VIA MEDICA

ORIGINAL PAPER / OBSTETRICS

Ginekologia Polska
2024, vol. 95, no. 6, 451–459

ISSN 0017–0011, e-ISSN 2543–6767

DOI 10.5603/gpl.96919

Clinicopathologic characteristics, treatment, prognosis and pregnancy outcomes in rhabdomyosarcoma of the uterine cervix: a case series

Xiuzhang Yu[1, 2], Mingrong Qie[1, 2], Liyan Huang[3], Minmin Hou[1, 2]

[1]Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Chengdu, China
[2]Key Laboratory of Birth Defects and Related Diseases of Women and Children (Sichuan University), Ministry of Education, Chengdu, China
[3]Department of Pathology, West China Second University Hospital, Sichuan University, Chengdu, China

ABSTRACT

Objectives: In this retrospective observational study, cases from our institution were included and the published literature reviewed to investigate the diagnosis and prognosis of cervical rhabdomyosarcoma, a rare group of tumours.

Material and methods: The clinicopathological data of 12 patients with cervical rhabdomyosarcoma (RMS) treated at the West China Second University Hospital of Sichuan University from January 2006 to May 2023 were collected, and their clinicopathological characteristics, diagnoses, treatments, prognoses and pregnancy outcomes were retrospectively analysed.

Results: (1) Clinical characteristics: The ages of the 12 RMS patients ranged from 15 to 50 years, with a median age of 17 years. Five of the patients were adults, and seven were adolescents. The initial symptoms were vaginal bleeding in 5 patients, vaginal tissue prolapse in 6 patients, and abdominal pain and urinary frequency in 1 patient. Two patients were considered to have "cervical polyps" and underwent polypectomy at the other hospitals, but the cervical mass recurred soon thereafter. (2) Pathological features: The maximum tumour diameter ranged from 3 to 25 cm. The twelve cases of cervical RMS consisted of embryonal rhabdomyosarcoma (ERMS) in 7 adolescents, ERMS in 3 adults, and pleomorphic rhabdomyosarcoma (PRMS) in 2 adults. Immunohistochemical results showed the expression of one or more characteristic markers of RMS. We reclassified tumour stage according to the Intergroup Rhabdomyosarcoma Study (IRS) clinical group and tumour node metastasis (TNM) classification. (3) Treatment: Eight patients underwent radical surgery (66.7%, 8/12), including all 5 of the included adults and 3 of the adolescents, 2 of whom were treated 10 years ago. Conservative surgical resection was performed on four patients (33.3%, 4/12), all of whom were adolescents. Postoperative chemotherapy was given to all patients except one, but one patient who underwent radical surgery discontinued chemotherapy on her own without receiving a full course. Two of the ERMS patients underwent preoperative chemotherapy, and the lesions were significantly reduced. (4) Prognosis: One of the 12 patients with cervical RMS was lost to follow-up. Of the remaining 11 patients, 10 (including seven adolescents and three adults) survived tumour free (90.9%, 10/11), and 1 adult patient with existing pulmonary multiple metastases (IRS stage IV, T2N0M1) at the initial diagnosis survived 9 months with progression-free disease (9.1%, 1/11). The median survival time was 91 months (5 to 213 months). Among 4 patients receiving fertility-sparing management, 1 conceived and delivered successfully (25%).

Conclusions: The treatment of cervical RMS must take the patient's age and reproductive intent into account. The overall prognosis for cervical RMS in children and adolescents is good, and conservative surgical resection combined with chemotherapy is recommended to preserve fertility. The pregnancy outcome is also worth anticipating. For patients who have completed childbirth, radical surgery is preferred. Approaches to accurately assessing the patient's condition, grasping the indications and scope of surgery, and developing chemoradiotherapy regimens deserve further exploration.

Keywords: cervical sarcoma; rhabdomyosarcoma; fertility preservation; chemotherapy; prognosis

Ginekologia Polska 2024; 95, 6: 451–459

Corresponding author:
Minmin Hou
Department of Obstetrics and Gynecology, West China Second University Hospital, Sichuan University, Number 20, 3rd section, South Renmin Road, Chengdu, Sichuan 610041, China
e-mail: mminnh789@163.com

Received: 11.08.2023 Accepted: 23.11.2023 Early publication date: 20.12.2023

INTRODUCTION

Rhabdomyosarcoma (RMS) represents a rare group of tumours that are classified into four major subtypes according to the 2020 WHO Soft Tissue Tumour Classification: embryonal rhabdomyosarcoma (ERMS), alveolar rhabdomyosarcoma (ARMS), spindle cell/sclerosing rhabdomyosarcoma, and pleomorphic rhabdomyosarcoma (PRMS). Among these, ERMS is the most common type, usually occurring in the mucosa or near the mucosa of the head, orbit, or lower genitourinary tract. Only 0.5% of primary RMSs are located in the cervix, and they usually appear in the first two decades of life. Cervical RMS that appears in adults is even rarer [1]. Most of the current knowledge about RMS comes from case reports, clinical studies by the Intergroup Rhabdomyosarcoma Study Group (IRSG) and Children's Oncology Group (COG), and the consensus of the International Soft-Tissue Sarcoma Consortium (INSTRuCT) [2]. Clinical studies of female genital tract RMS are primarily in children; there is a lack of prospective studies of adult female genital tract RMS, and there are only a few reported cases of adult cervical RMS (fewer than 40 cases) [3]. The therapeutic regimen is based mainly on the experience of RMS at sites other than the cervix. Paediatric RMS appears to have a better prognosis than adult RMS [4]. We clinically analysed 12 patients with cervical RMS treated at the West China Second University Hospital of Sichuan University from January 2006 to May 2023, and we discuss the clinicopathologic features, treatments, prognoses and pregnancy outcomes of this disease in the context of the relevant literature, with the objective of improving the diagnosis and treatment experience of this disease.

MATERIAL AND METHODS

Patients with cervical RMS were treated at the West China Second University Hospital of Sichuan University from January 2006 to May 2023. The study was conducted following the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the West China Second University Hospital, and informed consent was obtained from all patients.

The inclusion criteria were as follows: 1) patients with a confirmed pathological diagnosis of cervical RMS; 2) patients with both pathological consultation records and clinical consultation records; and 3) patients diagnosed with cervical rhabdomyosarcoma that was not part of a biphasic tumour or germ cell tumour and with a pathology report confirming that the tumour did not originate elsewhere (*e.g.*, the uterus).

The general data, clinical manifestations, auxiliary examinations, pathological features, treatment modalities and prognoses of the patients were retrospectively analysed. Follow-up was also performed by telephone. The follow-up cut-off date was October 15, 2023. The follow-up period ranged from 5 to 213 months, with a median follow-up time of 91 months. One patient was lost to follow-up. The limitation and bias of this study is the small number of cases, but a large-scale study of this rare disease is not possible.

RESULTS

Clinical characteristics: The ages of the 12 patients with cervical RMS ranged from 15 to 50 years, with a median of 17 years (the youngest patient with female genital tract RMS at our hospital was two months old and was not included in this study because she did not receive clinical treatment). There were 7 adolescent patients and 5 adult patients. One patient had the "congenital pulmonary cyst", and two patients had the "thyroid cyst". Three patients had a family history of tumours. The initial symptoms were vaginal bleeding in 5 patients, vaginal tissue prolapse in 6 patients, and abdominal pain and urinary frequency in 1 patient. Two patients were considered to have "cervical polyps" and underwent polypectomy at other hospitals, but the cervical mass recurred soon thereafter (Tab. 1). Patients 4, 5, 6, and 7 underwent magnetic resonance imaging (MRI), and patients 2, 3, 8, 9, 10, 11, and 12 underwent computed tomography (CT). The results of the examinations were consistent with the B-ultrasonography findings, and there was no specificity. The lung CT of Patient 11 indicated multiple lung metastases.

Pathological characteristics: The lesions of the included patients were located at the cervix/cervical junction. The maximum tumour diameter ranged from 3 to 25 cm. We obtained the MR images of patient 6, as shown in Figure 1. The immunohistochemical findings revealed the expression of one or more characteristic markers of RMS, including vimentin (Vim), desmin, myoglobin (Mb), myogenin, and myogenic differentiation protein (MYOD), as shown in Table 2. Among the 12 patients with cervical RMS, all the adolescent patients had ERMS, one of whom had embryonal rhabdomyosarcoma (differentiated) with chondrogenesis and one of whom had ERMS with the focal area containing the adenoid rhabdomyosarcoma component. Three patients underwent genetic testing. The patient with ERMS combined with ARMS had no meaningful FOXO1 (FKHR) gene allele detected, and 2 patients with ERMS who underwent DICER1 genetic testing had a 50% mutation rate (1/2). The pathologic characteristics of patient 6, a 17-year-old patient with typical cervical ERMS, are shown in Figure 2. Three of the adult patients had ERMS, and two, aged 49 and 50 years, had PRMS. Details are shown in Table 2.

Treatment approaches: 1) of the 7 adolescent patients included in this study, 3 underwent radical surgery, two of whom were treated 10 years ago, and the other, whose

Table 1. Clinical features of 12 patients with cervical rhabdomyosarcoma (RMS)

No	Age [yr]	BMI [kg/m^2]	Parity (at first visit)	Age of menarche	History of surgery and previous illnesses	Family history of cancer	Initial symptom
1	17	Unknown	G0P0	13	None	None	Vaginal tissue prolapse
2	17	17.9	G0P0	13	Surgery for "pulmonary cyst"	None	Vaginal bleeding
3	17	21.9	G0P0	12	Excision of left ovarian cyst	None	Vaginal bleeding
4	17	20.5	G0P0	12	None	Head cancer (mother)	Vaginal tissue prolapse
5	16	20.6	G0P0	12	None	None	Vaginal tissue prolapse
6	15	19.3	G0P0	13	Thyroid mass ablation	None	Vaginal bleeding
7	16	22.2	G0P0	11	Thyroid mass ablation	None	Vaginal tissue prolapse
8	38	22.0	G2P1 + 1	16	Caesarean section	None	Vaginal tissue prolapse
9	48	21.1	G3P1 + 2	13	Cholecystectomy	Stomach cancer (father)	Vaginal bleeding[a]
10	46	23.8	G2P1 + 1	14	Caesarean section	Lung cancer (father)	Vaginal bleeding[a]
11	50	21.4	G2P2	16	None	None	Vaginal tissue prolapse
12	49	29.1	G3P2 + 1	19	Appendectomy	None	Abdominal pain and urinary frequency

[a]Two patients were considered to have "cervical polyps" and underwent polypectomy at other hospitals, but the cervical mass recurred soon thereafter; BMI — body mass index

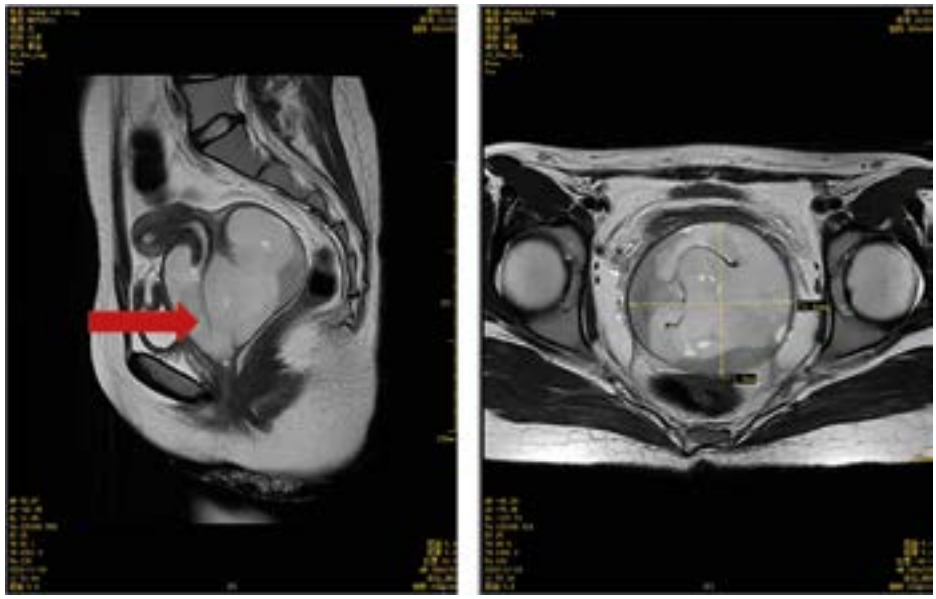

Figure 1. Magnetic resonance images of Patient 6: mixed signal mass in the external cervix and vagina

family requested radical surgery intraoperatively, was diagnosed with cervical malignancy tendency to sarcoma by frozen section during operation. The lesions were found to be significantly reduced in the two patients who were treated with neoadjuvant chemotherapy prior to radical surgery. Four patients underwent conservative surgery. Patient 1 refused radical surgery, and only a lesion biopsy and cervical biopsy were performed. Patients 4, 5 and 7 all underwent cervical mass excision/biopsy first, with postoperative pathology that was considered RMS, and then they accepted cervical conization at our institution. All of them underwent postoperative chemotherapy, but one patient discontinued chemotherapy on her own without receiving a full course (Tab. 3); 2) all five adult patients underwent radical surgery, four received chemotherapies, and one was lost to follow-up.

Prognosis: 1) all 7 adolescent patients were stage I according to the IRSG staging criteria and survived tumour free. The median survival time was 91 months (5 to 213 months). Among 4 patients receiving fertility-sparing management, 1 conceived and delivered successfully (25%). The remaining three patients did not become

Table 2. Pathological features of 12 patients with cervical rhabdomyosarcoma (RMS)

No	Tumour site	The longest tumour diameter [cm]	Immunohistochemistry					Pathological type	Genetic test
			Desmin	Myogenin	MyoD	Myoglobin	Others		
1	Cervix	Unknown	++	–	–	–	/	ERMS (botryoid)	–
2	Cervix	8	++	++	–	Focal+	/	ERMS	–
3	Cervix	9	+	++	+	++	/	ERMS (differentiated with chondrogenesis)	–
4	Cervix	3	Focal+	–	+	/	Vim(+)	ERMS	–
5	Cervix	6	+	+	/		CD56 (+), PCK (focal+)	ERMS + ARMS	No significant heterotopic FOXO1 (FKHR) gene was detected
6	Cervix	11	Focal+	Focal+	+	/	Vim (+), BRG –1 (+)	ERMS[a]	No DICER1 gene mutation was detected
7	Cervix	7.6	+	+	+	+	P53 wild –type expression, caldesmon (focal+), CD10 (+)	ERMS	DICER1 gene mutation was detected
8	Cervix	5.4	/	/	/	/	/	ERMS (botryoid)	–
9	Cervix	3	+	Focal+	+	Focal+	P53 wild-type expression, Vim (+)	ERMS (botryoid)	–
10	Cervix	4	+	Focal+	+	Focal+	P53 wild-type expression	ERMS	–
11	Cervical junction	5.8	+++	Focal+	–	Focal+	SMA (++), caldesmon (++), CD10 (focal+), ER (++)	PRMS (involved vagina)	–
12	Cervix	25	–	+	+	–	/	PRMS (metastasized to the lymph node and omentum)	–

[a]Intraoperative freezing pathology showed a malignant tumour with sarcomatous tendencies; PCK — pan cytokeratin; BRG — BRM/SWI2 related gene; SMA — smooth muscle actin; ERMS — embryonal rhabdomyosarcoma; ARMS — alveolar rhabdomyosarcoma; PRMS — pleomorphic rhabdomyosarcoma

pregnant because they had no immediate pregnancy plans rather than trying and failing to conceive; 2) of the 5 adult patients, 3 had stage I disease, and 2 patients had stage IV disease (all pathological types were PRMS). All patients with PRMS were staged later, as detailed in Table 3. One patient was lost to follow-up. Three patients survived tumour free, and 1 patient with existing pulmonary multiple metastases (IRS stage IV, T2N0M1) at the time of initial diagnosis survived 9 months (as of the follow-up date) with no tumour progression. The median survival time was 21.5 months (9 to 138 months).

DISCUSSION

Aetiology of cervical RMS

The aetiology of cervical RMS is currently unclear. Recent studies have found that RMS, especially ERMS, is more common in children with certain genetic syndromes [5]. These patients often have multiple primary cancers, and a possible correlation between ERMS, especially cervical ERMS, and DICER1 pathogenic variants has been found [6–8]. PAX-FOXO1 fusions are present in approximately 80% of ARMS, and missense mutations in MYOD1 are the most common molecular alterations in adult spindle cell/sclerosing RMS [5]. Of note, three of the cervical RMS patients had either "pneumocyst" or "goiter", and it is unclear whether this was multinodular goiter/pleuropneumoblastoma, which requires a high degree of caution for DICER1 syndrome. In this study, 3 adolescent patients underwent genetic testing, 1 patient with ERMS combined with ARMS had no meaningful FOXO1 (FKHR) gene allele detected, and 2 patients with ERMS who used to have "goiter" who underwent DICER1 genetic testing had a 50% mutation rate (1/2). The genetic susceptibility and molecular driving mechanisms of RMS warrant further investigation.

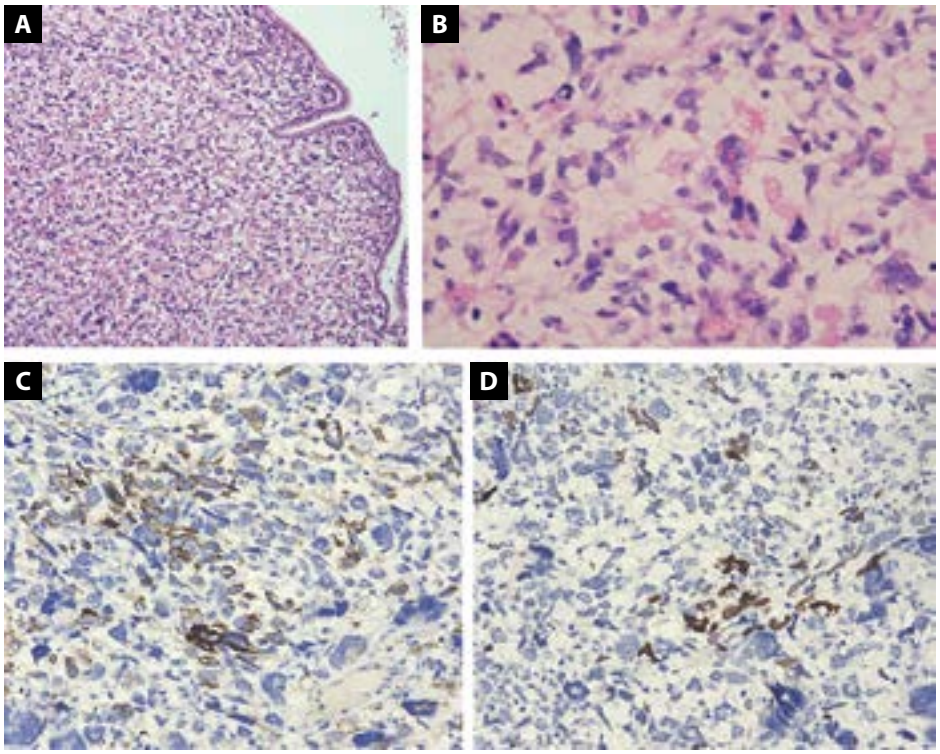

Figure 2. Pathologic characteristics of Patient 6; **A.** The tumour was growing in the cervical stroma (HE stain, ×100); **B.** The tumour cells were round or spindle-shaped, with oval nuclei, empty chromatin, insignificant nucleoli, and occasionally striated myoblasts (HE stain, ×400); **C.** Immunohistochemistry showed that the tumour cells were positive for desmin (×400); **D.** Immunohistochemistry showed the tumour cells to be positive for myoD1 (×400)

Clinical and pathological characteristics of cervical RMS

The median age at diagnosis of primary RMS of the cervix has been reported to be 13.5 years [2]. The median age of gynaecologic RMS in adult women is 32 years, and nearly one-third of patients are diagnosed after the age of 50 years [9]. The ages of the adolescent patients in this study were concentrated between 15 and 17 years, and the ages of the adult patients were between 38 and 50 years, which is generally consistent with previous reports. The clinical presentation of cervical RMS is mainly cervical masses or vaginal bleeding. This study is consistent with previous reports, and one of the patients even had vaginal bleeding leading to severe anaemia (Patient 6, HGB 34 g/L). Because many patients with cervical RMS are children and adolescents and are not sexually active, diagnosis and treatment may be delayed. One patient in this study presented with the initial symptom of abdominal pain and urinary frequency, mainly due to a large mass (25 cm) that partially protruded into the broad ligament and compressed the bladder and ureter. Typical ERMS lesions are nodular, papillary, polypoid, or grape-like masses, which may also grow infiltratively, involve surrounding tissues or metastasize distantly. Due to the relative rarity of cervical RMS, misdiagnosis occurs in up to a quarter of women [1], and cervical ERMS can easily be misdiagnosed as cervical polyps or leiomyosarcoma. In this study, 2 patients were considered for "cervical polyps" to undergo polypectomy in other hospitals, but their cervical mass quickly recurred. Pathologists must improve their understanding of this disease. Careful microscopic observation of RMS can reveal evidence of striated muscle differentiation, with cytoplasmic red staining and transverse fibres. Immunohistochemical staining of MSA, desmin, myoglobin, and myogenin can assist in the differential diagnosis. Microscopically, the tumour cells were round or spindle-shaped, with oval nuclei, empty chromatin, insignificant nucleoli, and occasionally striated myoblasts. Botryoid RMS is a subtype of ERMS characterized by a neoplastic layer that is visible microscopically beneath the intact epithelium [10]. PRMS microscopically shows pleomorphic cells with round, spindle, or polygonal tumour cells. ARMS tumour cells may form glandular vesicle-like or pseudoglandular-like structures and require FISH if necessary. Spindle cell/sclerotic RMS consists of fasciculated spindle cells and has been previously classified as a subtype of ERMS. ERMS is the most common form, occurring in children and adolescents; ARMS is the second most common, occurring mainly in adolescents aged 10–25 years; PRMS is less common, occurring in adults aged 45 years and older, but is highly aggressive; and spindle cell RMS is rare [11]. Most of the patients included in this study had ERMS, and only 2 adult women had PRMS, which is consistent with previous reports. Of note, one 16-year-old

Table 3. Diagnosis, treatment, prognosis and pregnancy outcomes of 12 patients with cervical rhabdomyosarcoma (RMS)

No	Stage (IRSG)	Stage (TNM)	Operative method	Chemotherapy regimen	Survival time [month]	Status at last follow-up	Delivery after treatment
1	I	TXN0M0	Conservative surgery (mass excision)	4 IEP (postoperation)	213	NED	G1P1 (17 years later)
2	I	T2N0M0	Radical surgery (MRH + PPLND + bilateral partial ovariectomy)	4 BEP (before operation); 6 BVP (postoperation)	183	NED	–
3	I	T2N0M0	Radical surgery (RH + PPLND)	2 BEP (before operation); 2 BEP (postoperation); then discontinued chemotherapy on her own	153	NED	–
4	I	T1N0M0	Conservative surgery (cervical conization)[a]	4 VIA (postoperation)	111	NED	No pregnancy plan
5	I	T2N0M0	Conservative surgery (cervical conization)[a]	1 VIA (post mass excision), 1 VIA and 3 vindesine/mycin/ifosfamide (post cervical conization)	91	NED	No pregnancy plan
6	I	T3N0M0	Radical surgery (RH + BS + PPLND)	6 VAC (postoperation)	10	NED	–
7	I	T2N0M0	Conservative surgery (cervical conization)[a]	2 VAC (post mass excision); 2 VAC (post cervical conization)	5	NED	No pregnancy plan
8	I	T2N0M0	Radical surgery (RH + BSO + PPLND)	6 VAC (postoperation)	138	NED	–
9	I	T1N0M0	Radical surgery (RH + BSO + PPLND)	4 VAC (postoperation)	27	NED	–
10	I	T1N0M0	Radical surgery (MRH + BSO + PPLND)	7 VAC (postoperation)	16	NED	–
11	IV[b]	T2N0M1	Radical surgery (TAH + BSO + vaginal partial excision)	4 epirubicin/etoposide/cisplatin (before operation), 3 epirubicin/ifosfamide and 1 ifosfamide (postoperation)	9	Survived without tumour progression	–
12	IV	T4N1M1	Radical surgery (MRH + BSO + PPLND + partial greater omentum excision)	No chemotherapy	Loss to follow-up	Lost to follow-up	–

[a]Cervical mass excision/biopsy was performed with/without chemotherapy before cervical conization; [b]The lung CT prior to initial treatment indicated multiple lung metastases
BEP — bleomycin, etoposide, cisplatin; BS — bilateral salpingectomy; BSO — bilateral salpingo-oophorectomy; BVP — bleomycin, vincristine, cisplatin; IEP — etoposide, cisplatin, ifosfamide; MRH — modified radical hysterectomy; NED — no evidence of disease; PPLND — pelvic/para-aortic lymph node dissection; RH — radical hysterectomy; TAH — total abdominal hysterectomy; VAC — vincristine, actinomycin-D, cyclophosphamide; VIA — vincristine, ifosfamide, actinomycin-D

female patient with ERMS was found to have focal areas containing ARMS components by microscopy, suggesting that multiple different types of RMS can coexist.

Treatment of cervical RMS

Previously, the main surgical approach was considered an extensive hysterectomy with pelvic and para-aortic lymph node dissection. However, patients with cervical RMS are very young, and the inability to have children or even normal development of female sexual characteristics after radical surgery causes great physical and psychological harm to patients. The scope of surgery has now evolved from extensive to limited, and conservative resection has provided adequate local control [2, 8, 12, 13]. The IRSG recommends low-intensity surgical resection combined with chemotherapy to treat uterine RMS [14]. INSTRuCT recommends chemotherapy alone in patients with complete response or organ-sparing surgery in combination with intracavitary brachytherapy (BT) or EBRT; fertility preservation should be considered in all children unless persistent tumours at the corpus uteri require treatment with hysterectomy [2]. Recent international data suggest that only 12% of patients with cervical tumours are treated with radical surgery, and the local control rate is 88% [2]. Surgery (*e.g.*, simple mass excision, polypectomy, cervical conization, radical cervical hysterectomy) to remove the primary tumour and some normal tissues around its periphery for a lesion-free margin should be performed and supplemented by chemotherapy. If complete resection is not possible with initial surgery, cystoscopy, colposcopy, rectal examination under general anaesthesia, and MRI of the abdominopelvic region, if necessary, may be performed

after 3 courses of induction chemotherapy. After 6 courses of treatment, patients need to be re-evaluated. In patients with signs of tumour, local control with excision or radiotherapy is attempted [2]. The specific surgical approach and extent of the procedure will depend on the patient's age, the size of the lesion, the type of tissue, and whether it infiltrates the surrounding organs. However, it should be noted that recurrence after conservative treatment is not uncommon, especially in patients who have not received postoperative chemotherapy or who have had inadequate cycles of chemotherapy [15]. However, most adults with genitourinary RMS have a late diagnosis, extensive lesions, and a high risk of metastasis; most have completed childbirth, in which case more aggressive multimodality therapy, such as radiation and chemotherapy combined with total hysterectomy and local lymph node dissection, is needed [16]. RMS is a chemosensitive tumour. Even in IRSG Group I (localized disease, completely excised, no microscopic residual tumour), postoperative chemotherapy is recommended. In Europe, the standard chemotherapy regimens for RMS are vincristine, ifosfamide, and actinomycin (VIA). The IRSG consensus is to recommend vincristine, actinomycin D, and cyclophosphamide (VAC) [17]. In the IRS-IV study, it was found that VAC, vincristine + ifosfamide + etoposide (VIE), and VIA offered no difference in effectiveness for patients with localized or regional rhabdomyosarcoma. There was no difference in patient outcomes [18]. US researchers chose VAC as the gold standard because cyclophosphamide is less costly and less nephrotoxic [3]. The intensity of chemotherapy was increased in four consecutive trials conducted at IRSG, with detailed protocols available from Arndt CA [19]. The most common toxic side effect was bone marrow suppression, followed by sepsis [18]. Local radiotherapy (brachytherapy) is recommended for patients with limited vaginal or cervical tumours with incomplete response after induction chemotherapy [2]. Experience in the treatment of adults with RMS is limited, and the choice of chemotherapy regimen is usually based on the results of paediatric studies [9]. In the IRS-V trial, the introduction of neoadjuvant chemotherapy was emphasized [4]. Two patients in this study underwent chemotherapy before radical surgery, and the apparent finding of lesion reduction provides additional indirect support for the clinical significance of neoadjuvant chemotherapy. The great variety of treatment regimens received by the patients included in this study was due to the wide age range of patients and the long time span of this study. These results fully reflect the changing philosophy regarding the treatment of cervical RMS during its historical evolution and the principle of individualized treatment. In terms of the choice of surgical modality, all adult patients in this study opted for radical surgery, while more than half of the adolescent patients opted for conservative surgery. In general, in the past, children and adolescents underwent mainly radical surgery, and in the last 10 years, conservative resection was the main operation. However, there are exceptions. For example, in patient 1, only lesion excision and cervical biopsy were performed, and the postoperative chemotherapy regimen was nonclassical and not a full course; however, the patient was followed up for 213 months without recurrence and successfully conceived and delivered spontaneously. In patient 6, the patient was biopsied and then underwent radical surgery, the underlying reasons being a consideration of cervical sarcoma from the intraoperative frozen section and the family members of this patient's subsequent concerns about the disease. This shows that clinicians should both improve their knowledge of cervical RMS to reduce missed diagnoses and misdiagnoses and fully recognize the good prognosis of cervical RMS with reasonable treatment to avoid excessive radical surgery. Adequate doctor–patient communication and description of the disease are also important.

Prognosis of cervical RMS

The National Cancer Database's 5-year overall survival rate for cervical RMS was 66.2% (including adults and children) [20]. The prognoses of children and adolescents and adult patients are different. In children and adolescents, the recently reported 10-year overall survival rate for vaginal and uterine RMS was 92%, and approximately half of the patients did not undergo radical surgery [2, 21]. Researchers in a multicentre study of adult RMS reported a 5-year overall survival rate of 78.2% and a progression-free survival rate of 58.2%, with no patients in the IRS I group dying of the disease [4]. The presence of residual lesions after initial surgery is the most important prognostic factor, and other factors associated with prognosis include disease stage, age, pathological subtype, regional lymph node involvement, whether distant metastases are present, and treatment modality [8, 12]. It is currently believed that polyp-like presentation, embryonal type, and superficial tumours are suitable for preserving reproductive function, and deep infiltrative disease and alveolar/pleomorphic RMS increase the risk of tumour recurrence [17]. The disease-free survival rate in this study was 91% (10/11), which is consistent with recent reports from other countries; patients who survived with tumours and those who were lost to follow-up were all patients with late-stage, adult, PRMS type. Our research shows a good overall prognosis for cervical RMS. Young age, pathological type of ERMS, and early TNM/IRS stage may be predictive of a good prognosis. PRMS is often diagnosed with metastasis, which indicates a poor prognosis.

Pregnancy outcomes of cervical RMS

As mentioned earlier, the current treatment philosophy for ERMS of the genital tract is to protect the patient's reproductive function as much as possible. Successful pregnancy and delivery are the primary goal of fertility-sparing treatment. However, there are fewer reports on pregnancy outcomes after treatment. Piątek S et al. reported a 22-year-old woman diagnosed with RMS of the cervix who had two successful deliveries without disease recurrence [22]. A recent systematic review found that of 35 enrolled patients with cervical ERMS, 3 had a successful pregnancy (3/35, 9%), and their pregnancy rates were lower than those of patients with other uterine sarcomas, such as low-grade endometrial stromal sarcoma (27/63, 43%), adenosarcoma (4/19, 21%), and smooth muscle tumour of uncertain malignant potential (29/84, 35%) [23]. The low pregnancy rates among patients with RMS may be caused by fertility impairment and multidrug chemotherapy, especially high doses of alkylating agents such as cyclophosphamide and ifosfamide [2, 22]. In our study, 4 patients received fertility-sparing treatment, and 1 successfully conceived and delivered (25%). The remaining three patients did not become pregnant because they had no immediate pregnancy plans rather than trying and failing to conceive. The birth rate was higher than that previously reported. This orients our focus towards future reports on the subsequent growth and pregnancy outcomes of other children and adolescents with genital tract RMS.

CONCLUSIONS

In summary, our findings suggest that the treatment of cervical RMS must take patient age and reproductive intent into account. ERMS is the most common subtype of cervical rhabdomyosarcoma in children and adolescent patients, while pleomorphic rhabdomyosarcoma is also common in adults, especially in postmenopausal women. Cervical rhabdomyosarcoma in adult patients, especially postmenopausal women, is often found in the advanced stage, and the prognosis is worse than that of young patients. Cervical rhabdomyosarcoma usually presents with vaginal bleeding and cervical swelling. This tumour occurs mostly in young women, and the families of patients often wish to see a preservation of fertility. In recent years, the treatment philosophy has changed from extensive surgical excision to conservative surgery combined with chemotherapy and radiotherapy for selected patients. The prognosis of this disease has improved significantly, and the pregnancy outcomes are worth anticipating. It is essential to emphasize the importance of chemotherapy in reducing recurrence. However, for patients who have completed childbirth, radical surgery is preferred. Further case reports and systematic evaluations are needed to provide valid data on how to accurately assess patients' conditions, grasp the indications and scope of surgery, and make decisions on chemoradiotherapy regimens.

Article information and declarations

Data availability statement

The clinical and pathological characteristics, treatment approaches and prognosis information will be shared if requested.

Ethics statement

The study was conducted following the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of the West China Second University Hospital and informed consent was taken from all the patients.

Author contributions

This manuscript has been read and approved by all authors. All authors contributed to the design of the research. Xiuzhang Yu: concerpt, study design, acquisition of data, analysis and interpretation of data, article draft; Mingrong Qie: analysis and interpretation of data, article draft; Liyan Huang: analysis and interpretation of data, revised article critically; Minmin Hou: concerpt, study design, revised article critically, corresponding author.

Funding

This work was supported by the Key Research and Development Program of Sichuan Province (2022YFS0076).

Conflict of interest

All authors declare no conflict of interest.

REFERENCES

1. Pop CF, Stanciu-Pop CM, Jungels C, et al. Uterine embryonal rhabdomyosarcoma in adult women: a case report on the challenging diagnosis and treatment. Rom J Morphol Embryol. 2023; 64(1): 83–88, doi: 10.47162/RJME.64.1.10, indexed in Pubmed: 37128795.
2. Lautz TB, Martelli H, Fuchs J, et al. INSTRuCT group. Local treatment of rhabdomyosarcoma of the female genital tract: Expert consensus from the Children's Oncology Group, the European Soft-Tissue Sarcoma Group, and the Cooperative Weichteilsarkom Studiengruppe. Pediatr Blood Cancer. 2023; 70(5): e28601, doi: 10.1002/pbc.28601, indexed in Pubmed: 32762004.
3. Jadhav T, Madakshira MG, Garud S. Embryonal rhabdomyosarcoma of the uterine cervix in an adult female. Autops Case Rep. 2023; 13: e2023419, doi: 10.4322/acr.2023.419, indexed in Pubmed: 36777814.
4. Ricciardi E, Plett H, Sangiorgio V, et al. Adult primary cervical rhabdomyosarcomas: A Multicentric cross-national case series. Int J Gynecol Cancer. 2020; 30(1): 21–28, doi: 10.1136/ijgc-2019-000821, indexed in Pubmed: 31780571.
5. Giannikopoulos P, Parham DM. Rhabdomyosarcoma: how advanced molecular methods are shaping the diagnostic and therapeutic paradigm. Pediatr Dev Pathol. 2021; 24(5): 395–404, doi: 10.1177/10935266211013621, indexed in Pubmed: 34107813.
6. Cowan M, Suntum T, Olivas AD, et al. Second primary rhabdomyosarcoma of the uterine cervix presenting with synchronous ovarian Sertoli-Leydig cell tumor: An illustrative case of DICER1 syndrome. Gynecol

Oncol Rep. 2018; 25: 94–97, doi: 10.1016/j.gore.2018.06.008, indexed in Pubmed: 30014022.
7. Apellaniz-Ruiz M, McCluggage WG, Foulkes WD. DICER1-associated embryonal rhabdomyosarcoma and adenosarcoma of the gynecologic tract: Pathology, molecular genetics, and indications for molecular testing. Genes Chromosomes Cancer. 2021; 60(3): 217–233, doi: 10.1002/gcc.22913, indexed in Pubmed: 33135284.
8. Devins KM, Young RH, Ghioni M, et al. Embryonal rhabdomyosarcoma of the uterine cervix: a clinicopathologic study of 94 cases emphasizing issues in differential diagnosis staging, and prognostic factors. Am J Surg Pathol. 2022; 46(11): 1477–1489, doi: 10.1097/PAS.0000000000001933, indexed in Pubmed: 35941719.
9. Elsebaie MAt, Elsayed Z. Is fertility-preservation safe for adult non-metastatic gynecologic rhabdomyosarcoma patients? Systematic review and pooled survival analysis of 137 patients. Arch Gynecol Obstet. 2018; 297(3): 559–572, doi: 10.1007/s00404-017-4591-6, indexed in Pubmed: 29159540.
10. Hermoza AD, de Macêdo Matsushita G, Dos Santos MH, et al. Botryoid embryonal rhabdomyosarcoma of the cervix: A case report. Int J Surg Case Rep. 2023; 102: 107858, doi: 10.1016/j.ijscr.2022.107858, indexed in Pubmed: 36621217.
11. Hollowood K, Fletcher CD. Rhabdomyosarcoma in adults. Semin Diagn Pathol. 1994; 11(1): 47–57, indexed in Pubmed: 8202646.
12. Nasioudis D, Alevizakos M, Chapman-Davis E, et al. Rhabdomyosarcoma of the lower female genital tract: an analysis of 144 cases. Arch Gynecol Obstet. 2017; 296(2): 327–334, doi: 10.1007/s00404-017-4438-1, indexed in Pubmed: 28634755.
13. Terwisscha van Scheltinga S, Rogers T, Smeulders N, et al. Developments in the surgical approach to staging and resection of rhabdomyosarcoma. Cancers (Basel). 2023; 15(2), doi: 10.3390/cancers15020449, indexed in Pubmed: 36672397.
14. Corpron CA, Andrassy RJ, Hays DM, et al. Conservative management of uterine pediatric rhabdomyosarcoma: a report from the Intergroup Rhabdomyosarcoma Study III and IV pilot. J Pediatr Surg. 1995; 30(7): 942–944, doi: 10.1016/0022-3468(95)90317-8, indexed in Pubmed: 7472949.
15. Imawan DK, Oesman WS, Yuseran H, et al. Recurrent cervical sarcoma botryoides in a 3-year-old female: approach in a limited resource setting. Am J Case Rep. 2019; 20: 838–843, doi: 10.12659/AJCR.915608, indexed in Pubmed: 31197128.
16. Pawlik J, Pawlik W, Branecka-Woźniak D, et al. Rhabdomyosarcoma of the cervix in a post-menopausal woman-an unparalleled phenomenon. Int J Environ Res Public Health. 2021; 18(15), doi: 10.3390/ijerph18157851, indexed in Pubmed: 34360144.
17. Buruiana FE, Gupta B, Singh K. Rhabdomyosarcoma of the cervix in teenagers — Is fertility preservation a feasible option? Gynecol Oncol Rep. 2020; 34: 100677, doi: 10.1016/j.gore.2020.100677, indexed in Pubmed: 33304979.
18. Crist WM, Anderson JR, Meza JL, et al. Intergroup rhabdomyosarcoma study-IV: results for patients with nonmetastatic disease. J Clin Oncol. 2001; 19(12): 3091–3102, doi: 10.1200/JCO.2001.19.12.3091, indexed in Pubmed: 11408506.
19. Arndt CS, Donaldson S, Anderson J, et al. What constitutes optimal therapy for patients with rhabdomyosarcoma of the female genital tract? Cancer. 2001; 91(12): 2454–2468, doi: 10.1002/1097-0142(20010615)91:12<2454::aid-cncr1281>3.0.co;2-c.
20. Albert A, Lee A, Allbright R, et al. Primary sarcoma of the cervix: an analysis of patient and tumor characteristics, treatment patterns, and outcomes. J Gynecol Oncol. 2020; 31(3): e25, doi: 10.3802/jgo.2020.31.e25, indexed in Pubmed: 31912680.
21. Minard-Colin V, Walterhouse D, Bisogno G, et al. International Society of Pediatric Oncology Sarcoma Committee, the Children's Oncology Group, the Italian Cooperative Soft Tissue Sarcoma Group, and the European pediatric Soft tissue sarcoma Study Group. Localized vaginal/uterine rhabdomyosarcoma-results of a pooled analysis from four international cooperative groups. Pediatr Blood Cancer. 2018; 65(9): e27096, doi: 10.1002/pbc.27096, indexed in Pubmed: 29781567.
22. Piątek S, Szymusik I, Dańska-Bidzińska A, et al. Fertility-sparing management may be considered in young women with uterine sarcoma. J Clin Med. 2022; 11(16), doi: 10.3390/jcm11164761, indexed in Pubmed: 36012998.
23. Dondi G, Porcu E, De Palma A, et al. Uterine preservation treatments in sarcomas: oncological problems and reproductive results: a systematic review. Cancers (Basel). 2021; 13(22), doi: 10.3390/cancers13225808, indexed in Pubmed: 34830960.