

doi: 10.3978/j.issn.2095-6959.2021.01.006
View this article at: <http://dx.doi.org/10.3978/j.issn.2095-6959.2021.01.006>

15 例子宫肉瘤的临床分析

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[摘要] 目的: 对子宫肉瘤(uterine sarcomas, US)不同病理类型的临床资料进行分析。方法: 收集2016年5月至2019年4月中国科学技术大学附属第一医院妇科收治的US患者15例, 对其临床表现、年龄、绝经时间、术前实验室、影像学检查、手术及术后随访情况进行回顾性分析。结果: 1)子宫平滑肌肉瘤(leiomyosarcoma, LMS)患者年龄(56.38 ± 10.24)岁, 包块(91.75 ± 52.37) mm, 糖类抗原125(carbohydrate antigen 125, CA125) (31.9 ± 21.81) U/mL, 乳酸脱氢酶(lactate dehydrogenase, LDH) (222.68 ± 146.58) U/L, 术后2人予以放射与化学药物治疗结合, 4人行化学药物治疗, 在随访过程中3人出现转移。2)子宫内膜间质肉瘤(endometrial stromal sarcoma, ESS)患者年龄(58.4 ± 13.35)岁, 包块直径(92.6 ± 23.11) mm, CA125 (25 ± 13.04) U/mL, LDH (237.6 ± 78.72) U/L, 术后1人予以放射与化学药物治疗结合, 1人行化学药物治疗, 随访均存活。3)子宫腺肉瘤(adenosarcoma, AS)患者平均年龄42岁, 包块直径75 mm, CA125 39.63 U/mL, LDH 163 U/L, 术后均行化学药物治疗, 在随访过程中1人死亡。结论: US患者多以盆腔包块及阴道流血就诊, LDH>199 U/L及盆腔包块直径 ≥ 8 cm, 包块快速增长可作为鉴别指标。手术中淋巴结清扫对患者是否有益尚不明确, 术前评估淋巴结有无转移值得研究。US虽好发于围绝经期和绝经女性, 但对于盆腔包块伴阴道流血年轻女性, 需考虑子宫腺肉瘤的可能性, 避免延误病情。

[关键词] 子宫; 肉瘤; 放射治疗; 化学药物治疗; 淋巴结

Clinical analysis of 15 cases of uterine sarcoma

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Abstract **Objective:** To analyze the clinical data of different pathological types of uterine sarcoma. **Methods:** From May 2016 to April 2019, 15 patients with uterine sarcoma were treated in the Gynecology Department of the First Affiliated Hospital of University of Science and Technology of China. Clinical features, age, menopausal time, preoperative laboratory, imaging examination, operation and postoperative follow-up were analyzed retrospectively. **Results:** 1) The average age of uterine leiomyosarcoma patients was (56.38 ± 10.24) years old; the size of the mass was (91.75 ± 52.37) mm, carbohydrate antigen 125 (CA125) (31.9 ± 21.81) U/mL, lactate dehydrogenase (LDH) (222.68 ± 146.58) U/L. After surgery, 2 patients received chemoradiotherapy; 4 received

收稿日期 (Date of reception): 2020-01-13

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基金项目 (Foundation item): 安徽省自然科学基金青年基金 (1808085QH274)。This work was supported by Anhui Provincial Natural Science Foundation Youth Fund, China (1808085QH274).

chemotherapy; and metastasis occurred in 3 patients during follow-up. 2) The average age of patients with endometrial stromal sarcoma was (58.40 ± 13.35) years old; the size of the mass was (92.60 ± 23.11) mm, CA125 (25.00 ± 13.04) U/mL, LDH (237.60 ± 78.72) U/L. One patient received chemotherapy and radiotherapy, and one patient received chemotherapy. All patients survived during follow-up. 3) The average age of uterine adenosarcoma patients was 42 years old; the mass size was 75 mm, CA125 39.63 U/mL, and LDH 163 U/L. All patients received chemotherapy after surgery. One patient died during follow-up. **Conclusion:** Patients with uterine sarcoma are mostly treated with pelvic mass and vaginal bleeding. LDH >199 U/L and pelvic mass ≥ 8 cm in diameter, the rapid growth of mass can be used as distinguishing indicators. It is unclear whether lymph node dissection has benefited patients during surgery, and it is worth studying whether the lymph node metastasis is evaluated before surgery. Although uterine sarcoma occurs in perimenopausal and menopausal women, for young women with pelvic mass and vaginal bleeding, the possibility of uterine adenosarcoma should be considered to avoid worsening the patient condition.

Keywords uterine; sarcoma; radiotherapy; chemotherapy; lymph nodes

子宫肉瘤(uterine sarcomas, US)占子宫恶性肿瘤的3%~7%，恶性程度较高，易复发及远处转移，预后不佳^[1]。据2015年国际妇产科协会(Federation International of Gynecology and Obstetrics, FIGO)分期^[2]，US分为子宫平滑肌肉瘤(leiomyosarcoma, LMS)、子宫内膜间质肉瘤(endometrial stromal sarcoma, ESS)及腺肉瘤(adenosarcoma, AS)3种，癌肉瘤现已划归为子宫内膜癌的未分化型。US疾病罕见，恶性度高，无特异性肿瘤标志物；多数患者无特异性体征，临床表现常为阴道流血、腹痛、盆腔包块及其压迫症状^[3]，影像学表现易与子宫平滑肌瘤等良性疾病混淆，术前诊断困难。现就中国科学技术大学附属第一医院2016年5月至2019年4月收治的15例US患者的临床资料进行分析、总结。

1 对象与方法

1.1 对象

US患者15例，年龄15~79(55.13 ± 15.39)岁；

绝经患者9例，绝经时间最长30年；患者临床多表现为盆腔包块、尿频、阴道不规则流血或大量流血(表1)。术后病理诊断根据FIGO 2015年分期，LMS 8例，ESS 5例，AS 2例。

1.2 方法

15例患者术前均行B超检查，术前清晨空腹留取血液5 mL送糖类抗原125(carbohydrate antigen 125, CA125)、乳酸脱氢酶(lactate dehydrogenase, LDH)检查。所有患者行手术治疗，5例行经腹全子宫+双侧附件切除，3例行腹腔镜下全子宫+双侧附件切除，1例行经腹全子宫+双侧附件+大网膜+阑尾切除+腹膜后淋巴结清扫，2例系宫腔镜术后补充手术，2例系诊刮病理明确后补充手术，1例系外院肌瘤术后补充手术，1例系经腹全子宫+双侧输卵管术后补充切除卵巢。随访患者术后放射治疗(以下简称放疗)、化学药物治疗(以下简称化疗)及存活情况。

表1 子宫肉瘤患者基本情况及临床表现

Table 1 Basic conditions and clinical manifestations of uterine sarcoma patients

类别	n	年龄/岁			临床症状				绝经时间/年		
		<40	40~50	>50	盆腔包块	尿频	不规则流血	大量流血	未绝经	<10	≥10
LMS	8	0	3	5	4	1	4	0	3	0	5
ESS	5	0	2	3	1	0	3	1	2	1	2
AS	2	1	0	1	0	0	0	2	1	0	1

1.3 实验室阳性指标判断标准

CA125参考值范围为(0~35) U/mL, >35 U/mL为阳性; LDH参考值范围为(90~180) U/L, >180 U/L为阳性。

2 结果

2.1 US的CA125, LDH及包块大小情况

所有US患者CA125水平为(30.63 ± 17.99) U/mL, LDH水平为(219.69 ± 115.85) U/L, CA125阳性率为33.33%(5/15), LDH阳性率为60.00%(9/15), 包块直径为(89.93 ± 39.91) mm。按不同病理类型分组得到的US患者CA125, LDH及包块大小分布和均值

见表2~3。

2.2 US的超声检查结果

1例患者系外院行肌瘤挖除术后补充手术, 术前B超无法提供; 余14例患者术前均行B超检查(表4)。

2.3 治疗方案及随访

15例患者, 诊断Ia期3例、Ib期9例、Ic期1例、IIa期1例、IVb期1例(表5)。

3例术后追加放、化疗, 8例术后追加化疗。随访至投稿, 3例有远处转移, 1例死亡, 余患者随访尚无复发(表6)。

表2 子宫肉瘤患者CA125、LDH及包块大小的分布

Table 2 Grouping of CA125, LDH and mass size in patients with uterine sarcoma

类别	n	CA125/(U·L ⁻¹)		LDH/(U·L ⁻¹)		包块大小/cm		
		≤35	>35	≤180	>180	<5	5~10	>10
LMS	8	5	3	4	4	2	3	3
ESS	5	4	1	1	4	0	4	1
AS	2	1	1	1	1	0	2	0

表3 子宫肉瘤患者CA125、LDH及包块大小的均值

Table 3 Mean values of CA125, LDH and mass size in patients with uterine sarcoma

类别	年龄/岁	CA125/(U·L ⁻¹)	LDH/(U·L ⁻¹)	包块大小/cm
LMS	56.38 ± 10.24	31.9 ± 21.81	222.68 ± 146.58	91.75 ± 52.37
	40~68	12.36~60.52	115~560	35~177
ESS	58.4 ± 13.35	25 ± 13.04	237.6 ± 78.72	92.6 ± 23.11
	46~79	4.66~40.16	152~355	76~133
AS	42	39.63	163	75
	15~69	29.86~49.4	115~211	60~90

表4 子宫肉瘤患者B超检查描述情况分析

Table 4 Analysis of B-ultrasound description on uterine sarcoma patients

类别	血流分布		包膜		位置			包块内部	
	条状	丰富	清	不清	浆膜下	肌壁间	黏膜下	低回声	不均质
LMS*	4	3	6	1	3	3	1	3	4
ESS	3	2	2	3	0	5	0	2	3
AS	1	1	1	1	0	1	1	0	2

*1例患者系外院行肌瘤挖除术后补充手术, 术前B超无法提供。

*One patient came to our hospital for supplementary surgery after myomectomy in other hospitals, and B-ultrasound could not be provided before surgery.

表5 肉瘤患者临床分期(FIGO, 2015)

Table 5 Clinical staging of sarcoma patients (FIGO, 2015)

类别	I			II		III			IV	
	Ia	Ib	Ic	IIa	IIb	IIIa	IIIb	IIIc	IVa	IVb
LMS	3	3		1	0	0	0	0	0	1
ESS	0	5		0	0	0	0	0	0	0
AS	0	1	1	0	0	0	0	0	0	0

表6 15例子宫肉瘤治疗及随访情况

Table 6 15 cases of uterine sarcoma treatment and follow-up

类别	患者	分期	第1次手术	第2次手术	术后治疗	随访
ESS	1	Ib	经腹全子宫+双附件切除		IFO**+紫杉醇化疗6次	存活
	2	Ib	经腹全子宫+双附件切除			存活
	3	Ib	经腹全子宫+双附件切除		同步放、化疗2次	存活
	4	Ib	腹腔镜下全子宫+双附件			存活
	5	Ib	经腹全子宫+双输卵管	腹腔镜下双卵巢		存活
LMS	6	IVb	经腹全子宫+双附件切除		放疗1次, IA**方案化疗5次	多发转移
	7	Ia	宫腔镜活检	经腹全子宫+附件		存活
	8	Ib	诊刮	经腹全子宫+附件	IAP**方案化疗1次	存活
	9	Ib	子宫肌瘤挖除	经腹全子宫+双附件	IAP化疗4次	多发转移
	10	Ib	经腹全子宫+双附件切除		放疗1次, IA方案化疗3次后发现转移, 改为安罗替尼维持治疗	肺部转移
	11	Ia	腹腔镜下全子宫+双附件切除			存活
	12	IIa	经腹全子宫+双附件+大网膜+ 阑尾切除+腹膜后淋巴结清扫		IAP化疗2次, 艾恒+泽菲化疗3次	存活
	13	Ia	腹腔镜下全子宫+双附件切除		IAP化疗5次	存活
	14	Ic	诊刮	腹腔镜下全子宫+ 双附件	泽菲+多西他赛化疗2次	存活
	15	Ib	宫腔镜下宫腔占位切除	经腹全子宫+ 双输卵管	泽菲+多西他赛化疗5次	死亡

**I:异环磷酰胺; A: 阿霉素; P: 铂类药物。

**I: ifosfamide, IFO; A: adriamycin; P: platinum drugs.

3 讨论

US作为一种易复发及转移的间质肿瘤, 5年生存率为15%~40%^[4], 最常见的病理类型为LMS, 其次是ESS及AS^[5]; 临幊上最常见症状为异常阴道流血, 其次是腹部包块、腹痛等不适。对于US, 目前尚无特异性的肿瘤标志物。较多学者^[6]

认为LDH在US诊断上具有一定价值, 本研究发现: LDH的肉瘤诊断阳性率为60.00%(9/15), LDH水平为(219.69 ± 115.85) U/L, 与文献[7]报道的LDH值>199 U/L时应高度怀疑US结果相符。CA125临幊主要用于间皮细胞及苗勒管衍生物病变的诊断及监测, 本组病例的CA125阳性率为33.33%(5/15), CA125水平为(30.63 ± 17.99) U/mL,

未提示有明显预测价值。

术前影像学检查方面，B超因其无创、简单易行，能较准确地提示子宫内膜及肌层的病变，是首选的辅助检查方式^[8]。文献[9-10]提示：子宫肿瘤直径大(≥ 8 cm)、快速增长是US的独立危险因素。本研究对肿瘤的大小、位置、包膜、血流及回声情况进行分析，包块直径为(89.93±39.91) mm，与文献相符。其余观察指标是否存在临床价值需扩大样本分析。磁共振成像(MRI)在软组织成像方面有独特的优势，已广泛应用于US的术前诊断，但当肌瘤存在变性时，两者鉴别仍较困难^[11]，且LMS，ESS，AS的MRI特征存在重叠^[12]，使用MRI鉴别子宫肿瘤仍需进一步研究。

对于所有类型的US，治疗方式均首选手术；早期ESS及AS的手术方式首选全子宫+双侧附件切除^[13-14]。对于LMS切除子宫时是否切除附件仍存在争议。在FIGO分期中，淋巴结转移情况虽明确被纳入IIIC期判断标准，目前关于淋巴结清扫仍有异议。文献[15]指出：早期LMS淋巴结转移率仅为5%~11%，清扫淋巴结未必使LMS患者获益。在本组LMS患者术后转移的3例中，2例为Ib期，其中1例为子宫肌瘤术后补充手术，手术方式均为经腹全子宫+双侧附件切除；术后予以正规化疗，随访至13个月与6个月时分别出现肝、肺、脑、骨与肺部转移。两例早期(Ib)患者，术后短时间出现广泛转移现象，是否淋巴结术前已有转移，分期是否正确尚不得知；腹膜后淋巴清扫分期对LMS患者是否有益需多中心大样本的观察和随访，必要时术前可行PET/CT检查了解淋巴结情况。放化疗作为有效的术后辅助治疗^[16-18]，可根据术后病理分期或随访结果使用，常用的化疗药物包括异环磷酰胺、阿霉素、铂类、吉西他滨及紫杉醇等。

本组患者中最小年龄仅15岁，术后病理诊断为AS。在年龄方面，US虽好发于围绝经期和绝经期女性，但近年来有数篇年轻女性AS的报道^[19-20]，临床表现常为频繁阴道流血伴盆腔包块；对于该类患者临幊上应予以重视，必要时可行处女膜切开后诊刮或宫腔镜检查，不应因患者无性生活史，无法检查而耽误病情。

综上，US临床表现不典型，尚无特异性肿瘤标志物，临幊上常与子宫肌瘤混淆，存在术式选择不当、增加复发、转移风险。临幊上子宫肌瘤患者如术前LDH>199 U/L或盆腔包块直径 ≥ 8 cm，包块快速增长需考虑肉瘤的可能性。手术中淋巴结清扫对患者是否有益尚不明确，术前评估淋巴结有无转移值得研究。US虽好发于围绝经期和绝经

女性，但对于盆腔包块伴阴道流血的年轻女性，需考虑子宫腺肉瘤，避免延误病情。US临床少见，本组患者的随访时间尚未满5年，需进一步扩大样本、延长随访时间，以获得高级别循证医学证据。

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本文引用: 蒋来. 15例子宫肉瘤的临床分析[J]. 临床与病理杂志, 2021, 41(1): 39-44. doi: 10.3978/j.issn.2095-6959.2021.01.006

Cite this article as: JIANG Lai. Clinical analysis of 15 cases of uterine sarcoma[J]. Journal of Clinical and Pathological Research, 2021, 41(1): 39-44. doi: 10.3978/j.issn.2095-6959.2021.01.006