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The Outcomes of Uterine Sarcoma: A Case-series of 5-Years Survey

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ABSTRACT

Uterine sarcomas (US) are relatively rare malignant tumor of the uterine mesenchymal tumor. The present study evaluated the outcomes of patients with different types of uterine sarcoma in Iranian women during a 5-years survey. During 2014-2019, a case series of twenty-three patients of US (four cases of leiomyosarcoma (LMS), nine cases of endometrial stromal sarcoma (ESS), seven cases of carcinosarcoma (CS), and three cases of adenosarcoma (AS)) were studied. One case of AS needed adjuvant radiotherapy and a recurrence was occurred in this case four years later. Two cases of CS have died during study period. All of ESS cases were alive by the study duration. One case who did not receive radio/chemotherapy experienced a bronchial recurrence after 8-years of ESS diagnosis Immunohistochemistry test on tumoral cells of three patients for vimentin+Ki67, BCL2+CD64+Ki67, ER+PR+WT1+Ki67 expressions were 30%, 30%, 15% respectively. Two cases of CS died during the study period. Even with multimodalities of treatment, the prognosis of uterine sarcoma is still poor and early diagnosis seems to improve the prognosis of the patients.

Keywords: Adenosarcoma, Carcinosarcoma, Endometrial stromal sarcoma, Leiomyosarcoma, Outcome, Uterine

Introduction

Uterine sarcomas (US) are relatively rare malignant tumor of uterine mesenchymal origin, representing 1% of gynecologic malignancies and 3–7% of all malignant uterine tumors **(1, 2)**. The prognosis of uterine sarcoma is worse compared with common endometrial cancer, and its clinical behavior tends to be more aggressive with early lymphovascular spreading **(3, 4)**; which are associated with a 5-year survival rate of less than 30% for women with advanced disease **(5)**. Uterine sarcoma classifications have traditionally included leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and carcinosarcoma (CS) **(5)**.

Leiomyosarcoma (LMS) is highly malignant with an adverse prognosis, and even in stage I, its 5-year survival rate is approximately 50% **(6)**. The prognosis for uterine LMS is poor, with 5-year overall survival rates in uterine LMS around 19–65% in all stages, and 52–85% in women with stage I–II disease **(7)**.

Carcinosarcoma (CS) is the most common type of uterine sarcoma (8.2 cases per million), typically followed by leiomyosarcoma (LMS) (6.4 cases per million) and endometrial stromal sarcoma (ESS) (1.8 cases per million) **(3)**. Five-year overall survival rate in uterine carcinosarcoma is around 6–38% in all stages, and 44–74% in women with stage I–II disease **(7)**. These tumors are characterized by dense uniform stromal cells with a low mitotic index and without significant atypia **(8)**. The uterine ESS showed relatively better survival than CS and LMS, and 5-year overall survival rate in uterine ESS was around 50–65% in all stages, and 89% in women with stage I–II disease **(9)**.

Clinical presentation patterns of uterine sarcomas differ for the histologic subtypes, such as enlarged uterine size or abdominal pain in LMS or ESS and abnormal uterine bleeding in pre- or postmenopausal women in carcinosarcoma or ESS **(10)**.

Adenosarcomas (AS) of the uterus are rare and seen far less frequently than other more common uterine sarcomas which are composed of benign, but occasionally atypical glandular epithelium, in combination with a malignant mesenchymal component **(11)**. Despite the fact that adenosarcomas are typically considered low-grade tumors, recurrences have been reported in up to 30–40% of patients while 20–25% of women ultimately die from their tumors **(11)**.

The present study evaluated the outcomes of patients with different types of uterine sarcoma in Iranian women during a 5-year survey.

Case Report

A case series of Twenty-three consecutive patients with uterine sarcomas who referred to Bahman hospital, Tehran, Iran during 2014-2019 were studied. The mean age of the cases was 51.69 years (range: 28-84 years). There were nine cases of ESS, three cases of AS, seven cases of CS, and four cases of LMS. The descriptions of patients in each group are presented below.

Cases of AS

Three cases were detected for adenosarcoma; only one of them needed radiotherapy and chemotherapy. This case showed a recurrence 4-years after the termination of therapies. This patient has a familial history of breast cancer (her aunt). The clinical characteristics of these cases are listed in Table 1.

Cases of CS

Seven cases of CS were studied. Two patients with stages IVB and IA had familial history of cancer in their sister (liver cirrhosis and hepatocellur carcinoma) and aunt (colon cancer), respectively. The clinical characteristics of CS cases are presented in Table 2.

Cases of ESS

Nine cases were diagnosed with ESS all of which were alive by the end of the study duration. The mean age of these cases was 45.77 years. Cytology examination was negative for malignant cells in all ESS cases. Adjuvant radiotherapy and/or chemotherapy was done for five cases. One case who did not receive radio/chemotherapy experienced a bronchial recurrence after 3-years of ESS diagnosis. Immunohistochemistry test on tumoral cells in three patients was positive for following markers expressions: vimentin+Ki67 (30%), BCL2+CD64+Ki67 (30%), and ER+PR+WT1+Ki67 (15%), respectively. In one patient with FIGO stage IIA, ovarian, paramaterial and lymphovascular invasions were seen. In another patient with high grade ESS, myometrium and uterine-cervical stroma and vascular invasions were present. Both of these patients with tumoral invasion received adjuvant radio/ chemotherapy.

Cases of LMS

There were four detected cases of LMS during study time; two of them died. The clinical characteristics of LMS cases are listed in Table 3.

Table 1. The clinical characteristics of adenosarcoma patients

variable	Case 1	Case 2	Case 3
Age	28	46	68
Past Medical History	Single Regular menses	1 Cesarean section 2 Induced Abortion	5 NVD[8] 2 Induced Abortion DM[9]
Chief Complaint	Abdomino-Pelvic mass History of hysteroscopy x2 & Laparotomy	Cervical mass Severe vaginal bleeding CA-125: 20.7 U/mL Colposcopy	PM[10] bleeding CA-125: 20.7 U/mL ET[11] :19.8 mm
Radiology*	Loculation with multiple septation around ovaries Changed intramural signal in left lateral of servical canal Left ovarian hemorrhagic luteal cyst	A relatively hypo-echo focus in the cervical canal with cystic changes without blood vessels (32*15 mm)	-
Operation	Date: 2/23/2015 TAH[4]+BSO[5] LND[6] Removal of huge sarcoma tumor Omentectomy	Date: 2/16/2019 TAH+RSO[7]	Date: 5/30/2016 TAH+BSO LND Omentectomy
Cytology	Neg.	-	Neg.
FIGO[1] staging	IIA	IA	IA
Tumor size	7*10*7 cm	3.5*2*2 cm	4*3*0.5 cm

variable	Case 1	Case 2	Case 3
Surrounding tissues involvement	Myometrium into serosa Peritubal soft tissue and muscular layer of the left fallopian tube Left ovarian surface and parenchyma Vascular invasion	Stromal invasion up to 12 mm	No invasion to surrounding tissues was identified.
Adjuvant RT[2] and ChT[3]	End: 9/19/2015	No needed	No needed
Outcome	Recurrence in Pelvic, Nov/ 2019	Alive in good condition	Alive in good condition

Table 2. The clinical characteristics of carcinosarcoma patients

variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age	84	62	66	47	65	64	67
PMH[1]	4 NVD HTN[2]	3 NVD 2 Abortion Menopause: 15 yrs. ago	4 NVD Hypophysis and renal surgery Menopause: 14 yrs. ago	1 C/S[6] Divorced Psoriasis Breast cancer Uterine surgery: uterine mass 66*48 mm Menopause: 6 yrs. ago	1 NVD Uterine surgery: Intramural myomas: 47*44 & 36*25 mm Menopause: 15 yrs. ago	2 NVD Smoker 40 yrs Menopause: 14 yrs. Ago Psychosis Hypothyr.	3 C/S Nullipara HTN
Chief Complaint	Pap smear: Suspicious for endometrial AC[3]	Pelvic mass CA-125: 353 U/mL	HTN DM	Severe PM bleeding HE4: 71 pmol/L CA-125: 34 U/mL ROMA: 26%	PM bleeding	Tumoral mass expulsion	Spotting CA-125: 172 U/mL
Radiology	Uterine dimension larger than normal (92*56 mm) containing hetero-echo lesion with unclear border	-	-	Hypoeco-heterogeneous mass with hypovascular blood vessels (66*48 mm) coated by an endometrial layer	Larger uterus than normal (122*74 mm) with heterogen. echo. A hypo-eco mass in the middle of the fundus with internal cystic areas (75*70 mm) with irregular borders. Intermoral and submucosal diffuse myomas	-	Larger (114*99 mm) and thicker (39 mm) uterus than normal A large mass in endometr. cavity

variable	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Operation	Date: 11/14/2016 TAH+BSO Omen.[4]	Date: 6/9/2018 TAH+BSO Omen. LND	Date: 3/11/2019 TAH + BSO Omen. LND	Date: 11/24/2018 TAH+BSO Omen. LND	Date: 0/13/2018 TAH+BSO Omen. LND	Date: 5/18/2018 TAH+BSO Omen. LND	Date: 8/30/2019 TAH+BSO Omen. LND
Cytology	Neg.	Degenerated atypical cell	Undifferentiated carcinoma with focal serous differentiation	Heterologous elements (malignant osteoid)	Few atypical/ suspicious malignant cells	Neg.	Neg.
FIGO staging	IA	IVB	IVB	IA	IIIB	IB	IIIA
Tumor size	4*4*3 cm	6*6.5*3 cm	4.5*3*1 cm	10*7*4 cm	9*5*3 cm 3*1*1 cm	3.5*2*0.6 cm	10*7*3.5 cm
Pathology	CS (MMMT[5]) Papillary serous type	CS (MMMT) Papillary serous type	CS (MMMT)	CS (MMMT)	CS (MMMT) Endocervix: malig. tumor Endometrium: malignant epithelioid tumor Papillary serous type	CS (MMMT) EIC[7]	CS (MMMT) Carcinomatous component: High grade serous carcinoma Sarcomatous components: Epithelioid LMS
Surrounding tissues involvement	Myometrium (<50% of its thickness)	Bilateral ovary and omentum Lymphovas. invasion	Myometrium (<50% of its thickness) Lower uterine segment Cervix stroma Omentum Lymphovascular invasion	Myometrium (<50% of its thickness) Sarcomatous component: LMS Epithelial component: serous carcinoma	Myometrium (superficially) Right parametrium	Myometrium (deep)	Myometrium (full thickness) Uterine serosa Lower uterine segment Cervical stroma
Adjuvant RT and ChT	-	4 courses End: 5/2018	External RT & Brachy. + ChT.	-	Adjuvant ChT. and RT	-	Adjuvant ChT. and RT
Outcome	Alive following up	Death	Alive following up	Alive following up	Alive in good condition	Death	Alive following up

1: Past medical history; 2: Hypertension; 3: Adenocarcinoma; 4: Omentectomy; 5: Malignant Mixed Mullerian Tumor; 6: Cesarean section; 7: Endometrial intraepithelial carcinoma

Table 3. The clinical characteristics of leiomyosarcoma patients

variable	Case 1	Case 2	Case 3	Case 4
Age	40	48	52	40
PMH	2 C/S LMP[1]: 3 yrs. ago	3 NVD	2 NVD 1 C/S HTN DM	1 C/S Myomectomy 5 yrs. ago
Chief Complaint	Malig. mesenchymal tumor	Cancer recurrence Known case of LMS	AUB[4] Cervical mass	AUB HE4: 53 pmol/L

variable	Case 1	Case 2	Case 3	Case 4
	(LMS) in biopsy examination	1st laparos. myomectomy then TAH 3 yrs ago		CA-125: 4.3 U/mL ROMA: 7.8%
Radiology	-	-	Endometrium is thick (27 mm) with 32 mm enhancing polypoid mass in the left side of fundus Uterus is large with multiple myomas (the largest is 10 mm)	Large retroverted uterus (91*54*58 mm) with hetero-echo submucosal (34*22 mm) and transmoral (25*21 mm) myomas in posterior wall multiple hypo-echo myomas in anterior wall (8-10 mm)
Operation	Date: 5/14/2016 EUA[2] Radical TAH + RSO Systematic LND	Date: 10/30/2016 Pelvic mass & small intestine mass resection of adnexa including fallopian tubes Optimal debulking Omentectomy	Date: 5/11/2019 TAH+BSO Omentectomy LND	Date: 1/5/2019 TAH+BSO Omentectomy LND
Cytology	Neg.	Neg.	Neg.	Neg.
FIGO[1] staging	IIB	IB	IB	IA
Tumor size	Greatest diameter: 14 cm	Pelvic: multiple tumoral creamy tissue fragments 15*15*7cm in aggregate vagina: 5*4*3 cm	14*10*8 cm Tumoral tissue fragments: 15*12*3 cm	4.6*2.5*1 cm two intramural myomas measuring 0.5cm and 0.7cm
Pathology	Malig., Adenosarcoma (LMS) Necrosis identified Mitotic rate: 40/10 HPFs[3]	LMS consistent with recurrence of tumor Extensive coagulative tumor cell necrosis Mitotic rate: 40/10 HPFs	Malignant spindle cell tumor (LMS): epithelioid type of uterus Polypoid adenomyoma of uterus	Leiomyosarcoma of myometrium, myxoid type, arising in leiomyoma Simple cyst 2.5cm on the surfaces of each ovary
Surrounding tissues involvement	uterine corpus and cervix vascular invasion one out of five lymph node perilymph node adipose tissue	Omentum: Extensive coagulative tumor cell necrosis	Myometrium (full thickness) Uterine serosa Lymphovascular invasion Omentum: Reactive mesothelial hyperplasia	Myometrium (deep)
Adjuvant RT and ChT	Adjuvant ChT. and RT	-	ChT. & RT , End of Adj. : 10/2/2019	-

variable	Case 1	Case 2	Case 3	Case 4
Outcome	Death	Death	Alive following up	Alive following up

Discussion

Compared to the more common types of endometrial cancer, women with uterine sarcomas have a poor prognosis due to the aggressive nature of this tumor **(4, 12)** The most frequent prognostic factors in uterine sarcomas include tumor stage, histological subtype, grade, lymphovascular invasion and menopausal status **(4)**. As the results of the study of Putikul *et al.* show **(13)**, abnormal uterine bleeding was the most common presenting symptom in the present cases.

According to the results of a study by Arend *et al.*, patients with AS turned to be younger and were more likely to have early-stage tumors and patients with AS were 65% less likely to die from their tumors than women with CS **(11)**. In the present study, the mean ages for AS and CS patients were 47.33 and 67 years, respectively. Two cases of AS were in IA stage and one of them was in IIA stage; while 4 cases of CS were in III and IV stages. All three cases of AS were alive by the study duration and two CS patients died in this period. Also, patients with carcinosarcoma have been reported that are more likely to receive adjuvant radiotherapy **(11)**. In the present cases one out of three AS patients needed adjuvant radiotherapy; while 4 out of seven cases of CS received this therapy. Surgery followed by adjuvant radiotherapy with or without chemotherapy in CS cases has been significantly associated with improved overall survival **(14)**. Three out of four CS cases who received these therapies were alive by the end of the study duration.

The LMSs are rare but aggressive tumors with poor clinical outcomes regardless of stage **(15)**. Two-cases out of four LMS patients had IB stage in this study; which was in accordance with some other studies **(16, 17)**. Two LMS patients received adjuvant radiotherapy and chemotherapy; one of them, with IIB stage, died during the study. It has been claimed that adjuvant radiotherapy may provide a survival benefit for uterine carcinosarcoma, but not leiomyosarcoma **(18)**. In the studied cases, 3 out of four CS cases who received this therapy were alive at the study termination; but one of two cases of LMS undergone adjuvant radiotherapy died. On the other hand, mitotic count >10-15/HPF has been associated with poorer prognosis in patients with LMS and mitotic count was defined as the most significant predictor of overall survival in uterine sarcomas **(19-21)**. Both LMS patients studied in the present study, had mitotic count 40/10 HPF.

Histological subtypes of LMS and CS (MMMT) have been associated with a poorer overall survival than ESS **(12)**. Two out of four LMS cases and two out of seven CS patients in this study died before study termination; however, all nine ESS cases were alive at that time. Extra-uterine spread were associated with poorer outcome in uterine sarcomas **(22)**. Lymphovascular invasion was the most common extra-uterine tissues involvement in patients with poor outcome in the present cases.

Comparing histological types of uterine sarcomas, ESS are related with better survival (4). All the nine cases of ESS in the present study were alive till the end of the study.

Conclusion

Advanced age and higher FIGO staging were observed to have poorer outcomes in patients with different histological types of uterine sarcomas. So, an early diagnosis seemed to improve the prognosis of the patients. This study is limited by small sample size and further studies with larger sample size could improve the findings.

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Ethical Permission

This study is with patient permission publish her medical data. The identity of the patient was confidential and not disclosed in the study.

Conflict of Interest

The authors declared no conflict of interest regarding the publication of this article.

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