Uterine sarcomas in RIPAS Hospital, Brunei Darussalam: A 10-year Experience

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ABSTRACT

Introduction: Uterine sarcomas are rare but aggressive malignant tumours of the smooth muscle or supporting tissues of the uterus. Currently, there are no published data available in Brunei Darussalam. This study was done to evaluate the demographic profile, risk factors, diagnostic issues and the clinical outcome of patients with uterine sarcomas in the Raja Isteri Pengiran Anak Saleha (RIPAS) hospital, a tertiary hospital in Brunei Darussalam. **Patients and Methods:** All patients with uterine sarcoma registered in the Department of Obstetrics and Gynaecology during a period of ten years (2001 to 2010) were studied. Cases were identified through the Gynaecology Oncology registry and the case notes were retrospectively reviewed. **Results:** Over this period, there were 156 cases of uterine tumour and of these, 37 cases (23.7%) were uterine sarcoma. The majority were local (n=34, Bruneian 81.1%; 30 Malays and four Chinese) with a mean age of 47.8 years. High risk factors were identified in 29 (78.4%) patients. Abnormal uterine bleeding and mass per abdomen were the most common clinical presentations. A preoperative diagnosis was possible only in five cases (13.5%) and in two patients (5.4%) the diagnosis was suspected during surgery and confirmed by frozen section. At the completion of a five-year follow up in the first five year group (2001 to 2005) 62.5% patients are alive and disease free. There were six deaths from the disease during the entire study period. **Conclusion:** A high proportion of uterine tumours were uterine sarcoma. The majority of the patients (78.4%) had one or more risk factors. Unlike endometrial carcinoma a preoperative diagnosis is difficult in uterine sarcoma. At the time of this study 70.3% of patients with uterine sarcoma were alive and disease free.

Keywords: Clinical outcomes, diagnosis, risk factor, uterine sarcomas

INTRODUCTION

Uterine sarcomas are rare mesodermal tumours that account for 3% to 7% of uterine cancers. Uterine sarcomas can arise from the myometrium (leiomyosarcoma), stroma (endometrial stromal sarcoma and endometrial sarcoma) or connective tissues of the myometrium. Leiomyosarcomas, endometrial stromal sarcomas and endometrial sarcomas are single cell type tumours whereas carcinosarcoma or malignant mixed mesodermal tu–

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mours (MMMT) and adenosarcoma are from more than one type of cell (mixed – both mesodermal and epithelial components are present). Adenosarcoma is rare where the benign epithelial component is mixed with a sarcomatous component. These tumours may also be subdivided into homologous or heterologous depending on the malignant mesodermal element that is normally present in the uterus or not. Zelmanowicz *et al* reported that carcinoma of endometrium and MMMT have similar risk factor profiles. [2] Black women have approximately twice the incidence of that reported for white women. Although most now agree that uterine MMMT/carcinosarcoma is actually metaplastic carcinoma of the endometrium that is monoclonal in origin, these tumours used to be reported together with other uterine sarcomas. [4, 5]

Leiomyosarcoma usually arise de novo or rarely from a pre-existing fibroid (0.7% risk). [2, 4] Reported risk factors for this tumour include pelvic irradiation [5] and use of tamoxifen and oestrogen. Currently, there are no screening tests available for uterine sarcomas. Abnormal uterine bleeding, pain and or abdominal swelling are common clinical manifestations but these are also seen in other uterine pathologies. Standard ultrasound scan is not helpful in the pre-operative diagnosis for differentiating sarcomas from fibroids as the imaging findings can be very variable and overlap. Advanced imaging techniques like computed tomography (CT) scan, magnetic resonance imaging (MRI) and colour Doppler ultrasound are not usually carried out if the clinical diagnosis is fibroid. Most are diagnosed after surgery by histopathological examination. Immunohistochemistry is useful to differentiate sarcoma from other tumours.

The clinical experiences with all subtypes are limited due to the rarity of the disease. There are currently no published data on uterine sarcomas in Brunei Darussalam and therefore the aim of this study was to evaluate the profiles and outcome of uterine sarcomas encountered locally.

MATERIALS AND METHODS

Patients diagnosed with uterine sarcoma between January 2001 and December 2010 were identified from the Gynaecology Oncology registry and retrospectively studied. There were altogether 37 cases identified. However only 35 case files could be retrieved and included in the study. For the two case files that could not be retrieved, details from the registry were used for the study. Patients who had defaulted follow-up were contacted and the latest status was ascertained. Three patients (expatriates) had returned to their countries for further treatment and were lost to follow up at various periods. Age, parity, race, risk factors (pelvic irradiation and hormone use), menopausal status, presenting symptoms, staging, treatment and follow-up status were analysed.

RESULTS

Among the 37 patients with uterine sarcoma, eight were in the first five years of the study period and the remaining in the second part (Figure 1).

Thirty-four patients (91.9%) were Bruneians. The age of the study population ranged from 29 to 80 years with a mean of 47.8 years. The demographic of patients are shown in Table 1. None of the patients had any of the established risk factors. Six patients had histories of fibroid for more than

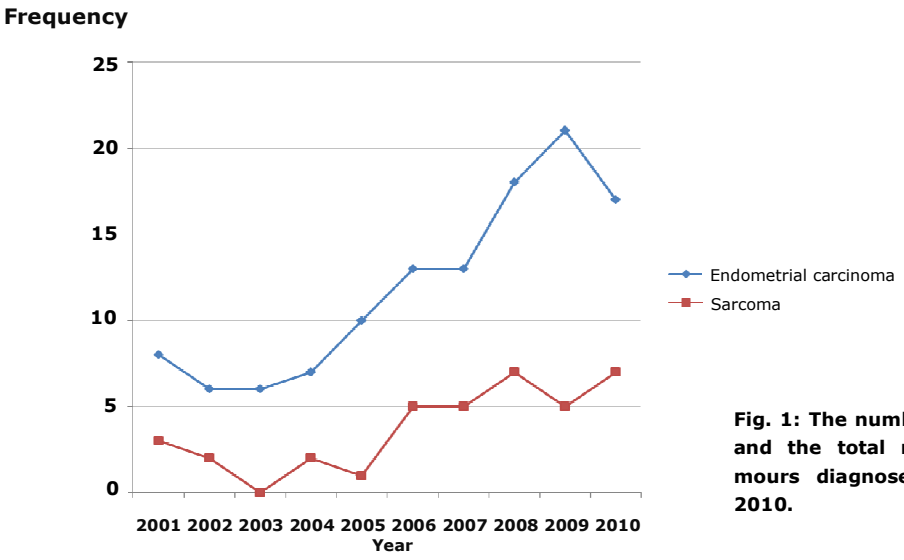

Fig. 1: The number of uterine sarcomas and the total number of uterine tumours diagnosed between 2001 and 2010.

one year, one patient had a history of breast cancer, one had a family history of colorectal cancer and one was of advanced age. Hypertension and diabetes were the most common comorbid conditions. The majority were multiparous and premenopausal.

Table 1: Demographic details of patients.

Age groups	**n (%)**
20-29	1 (2.7)
30-39	4 (10.8)
40-49	21 (25.8)
50-59	6 (16.2)
60-69	4 (10.8)
70-79	0 (0)
>80	1 (2.7)
Ethnicity	
Malay	30 (88.2)
Chinese	4 (10.8)
Others *	3 (8.8)
Comorbid conditions	
Hypertension	14 (37.8)
Diabetes mellitus	8 (21.6)
Overweight	6 (16.2)
Parity	
Nulliparous	7 (18.9)
Parity 2 to 4	23 (62.2)
Parity 5 or more	7 (18.9)
Menopausal status	
Pre	29 (78.4)
Post	8 (21.6)

* Comprise of a Nepalese, an Indian and an African patient.

Leiomyosarcoma was the most common sarcoma comprising of 54.1% (n=20) of all the uterine sarcomas. Of these 20 patients, 13 were categorised as low grade and seven as high grade. Of the eight patients with endometrial stromal sarcoma, four patients each were categorised as low and high grade respectively. One patient with endometrial stromal sarcoma also had concomitant squamous cell carcinoma of the cervix. MMMT/carcino-sarcomas and adenosarcoma were diagnosed in eight patients and one patient respectively.

The average ages of the various subtypes of uterine sarcomas were 42.9 years for leiomyosarcoma, 46.6 years for endometrial stromal sarcoma and 60.8 years for MMMT/carcinosarcoma. The only patient with adenosarcoma was 63 years old.

The most common symptoms at presentation were abnormal uterine bleeding and abdominal mass (Table 2).

The majority (70.3%) of the disease

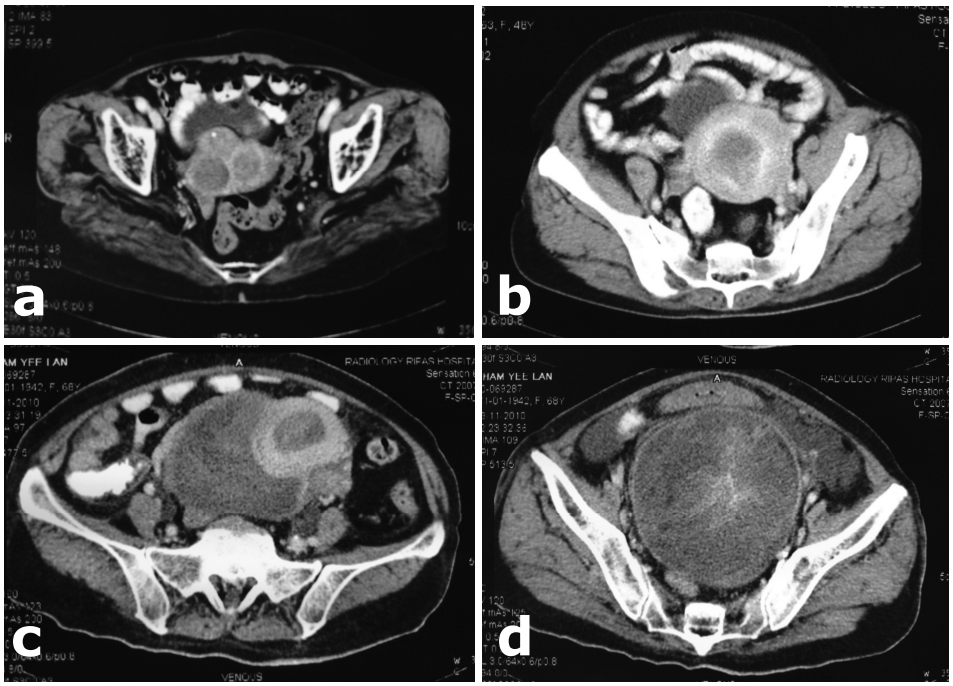

Fig. 2: Axial computed tomography (CT) images showing uterine sarcomas of various sizes; a) small sarcoma that resembled uterine fibroids, b) sarcoma with hydrometria, c) sarcoma of moderate size and, d) a large uterine sarcoma.

was categorised as Stage I. Stage II, III and IV disease accounted for 5.4%, 10.8% and 13.5% respectively.

Overall, 35 patients underwent surgery. Twenty-one were treated with surgery only and 14 subsequently received adjuvant treatment. Six patients with high grade tumour were not given adjuvant treatment despite having indications. The reasons included old age, patient's refusal and co-morbidities. One patient received chemotherapy as the only treatment whilst one patient with advanced disease received only palliative care.

Table 2: Clinical presentations of patients.

Pelvic mass	26 (70.3%)
Abnormal uterine bleeding	25 (67.6%)
Pain	4 (10.8%)
Pressure or mass symptoms	3 (8.1%)
Vagina discharge	1 (2.7%)

For complete breakdown, please refer to supplementary text.

During this study, 62.5% of patients diagnosed in the first five years (2001 to 2005) are alive and disease free. Two patients have died from the disease. In the second five years (2006 to 2010), 72.4% of patients (n=21/29) are alive and well. Four patients in this group died from the disease. Four patients were lost to follow up as they went abroad for treatment (n=2) or defaulted (n=2) and could not be contacted.

DISCUSSION

Uterine sarcomas are uncommon and account for between three and seven percent of all corpus or uterine cancers. In our study the proportion of uterine sarcoma was found to be much higher (23.7%) than any other previous reports.

The mean age at diagnosis among our patients was 42.9 years with differences seen between the various types of sarcomas. Generally our findings are similar to what has been reported in the literature. Patients with MMMT/carcinosarcoma were older. Patients with leiomyosarcoma are usually 10 years younger than those with endometrial stromal sarcomas and MMMT/carcinosarcoma. [7] Leiomyosarcoma is reported to occur more commonly in the 45 to 55 year age group. [2] Among our patients, 60% were in the 40 to 49 years age groups. For MMMT/carcinosarcoma, the mean age at diagnosis is 60 years. In our study, this was 60.8 years.

The majority of the risk factors in uterine sarcoma are similar to those reported for non sarcoma endometrial cancer. Pelvic radiation and exogenous oestrogen use also increase the risk of uterine sarcoma. Among our patients, there was no history of pelvic radiation or oestrogen use.

Abnormal bleeding and abdominal mass were the most common presentations. Among our patients, 70.3% and 67.7% presented with abdominal mass and abnormal uterine bleeding respectively. Pain or pressure symptoms were less common. Overall, all the reported symptoms are non-specific and are also reported among common benign pathologies such as a fibroid. Currently, there are no screening tests to diagnose uterine sarcoma. Furthermore a firm diagnosis is only possible if there is a mass, usually a polypoidal or endometrial involvement to biopsy during hysteroscopy. Without a biopsy, it is difficult to differentiate based on radiological imaging and symptoms between early uterine sarcoma and fibroids. In such instances, cases which resemble fibroids on imaging would usually have been treated as fibroid with GnRH analogue or uterine artery embolisation and this could result in delayed diagnosis of uterine sarcoma, typically leiomyosarcoma. None of our patients were treated as fibroid. Therefore, it is important to always consider the diagnosis of a uterine sarcoma in patients with uterine mass.

Recently a new staging system has been introduced for uterine sarcoma by the international federation of gynaecology and obstetrics (FIGO). [8] Prior to this, there was no specific staging system for uterine sarcoma. Most including our study followed the staging system for uterine sarcoma to stage endometrial carcinoma. In our study, the majority were categorised as early with 70.3% having Stage I disease. Stage III and IV disease accounted 10.8% and 13.5% respectively. Early manifestations with uterine bleeding probably accounted for the large proportion diagnosed with Stage I disease.

Surgery remains the mainstay of treatment with total abdominal hysterectomy with bilateral salpingo-oophorectomies. Other approaches include radiation and chemotherapy. Most authors believe adjuvant pelvic radiation improves pelvic tumour control and there are some reports suggesting survival benefit in early stages. In our study 35 (94.6%) patients had surgery as the initial treatment and 37.8% received adjuvant treatment. Tumour histology, stage, grade and patients' performance status were important factors for deciding additional therapy. Overall 70.3% of our patients were alive at the time of study. This was dependent on the stage of the disease.

Most studies report the worst outcome for high grade leiomyosarcoma. Six of our seven patients with high grade tumours were categorised as Stage I and all are alive and well. Seventy-five percent of the patients with high grade endometrial sarcoma are alive and disease free at the time of writing. In contrast, only 37.5% of patients with carcinosarcoma are still alive. The overall five-year survival of carcinosarcoma is approximately 50% even for Stage I disease. [10] Six (75%) patients with carcinosarcoma our study had stage III or IV disease. Carcinosarcoma was the diagnosis in five out of the six (83.3%) patients who died. One patient with dual cancers died from the disease. Patients who died all had Stage III/IV disease and died within a year of diagnosis. The mortality were 50% and 80% respectively for stage III and IV tumours. There were no mortality in stage I or II disease or any of those with LMS, ESS and adenosarcoma. The stage of disease at diagnosis was the most important prognostic factor in our study.

In conclusion, we have shown that uterine sarcoma is not uncommon among our population accounting for almost a quarter of uterine tumours. Further research is required to find the reason for the high incidence of uterine sarcoma in this study population.

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