possible.

Descriptive statistics were presented as percentage, mean and standard deviation. Survival was calculated using the Kaplan-Meier method.

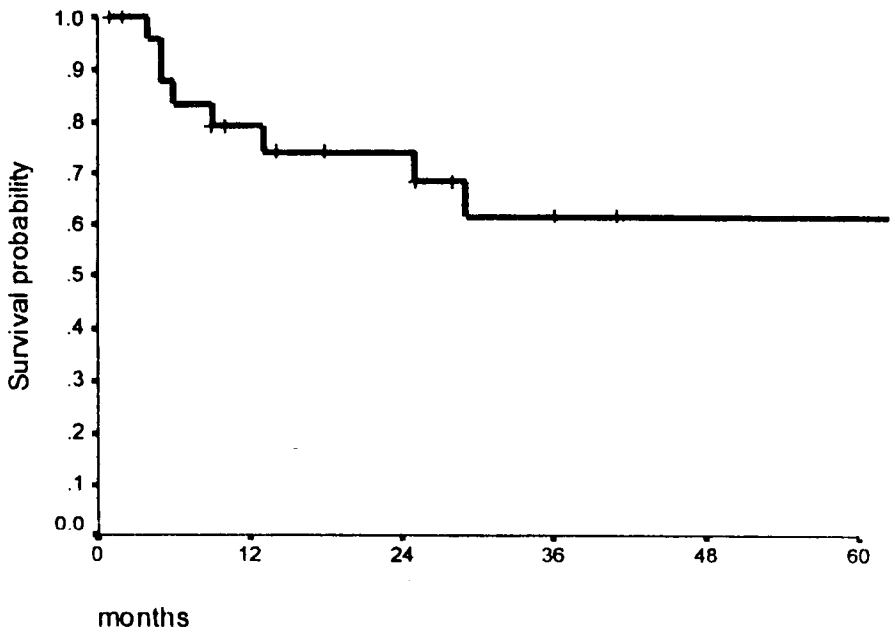

Fig. 1. Survival probability of the patients.

Table 1. Distribution of patients by histology, age, menopausal status and parity

Histologic diagnosis	No. (%)	Mean age (range) (years)	No. of menopausal patients (%)	Mean parity (range)
LMS	14 (53.9)	44.2 (29 - 61)	4 (28.5)	3.4 (0 - 9)
MMMT	5 (19.2)	57.2 (15 - 70)	4 (80)	3.2 (0 - 7)
High-grade ESS	4 (15.4)	40.0 (24 - 56)	1 (25)	2.0 (0 - 4)
Low-grade ESS	3 (11.5)	35.7 (24 - 47)	0 (0)	1.3 (0 - 3)
Total	26 (100)	45.1 (15 - 70)	9 (34.6)	2.9 (0 - 9)

Table 2. Distribution of patients by histology and presenting symptoms (n=26)

Presenting symptoms	No. (%)	Histologic diagnosis (numbers)			
		LMS	MMMT	High-grade ESS	Low-grade ESS
Abnormal bleeding	17(65.4)	7	4	4	2
Pelvic mass	12(46.2)	9	0	1	2
Abdominal pain	4 (15.4)	1	2	0	1
Leukorrhea	1 (3.8)	0	1	0	0

Note: Many patients had more than one presenting symptoms.

Table 3. Distribution of patients according to FIGO staging and histologic subtypes (n=26)

Stage	No. (%)	Histologic diagnosis (numbers)			
		LMS	MMMT	High-grade ESS	Low-grade ESS
I	19(73.1)	11	3	2	3
II	0 (0)	0	0	0	0
III	3 (11.5)	1	1	1	0
IV	4 (15.4)	2	1	1	0

Results

During our period of study, there were 26 cases of uterine sarcomas treated. The hospital-based incidence of the disease was 7.5% of uterine malignancy patients admitted (26/346) and 10.7/10,000 gynecologic admissions (total gynecologic admission = 24,357).

Of the 26 patients, 14 patients (53.9%) had leiomyosarcomas (LMS), 5 patients (19.2 %) had malignant mixed mesodermal tumor (MMMT), 4 patients (15.4%) had high-grade endometrial stromal sarcoma (ESS) and 3 patients (11.5%) had low-grade ESS.

The mean age ± SD at the time of diagnosis was 45.1 ± 15.8 years (range 15 - 70 years). The histologic and age distributions are presented in Table 1. Four out of five patients with MMMT were 64 years and older, with a median age of 68 years. Nine patients (34.6%) were post-menopausal at the time of diagnosis, most of whom had MMMT and LMS. Most of the ESS

patients were in their reproductive years.

The mean parity was 2.9 with the range of 0 - 9 (Table 1). Grand multiparity (para > 5) was seen in 5 cases, all of which had LMS and MMMT, while 7 were nulliparous.

The presenting symptoms are summarized in Table 2. The most common was abnormal uterine bleeding (17 cases, 65.4%), most of which were excessive while only one case had metrorrhagia. Six cases were post-menopausal. Diagnostic curettage was performed in 9 patients with abnormal bleeding. Correct pre-operative diagnosis was established in only 30.8% of cases. None of the patients in our series had any previous history of other primary malignancy nor receiving radiation therapy.

According to the modified FIGO staging, 19 patients (73.1%) were in stage I, none in stage II, 3 (11.5%) were in stage III, and 4 (15.4%) were in stage IV. The distribution of patients is demonstrated in Table 3.

Treatment was mainly hysterectomy. The procedure consisted of total abdominal hysterectomy (TAH), bilateral salpingo-oophorectomy (BSO), omental biopsy and peritoneal washing in 3 cases which could be diagnosed as uterine sarcoma pre-operatively. Simple hysterectomies were the minimal treatment in most of the remaining cases. Adjunctive radiation therapy or chemotherapy was given in selected advance cases as will be further described.

Follow-up time ranged from 1 - 115 months with the mean of 34.1 months, median follow-up time was 22 months. Five patients (19.2%) were lost to follow-up at the time of this study with a mean duration of follow-up of 6.2 months (range 1 - 10 months), and median follow-up time of 9 months.

Ten patients with stage I LMS had TAH; one in this group had pelvic recurrence 6 months after diagnosis. One patient with stage I LMS had myomectomy only, due to pre-operative diagnosis of myoma uteri. She received post-operative chemotherapy (doxorubicin and cis-platinum) but subsequently had recurrent disease 14 months after diagnosis. Despite whole pelvic radiation, she died of disease 25 months after diagnosis. The only patient with stage III LMS had TAH.BSO and adjunctive doxorubicin but is now still alive without disease after 77 months of follow-up. Both of the patients with stage IV disease, died of disease 6 and 29 months after diagnosis.

Three patients with stage I MMMT had different modes of treatment after surgery; one without adjunctive treatment, one received radiotherapy and one received doxorubicin. All of them had recurrent disease at 44, 10 and 6 months, respectively. The last patient died of disease 13 months after diagnosis. The only patient with stage III MMMT had complete surgical staging and post-operative radiation therapy while one patient with stage IV MMMT had palliative radiation and megestrol acetate. Both died of disease 5 months after diagnosis.

Among the two patients with stage I high-grade ESS who had surgical treatment alone, one is still alive without disease 14 months after diagnosis, while the other had distant metastasis with 7 months of disease-free period. The only patient with stage III disease had complete surgical staging with post-operative radiation. She had distant metastasis and died of disease 5 months after diagnosis. The patient with stage IV disease who had complete surgical staging alone died of disease 4 months thereafter.

All of the three patients with low-grade ESS were in stage I, thus were treated surgically. All are still alive without evidence of disease with follow-up times of 36,101 and 115 months respectively.

Using Kaplan-Meier survival analysis, the overall 5-year survival rate was 61.7% (Figure 1). The survival rate declined most rapidly during the first year after treatment and was stable after the third year. The 5-year survival rate of LMS, MMMT and low-grade ESS were 61.7%, 40% and 100%, respectively. The one-year survival rate of patients with high-grade ESS was 75%. The median survival in MMMT was 9 months. When compared by stage, 5-year survival rates for stage I, III and IV were 79.4%, 66.6% and 0%,

respectively. Median time for survival in stage IV patients was 5.5 months.

Discussion

Uterine sarcoma is a rare gynecologic neoplasm. In this study, we reported the incidence of 7.5% of uterine malignancy patients admitted. The incidence in our institution increases from 6 to 10.7 / 10,000 total gynecologic admissions when compared to our previous report.[6]

A decade ago, worldwide reports ranked LMS as the most common histologic subtype,[2,7,8] but more recent data revealed MMMT as the most common, followed by LMS and ESS.[9-12] In this series, the most common subtype is LMS which accounted for more than 50% of cases. The next most common is ESS (26.9%) with only 19.2% of patients having MMMT. These proportions are similar to the previous series of our institution 10 years ago.[6]

Most reports revealed a mean age of 55 - 60 years among patients with uterine sarcomas.[8,10,13] 7.2% of patients were post-menopausal.[8,13] Mean age for LMS patients is usually around 45 - 55 years which is 10 - 15 years younger than MMMT patients.[7,8,12,13] LMS patients in our series were slightly younger and there was a lower percentage of post-menopausal patients than in those reports but were quite similar to our previous study (45.7 years). Median age of our MMMT patients was comparable to other studies (approximately 70 years).

The wide range of parity among different histologic diagnoses may corroborate previous studies that could not demonstrate the relationship between uterine sarcomas and parity.[13]

The two most frequently presenting symptoms were abnormal uterine bleeding and abdominal mass, which are also found in other series.[1,2,7,8,11,13] Uterine sarcoma was diagnosed in only 30.8 %(8/26) of cases. The most common pre-operative diagnosis was myoma uteri, which would have diagnostic curettage only in patients with abnormal uterine bleeding other than hypermenorrhea. But correct diagnosis could be established in 88.9% of patients who underwent the procedure (8 out of 9 curettage cases). The rate of correct pre-operative diagnosis was comparable to the previous studies of our institution (4/15 cases). Other reports showed correct pre-operative diagnosis in 30.4 - 44%.[8,14] The reported incidence of positive uterine curettage was 52 in 75 cases.[14] These data still warrant the value of uterine curettage among patients with uterine bleeding.

None of the patients in our series had any history of pelvic irradiation nor other primary malignancy. But, when combined with the previous series of our institution, there was only one case with history of pelvic irradiation, thus yielding an overall rate of 2.4% (1/41) in 30 years. Others reported the incidence of 0 - 29%.[1,7,13]

The majority of our patients were diagnosed in stage I (73.1%) which was comparable to other series.[11,13] The early symptomatic character of the disease might contribute to such early detection.

Although most authorities regard surgery as the hallmark of treatment in uterine sarcomas,[1-3] the optimal management has yet to be defined. The minimal standard procedure is total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH.BSO). Peritoneal washings and pelvic/ para-aortic lymph nodes sampling were reported as useful in predicting the prognosis[15] but were not shown to increase survival.[1] The roles of adjuvant/ adjunctive radiotherapy or chemotherapy are also still controversial and most series showed benefit only among high risk or advanced diseases.[1,11,13,16] Approximately half of the patients in this series had undergone TAH.BSO or more. In the remaining patients whose uterine sarcomas were not realized until the pathology was reported, TAH with unilateral salpingo-oophorectomy or TAH or less were performed. Whole pelvic radiation and chemotherapy were given post-operatively in 4 cases.

Most series reported 5-year overall survival rates of 32 - 42%.[8,11,13,14] Our series reported a 5-year survival rate of 61.7%. The relatively better prognosis might be due to the higher proportions of stage I patients and inclusion of many ESS cases in our

series.

Considering five-year survival by histologic subtypes in this series, MMMT had the worst prognosis, with a five-year survival rate of 40%, leiomyosarcoma had a five-year survival rate of 74.1%, while low-grade ESS had an excellent prognosis with five-year survival rates of 100%.

In conclusion, the incidence of uterine sarcoma in Ramathibodi Hospital is 7.5% of uterine malignancy patients, or 10.7/10,000 gynecologic admissions. The most common histology was leiomyosarcoma (53.9%). Common presenting symptoms were uterine bleeding and abdominal mass. Treatment modalities were surgery, combined with chemo/radiotherapy in selected cases. The over all five-year survival rate of the studied group was 61.7%.

References

1. Curtin TP, Silverberg SG, Thigpen JT, Spanos WJ Jr. Corpus: mesenchymal tumors. In: Hoskins WJ, Perez CA, Young RC, editors. Principles and practice of gynecologic oncology. Philadelphia: Lippincott-Raven 1997: 897-918.
2. DiSaia PJ, Creasman WT. Clinical gynecologic oncology. St. Louis: Mosby 1997: 169-79.
3. Creasman WT. Cancer of the uterine corpus. In: Holzman GB, editor. Precis, oncology: an update in obstetrics and gynecology. Washington DC: American College of Obstetrics and Gynecologists, 1998: 31-7.
4. Zaloudex CJ, Norris HJ. Mesenchymal tumors of the uterus. In: Engolio C, Wolft M, editors. Progress in surgical pathology. Vol. 3 New York: Masson 1981: 1-35. Tangtrakul S, Srisupundit S, Linasmita V, Bullangpoti S, Bhamarapravati Y. Uterine sarcomas in Ramathibodi Hospital (1969 - 1986). J Med Assoc Thai 1990; 73: 11-4.
5. Levenback CF, Tortolero-luna G, Pandey DK, et al. Uterine sarcoma. Obstet Gynecol Clin of North Am 1996;23:457-73.
6. Tangtrakul S, Srisupundit S, Linasmita V, Bullangpoti S, Bhamarapravati Y. Uterine sarcomas in Ramathibodi Hospital (1969 - 1986). J Med Assoc Thai 1990; 73: 11-4.
7. Wen BC, Tewfik FA, Tewfik HH, Long JP, Anderson B. Uterine sarcoma: a retrospective study. J Surg Oncol 1987; 34 104-8.
8. Schwartz Z, Dgani K, Lancet M, Kessler I. Uterine sarcoma in Israel: a study of 104 cases. Gynecol Oncol 1985; 20: 354-63.
9. Harlow BL, Weiss NS, Lofton S. The epidemiology of sarcoma. J Natl Cancer Inst 1986; 76: 339-402.
10. Wolfson AH, Wolfson DJ, Sittler SY, Breton L, Markoe AM, Schwade JG et al. A multivariate analysis of clinicopathologic factors for predicting outcome in uterine sarcomas. Gynecol Oncol 1994; 52: 56-62.
11. Echt G, Jepson J, Steel J, Langholz B, Luxton G, Hernandez W et al. Treatment of uterine sarcomas. Cancer 1996; 66: 35-9.
12. Major FJ, Blessing JA, Silverberg SG, Morrow CP, Creasman WT, Currie JL et al. Prognostic factors in early-stage uterine sarcoma. A Gynecologic Oncology Group study. Cancer 1993; 71: 1702-9.
13. Piura B, Rabinovich A, Yanai-Inbar I, Cohen Y, Glezerman M. Uterine sarcoma in the south of Israel: a study of 36 cases. J Surg Oncol 1997; 64: 55-62.
14. Kahanpaa KV, Wahlstrom T, Grohn P, Heinonen E, Nieminen U, Widholm O. Sarcomas of the uterus: a ciinicopathologic study of 119 patients. Obstet Gynecol 1986; 64: 417-24.
15. Rose PG, Piver MS, Tsukada Y, Lau T. Patterns of metastasis in uterine sarcoma. An autopsy study. Cancer 1989; 63: 935-8.
16. Sorbe B. Radiotherapy and/or chemotherapy as adjuvant treatment of uterine sarcomas. Gynecol Oncol 1985; 20: 281-9.