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Botryoid Rhabdomyosarcoma of the cervix: A systematic review of the literature from 1937 to 2017 - all registered cases

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Abstract

Purpose: Embryonal rhabdomyosarcoma of the cervix (RMS) is a rare malignancy and occurs mainly in the first two decades of life. Botryoid rhabdomyosarcoma is a subtype of embryonal rhabdomyosarcoma and is an aggressive malignancy that arises from embryonal rhabdomyoblasts. It is often found in the genital tract of infants and young children.

Study design: we conducted a systematic review to accumulate the available evidence in the international literature. We searched Medline (1966–2021), Scopus (2004–2021), Clinicaltrials.gov (2008–2021), EMBASE (1980–2021), Cochrane Central Register of Controlled Trials CENTRAL (1999–2021), and Google Scholar (2004–2021) for relevant observational studies and case reports.

Results: We retrieved 156 cases with a mean age of 24.4 years with the oldest patient at the age of 89 years and the youngest 67-day-old infant. Twenty-four patients died. Ninety-seven patients were free of disease (85%). Of those 11 (11.3%) patients died. Fifteen patients (15%) developed relapse and 13 (86.6%) of them died. In 42 cases we could not extract information concerning their survival.

Discussion: The findings of our study are mainly limited to case reports and small case series, and there are no standard treatment guidelines available and no consensus on how to manage these cases. Surgery should be guided by the response to initial chemotherapy and should attempt to conserve the function of the bladder, rectum, vagina, and ovaries. As this is a disease of adolescence, fertility preservation in well-selected cases is of paramount importance.

Key words: Botryoid, Rhabdomyosarcoma, Cervix

Introduction

Embryonal rhabdomyosarcoma (RMS) is one of the types of rhabdomyosarcomas. The other types are alveolar, pleomorphic, and spindle cell/sclerosing RMS.¹⁻⁵ The embryonal RMS is further subdivided into

sarcoma botryoides and anaplastic variants. *Sarcoma botryoides*, also known as botryoid rhabdomyosarcoma, is a rare subtype of a highly malignant tumor called embryonal rhabdomyosarcoma.

The name botryoides originates from the Greek root bótry(s), which refers to the appearance of “a bunch of grapes”. Specifically, *sarcoma botryoides* is a variant of embryonal rhabdomyosarcoma that is characterized by the presence of a round, grape-like mass in the affected organ.^{6,8,12} Although more than 100 nomenclatures exist for this tumor, the term ‘sarcoma botryoides’ was first used by Pfanzenstiel in 1892.

Sarcoma botryoides most usually affect young people, however, it can also afflict the elderly. It usually appears on the walls of hollow organs, such as the vaginal, bladder, biliary tract, and nasopharynx of infants. It also appears to affect the cervix and uterus in teenagers and adults.^{6,7}

Material and methods

We retrospectively reviewed all patients with cervical rhabdomyosarcoma who presented to the literature using sources from PubMed, ResearchGate, UpToDate, and Google Scholar from 1932 to 2017. We reviewed pathologic and clinical information such as tumor characteristics, staging, treatment, and survival in 156 cases reported in international literature.

1. Types of studies and patients

Eligibility criteria for the inclusion of studies were predetermined. Observational studies (prospective and retrospective), case reports and case series that reported the progression-free and/or overall survival rates of patients with botryoid rhabdomyosarcoma were selected for inclusion. Studies were included irrespective of the stage of disease at initial diagnosis, age of participants, and use of adjuvant therapy.

2. Information sources and search methods

Two authors (E.L. and M.N.) searched Medline (1966–2022), Scopus (2004–2022), Clinicaltrials.gov (2008–2022), EMBASE (1980–2022), Cochrane Central Register of Controlled Trials CENTRAL (1999–2022) and Google Scholar (2004–2022) along with the reference lists of electronically retrieved full-text papers. The date of the last search was set at February 15, 2022. The Rayyan web app was used for the screening process. The search strategy included the text words “cervical cancer; perineural invasion; overall survival, progression free survival” and is presented in brief in Appendix.

Studies were selected in three consecutive stages. Following deduplication, the titles and abstracts of all electronic articles were independently screened by two authors (V.P and I.B.) to assess their eligibility. The decision for inclusion of studies in the present meta-analysis was taken after retrieving and reviewing the full version of articles that were considered potentially eligible. Discrepancies that arose in this latter stage were resolved by consensus from all authors.

3. Statistical analysis

Statistical analysis was performed with the SPSS statistical software (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). The differences of continuous variables were assessed using the Mann-Whitney and Kruskal-Wallis test (due to the abnormal distribution that was observed during the evaluation of normality) whereas dichotomous variables were analyzed with the chi-square test. Fisher’s exact test was applied wherever the number of observations was lower than five in the case of dichotomous variables. The Kaplan-Meier method was carried out to perform survival-analyses and estimate intervals to recurrence. The level of significance for all analyses was set to $p < .05$.

Results

1. Incidence

Oevrall 156 cases were retrieved, which had a mean age of 24.4 years with the oldest patient at the age (Figure 1) of 89 years and the youngest 67-day-old infant. In Figure 2, we categorized the cases into age groups of 11 years and listed the number of cases recorded in each age group. As can be seen in the column chart, the peak incidence of cases is found in the 11-22 years age group where 48.7% of cases (76 cases) belong. It is also observed that <22 years of age belongs to 60.4%, which coincides with the literature that the peak incidence occurs below 22 years of age and mainly in the second half of adolescence.¹³

Age group	0-11	11-22	22-33	33-44	44-55	55-66	66-77	77-88	88-99
No of cases	18 (11.5%)	76 (48.7%)	19 (12.1%)	11 (7%)	16 (10.2%)	5 (3.2%)	2 (1.2%)	0 (0%)	1 (0.6%)

2.Tumor characteristics.

2.1.Tumor size

We observed that the mean tumor size was 5.92cm. Of the 156 cases, 90 had no information regarding the tumor size (NR:90), so the remaining 66 cases were studied. The largest size was found in a female 16 years old and was 20cm²⁸ and the smallest size was 1.8cm in a 2 years old infant.¹⁴

2.2. Nodal status

Concerning the nodal status, 130 cases without lymph node dispersion were identified (98.5%), while in 26 cases no information about lymph nodes was found so they were excluded from the statistical analysis. Finally, 2 cases of lymph node dispersion (1.5%) were found, one in a 58-year-old woman with a 15cm tumor size who underwent polypectomy initially followed by abdominal total hysterectomy after appendages and died in 5 months, with only

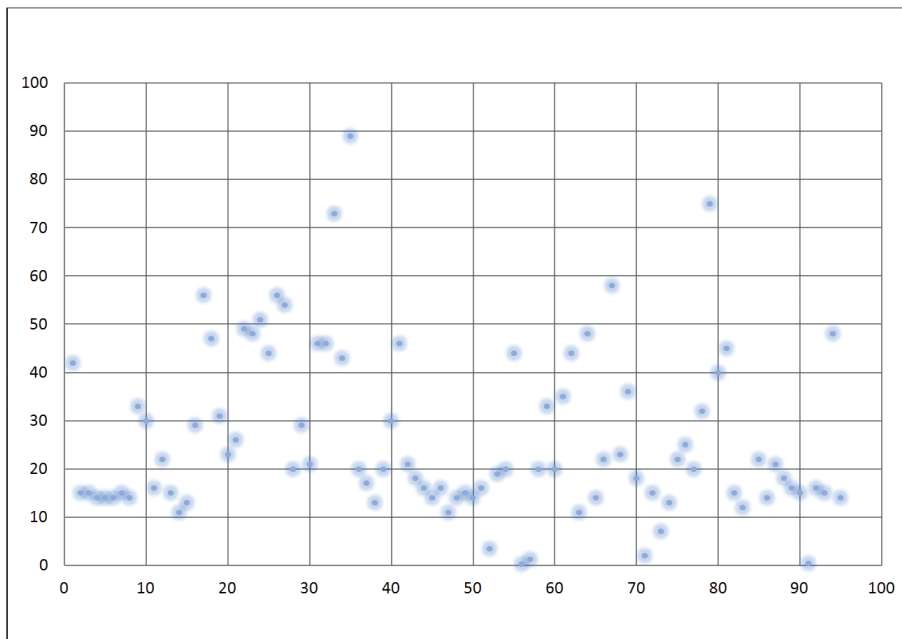


Figure 1. Scatter plot of cases by age of diagnosis. It is visually observed that the highest incidence of cases is in the second decade of life (vertical axis) where most cases are concentrated (horizontal axis).

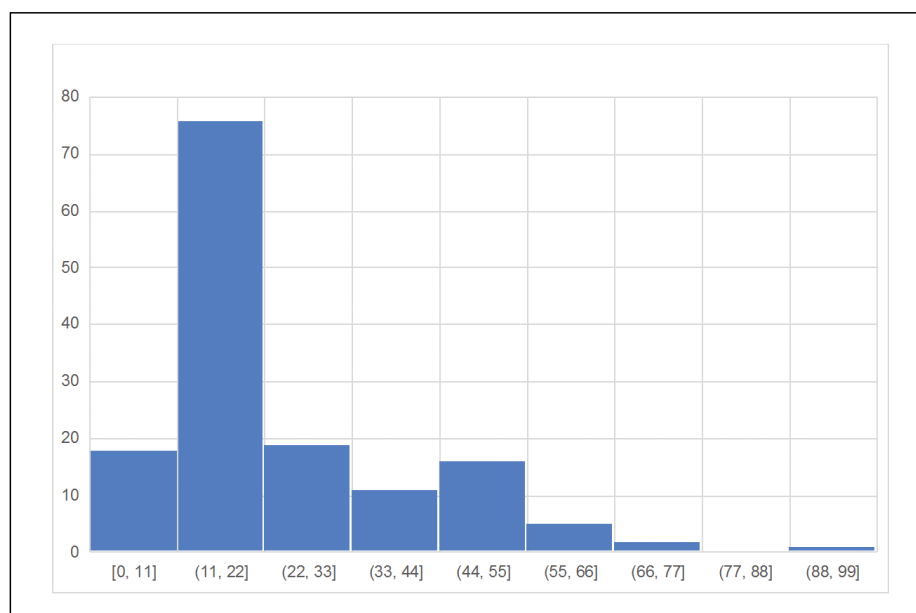


Figure 2. The horizontal line indicates the age groups the cases were divided into and the vertical line shows the number of cases falling into each age group.

one month of disease-free until recurrence where she received irradiation.²⁹ The second case involved a 21-year-old woman with unknown tumor size who had positive right external iliac lymph nodes, received adjuvant chemotherapy with VAC, doxorubicin, vinblastine and pelvic irradiation, and underwent radical hysterectomy and bilateral pelvic lymph node debulking. The patient died 4 months later.³⁰

2.3. Metastasis

Of the 156 cases, 136 did not have any sign of metastases during surgery, in 19 cases there were no relevant information from the published reports. In only one case we observed a reported metastasis to the lungs, bone, and brain. This was a 1.5-year-old child who received Vincristine, actinomycin D, cyclophosphamide, doxorubicin (12 months), and actinomycin D, cyclophosphamide, doxorubicin (10 months). This was alive after 8 years of follow-up, however, it did have a recurrence during the second

year of this period (relapse-free survival of 72+ months).³¹ The same study³¹ also reported a 17-year-old case with a 3cm N0 M0 tumor size who underwent TAH, BSO, and left iliac LND and also received external irradiation (5700 cGy through cobalt 60) and 2500 cGy irradiation and chlorambucil 8 mg/d due to spinal metastases. The overall survival of this case was 12 months and relapse-free was 2.5 months.

2.4. Tumor location

From the systematic review we performed, 135 cases (86.5%) were found in the cervix (endocervix, ectocervix, cervical lip, canal, cervical os). The remaining extracervical disease was detected in the uterus in 8 cases (5.1%) (in one case it also occupied the vaginal wall, exerting compression to the ureter and bladder³² and in two other cases it occupied the parametria^{33,34}). Also, in 11 cases there was a local extension, thus extending to the vaginal wall or/and vaginal fornix (7%) (with one of these cases also

showing vaginal nodules). Finally, two isolated cases were observed, one with bladder invasion³⁵ and the other in which the tumor was fixed to the sacrum.³⁰

3. Therapeutic approach and Treatment

3.1. Resectability

The review of the cases shows that of the 156 cases, 75 cases underwent hysterectomy (48%), 25 radical hysterectomy, 47 abdominal total hysterectomies, 2 vaginal hysterectomies, and 1 laparoscopic hysterectomy. Of these cases, bilateral salpingo-oophorectomy was performed in 33, bilateral pelvic lymph node lymphadenectomy in 39, and paraaortic lymphadenectomy in 14. More rarely omentectomy (4 cases), appendectomy (3 cases - 1 was accidental), and 4 ovarian transplantation was performed (1.5, 17, 20, 30 years old). More rarely, 4 cases underwent abdominal radical trachelectomy, in 3 cases anterior exenteration, and in 2 cases laparotomy and partial excision.

In local tumors confined to the cervix, polypectomy was performed (56 cases - 35.8%) of which 6 cases proceeded to hysterectomy in the second year. In 10 of these cases, curettage (endometrial/endocervical) was performed in parallel, while in 14 cases conization or loop excision was performed because the tumor was located in the cervical os or canal. Also in 15 cases, vaginectomy was performed because the tumor extended either to the vaginal wall or fornix. In addition, 18 cases underwent cervical wedge resection.

Finally, fewer cases either had no surgical intervention (2 cases) or only a biopsy was obtained (6 cases).

3.2. Radiotherapy

Radiotherapy is not a standard method of treatment for botryoid rhabdomyosarcoma of the cervix. Following review of the literature we found 8 cases that received pelvic irradiation as the sole treatment. Seven cases received adjuvant chemotherapy and irradiation, in 4 of those neoadjuvant and adjuvant

chemotherapy and irradiation was applied, whereas in 2 cases brachytherapy only was used.

3.3. Chemotherapy

First, we should mention that during the review of the literature 28 cases received no further treatment beyond surgical management and 3 deaths were recorded at 4, 6 and 12 months. It is important to mention that two of the previous cases presented with double primary malignancy, one was reoperated due to concurrent Sertoli Leydig cell tumor and the other received adjuvant chemotherapy because of endometrioid adenocarcinoma of the ovary. Also, in 17 cases there is no recorded information on further treatment.

An important part of the treatment of this malignancy is chemotherapy. It is recorded that 76 cases were given adjuvant chemotherapy alone (48.7%) with 51.3% of cases receiving VAC (Vincristine, Actinomycin D, Cyclophosphamide) of which 9 deaths were recorded. Of the remaining regimens, the second most common regimen was with vincristine and actinomycin D (10 cases). Also, the study reported 10 cases receiving neoadjuvant and adjuvant chemotherapy, 7 of them with VAC. In four chemotherapy regimens, the regimen was not reported.

4. Prognosis and Survival

Regarding the survival of patients with botryoid rhabdomyosarcoma of the cervix, of the 156 cases collected, 24 deaths (15.3%) were recorded; all but one death occurred during treatment after surgery. Of the total cases, survival greater than 5 years had 38 cases and less than 5 years 21 cases (with a mean survival of 12.92 months and minimum survival of 2 months) (Figure 3).

Ninety-seven patients were free of disease (85%). Of those 11 (11.3%) patients died. Fifteen patients (15%) developed relapse and 13 (86.6%) of them died. It is noted that 42 cases had an unknown

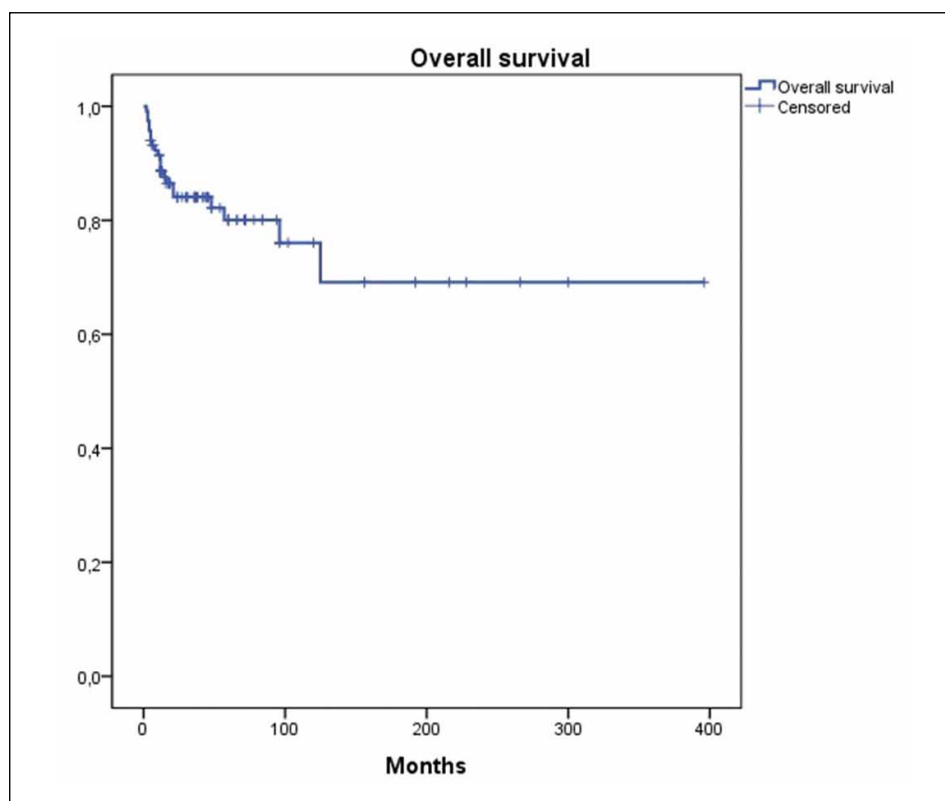


Figure 3. Visual representation of the survival analysis using the Kaplan-Meier curve.

disease-free period. From these, it can be concluded that 69.2% had a disease-free interval greater than 5 years, while 31.8% had less.

An important prognostic factor in botryoid rhabdomyosarcoma of the cervix is -the early disease stage at diagnosis-. In most of the patients 140 cases (89.7%), were diagnosed at stage IA (133 cases) and IB (7cases) according to the retrospective study. Patients with stage IA, i.e. tumor confined exclusively to the cervix and its complete exclusion survived 86.4% (115 cases) with only 18 recorded deaths.

Discussion

Sarcoma botryoides is a relatively rare malignancy that affects fewer than 4 children per million each

year. Despite its rarity, rhabdomyosarcoma is one of the most prevalent sarcomas in children, accounting for 4–6% of all cancer occurrences in children. The botryoides subtype of embryonal RMS is found under the mucosal surface of body orifices such as the vagina, bladder, and cervix, and accounts for around 10% of all RMS cases. Although sarcoma botryoides of the cervix has been documented in infants as young as five months old, it is more common in older people (i.e., children and young adults) than in vaginal sarcomas.^{9,10,11}

Due to the small number of cervical sarcoma botryoides cases documented in the literature, risk factors for the disease have remained unknown. Aging, a certain race (African-American women had double the incidence of white women), more than 5

years of tamoxifen use, and a history of radioactive exposure are all risk factors mentioned in several literature reviews. RMS has not been observed to be affected by parity, menarche age, or menopause.¹³ Chemical exposure, maternal age greater than 30 years, low socioeconomic position, and environmental factors all led to the development of RMS, according to one study.⁶²

The pathophysiologic pathways that lead to the formation of sarcoma botryoides remain unknown. The majority of children with sarcoma botryoides have no antecedent risk factors. Individuals with familial diseases that induce mutations in genes that control cell proliferation and death (such as Li-Fraumeni syndrome) are more likely to develop embryonal rhabdomyosarcoma and other malignancies. Although the majority of cervical RMS are sporadic, a small percentage have been linked to genetic diseases such as Li-Fraumeni cancer susceptibility syndrome, familial pleuropulmonary tumor, neurofibromatosis Type I, and Beckwith-Wiedemann syndrome.^{4,14,20-23} RMS has been linked to particular gene alterations, such as KRAS activation and p53 inactivation. Most embryonal rhabdomyosarcomas, in particular, have a point mutation in exon 6 of the p53 gene on chromosome 17. A heterozygous p53 germline mutation was revealed in a family as the source of the Li-Fraumeni cancer susceptibility syndrome, which manifests as a cluster of soft tissue cancers (including sarcomas). Dehner et al. also discovered a link between the blastoma family and pleuropulmonary tumors, as well as confirming DICER1 autosuggest, implying that RMS in children should be treated in a broader context to account for the possibility of pleuropulmonary blastoma familial tumor predisposition syndrome.^{8,14-16}

Mousavi and Akhavan⁸ revealed the occurrence of cervical sarcoma botryoides in two sisters, suggesting that hereditary factors may play a role in the development of sarcoma botryoides. Dehner et al.¹⁰

discovered a DICER1 germline mutation in a 9-year-old child who had cervical rhabdomyosarcoma and pleuropulmonary blastoma, suggesting a hereditary propensity to these cancers. Mutations in DICER1 have also been linked to familial pleuropulmonary blastoma syndrome. Three children with pleuropulmonary blastoma and Sertoli-Leydig tumors of the ovary were studied by Schultz et al.⁵⁹ Sertoli Leydig tumors were also found in three other family members of individuals with pleuropulmonary blastoma. The identification of a DICER1 mutation in this family condition is particularly interesting because this mutation is found in 60% of Sertoli-Leydig cancers.

The endoribonuclease enzyme Dicer is involved in microRNA biosynthesis and is encoded by the DICER1 gene, which is found on chromosome 14, location q32.13. Germline mutations in Dicer1 enhance the likelihood of developing rare cancers. Two of the 14 patients with cervical BRMS had pleuropulmonary blastoma, while another had ovarian Sertoli-Leydig cell tumor and thyroid nodular hyperplasia. A DICER1 mutation of the BRMS was found in one of them with cervical BRMS and pleuropulmonary blastomas. The DICER1 mutation could be the cause of extrauterine malignancies. The occurrence of BRMS in the cervix of two sisters in a family suggests that genetic factors may play a role in its development. Botryoid sarcoma has a better prognosis than other childhood RMSs, according to the International classification system. Malignant mixed Mullerian tumor, also known as carcinosarcoma, can grow exophytically from the uterine wall or cervix and have a sarcomatous gross and microscopic appearance; however, unlike ERMS, malignant mixed Mullerian tumor usually affects older people.^{17,18,19}

Finally, rhabdomyosarcoma has been linked to a number of hereditary illnesses, including Li-Fraumeni syndrome, neurofibromatosis type 1, Beckwith-Wiedemann syndrome, Costello syndrome, Noonan syndrome, and MEN2A syndrome.

Botryoid rhabdomyosarcoma of the cervix is a difficult diagnosis to make. Because of its rarity and high-risk malignant nature originating in the embryonic mesenchyme, which accounts for 4-6 percent of all cancers in children and young adults, clinical suspicion and early identification are required. Histopathology and post-surgery immunohistochemistry are used to diagnose sarcoma botryoides, while preoperative histopathology or intraoperative frozen section may be used in some situations.⁶³

Vaginal hemorrhage in children and irregular bleeding in adolescents and adults are the most common clinical presentations.^{7,8} The botryoid RMS appears when a tumor develops behind the mucosal membrane of the organs, forcing the growth to take on a typical grape-like form. Botryoid RMS is distinguished by a prominent cambium layer beneath the epithelium. The patient described here met all three of the necessary criteria for botryoid RMS (i.e. a polypoid appearance, an origin below a mucous membrane-covered surface, and the presence of a cambium layer).^{2,8}

A botryoid sarcoma might manifest itself clinically as abnormal vaginal bleeding, a vaginal mass prolapse, or an abdominal–pelvic mass. Abnormal vaginal discharge and bleeding, followed by uterine mass, abdominal discomfort, or pain, are some of the symptoms and indicators. Vaginal hemorrhage or discharge was evident in all individuals with early symptoms, and many had a tumor projecting from the vagina. Vaginal bleeding was the most common symptom, followed by leucorrhea and vaginal introitus mass. Similar findings were reported by other writers.^{4,5,20,25}

Clinicians must be aware of this unusual disease, particularly common places, as well as the aggressive nature and clinical implications of the tumor to avoid misdiagnosis and mismanagement. Because benign polyps in the vaginal or cervix are relatively uncommon in children, the authors advise that any polypoid mass discovered in a child should be assumed to be botryoid RMS unless proven otherwise.

Nuclear MRI is the gold standard for determining the tumor's origin (whether it's in the endometrium, myometrium, or cervix) as well as the spread and involvement of neighboring structures. In the face of the physical examination of the patient's cervical isthmus transition, a retrospective assessment of the pelvis MRI, performed with the surgical and postoperative pathological findings, was extremely significant for a better understanding of the surgical method.

Small, round cancer cells with hyperchromatic nuclei and large, polygonal-shaped cancer cells with rich eosinophilic cytoplasm, which typically exhibits diagnostic cross striations, have been found in embryonic rhabdomyosarcoma.

The importance of histology in RMS prognosis cannot be overstated. Although there are three types of RMS (embryonal, alveolar, and undifferentiated), the embryonal type is the more prevalent and has a better prognosis than the alveolar type, which is rare and has a worse prognosis.^{2,25} Embryonal RMS of the cervix must be distinguished pathologically from adenocarcinomas with heterologous elements, malignant mixed Müllerian favorable tumors, and low-grade stromal sarcomas because the best management strategies and clinical outcomes differ depending on the tumor site, deep myometrial invasion,² and lymphatic invasion. Cervical RMSs have a better prognosis than tumors in the female genital tract that develop in children.

(1) *Macroscopic Examination.* This tumor appears as a submucosal lesion with a characteristic “grape-like” appearance in female newborns and young children.

(2) *Microscopic Examination.* Botryoid rhabdomyosarcomas, also known as “sarcoma botryoides,” produced grape-like polypoid masses with a high level of subepithelial cellularity (the “cambium layer”) (Figure 4).

In newborns and adolescents, benign diseases

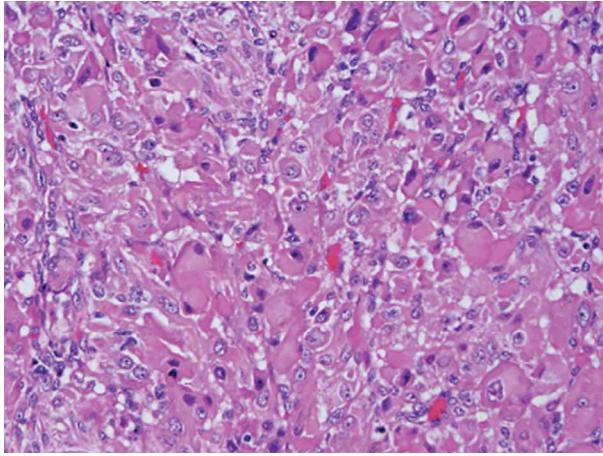


Figure 4. Botryoid rhabdomyosarcoma, organized into polypoid structures lined by squamous epithelium with underlying cellular aggregates.

including rhabdomyoma, pseudosarcoma botryoides (oedematous mesodermal cervical polyp), and malignancies like adenosarcoma and other small, round, bluetumors like neuroblastoma, rhabdomyosarcoma, non-lymphoma, Hodgkin’s and the Ewing’s family tumor.^{4,5,10}

The Intergroup Rhabdomyosarcoma Studies (IRS) classifies this cancer based on (i) the main site, (ii) tumor size, (iii) lymph node involvement, and (iv) surrounding tissue infiltration, and (v) the occurrence of metastases.²⁶

The stage was established using two systems: the Intergroup Rhabdomyosarcoma Study Group clinical categorization method (Table 1),⁵ and the TNM staging approach for rhabdomyosarcoma (Table 2).²⁰

The management of botryoid rhabdomyosarcoma represents a great challenge for gynecologists. In the past, these types of tumors were traditionally treated with exenterative procedures but today, fertility-sparing methods like polypectomy, conization, local excisions, and robot-assisted radical trachelectomy are the ones mostly implemented for the preservation of the reproductive ability.

Apart from the surgical resection of the tumor, multi-agent adjuvant chemotherapy with or without radiotherapy plays a crucial role in the effective treatment of sarcoma botryoides. Standardized schemes of chemotherapy can be used preoperatively to minimize the volume of the tumor or after surgical resection to limit the chance for recurrences. Chemotherapeutic combinations are based on protocols which are created by the Intergroup Rhabdomyosarcoma Study Group. The most common regimen of chemotherapy for children and young adults with the on-metastatic disease is the triplet of vincristine, actinomycin D, and cyclophosphamide (VAC), usually given in 6 to 12 cycles.⁵⁷

Table 1. Intergroup Rhabdomyosarcoma Study Group Clinical Classification System for Rhabdomyosarcoma.

CLINICAL GROUP	EXTENT OF DISEASE, RESECTABILITY, AND MARGIN STATUS
I	A: localized tumor, confined to site of origin, completely resected B: localized tumor, infiltrating beyond site of origin, completely resected
II	A: localized tumor, gross total resection, but with microscopic residual disease B: locally extensive tumor (spread to regional lymph nodes), completely resected
III	A: localized or locally extensive tumor, gross residual disease after biopsy only B: localized or locally extensive tumor, gross residual disease after major resection (≥ 50% debulking)
IV	Any size primary tumor, with or without regional lymph node involvement, with distant metastases, irrespective of surgical approach to primary tumor

Table 2. TNM Staging System for Rhabdomyosarcoma.

STAGE	SITES	T	TUMOR SIZE DESIGNATION	N	M
I	Orbit Head and neck* Genitourinary† Biliary tract	T1 or T2	a or b	Any N	M0
II	Bladder or prostate Extremity Cranial parameningeal Other‡	T1 or T2	a	N0 or Nx	M0
III	Bladder or prostate Extremity Cranial parameningeal Other‡	T1 or T2	a	N1	M0
IV	All	T1 or T2	a or b	N0 or N1	M1

T1, tumor confined to the anatomic site; T2, tumor extension; a, ≤ 5 cm in diameter; b, > 5 cm in diameter; N0, nodes not clinically involved; N1, nodes clinically involved; Nx, the clinical status of nodes unknown; M0, no distant metastases; M1, distant metastases present.

*Excluding parameningeal sites.

†Nonbladder and nonprostate.

‡Includes trunk, retroperitoneum, etc., excluding biliary tract.

Unfortunately, there are several toxic effects cancer patients may encounter under chemotherapeutic treatment. The most common side effects of cyclophosphamide are bone marrow suppression and subsequently susceptibility to infections, hemorrhage cystitis, cardiotoxicity, and gastrointestinal disturbances. Vincristine produces severe neurotoxicity in patients and less commonly SIADH, myelosuppression, and alopecia.⁶⁰

Other regimens include VAC plus VAI (vincristine, actinomycin D, and ifosfamide or VIE (vincristine, ifosfamide, and etoposide) plus VAC for 12 months. A randomized controlled trial by Amdt et al compared the VAC regimen and the combination of vincristine, topotecan, and cyclophosphamide for the treatment of moderated risk rhabdomyosarcoma. According to the results, topotecan didn't appear more efficient than actinomycin D with 68% and 73% survival 4 years survival rates respectively. Irinotecan is another

drug with is currently under investigation for its efficacy in the management of pediatric rhabdomyosarcoma when combined with the VAC regimen.^{2,60}

A recent study by the Children's Oncology Group reported no differences between VAC and VAC/ VI effectiveness for the treatment of intermediate-risk rhabdomyosarcoma although patients treated with VAC/VI regimen presented with less hematologic toxicity. In refractory cases, Intensity-modulated radiation and proton beam radiotherapy may be used complementary to assist the therapeutic approach and limit the high amount of chemotherapeutic toxicity.^{57,60}

Although the outcome is not always favorable for the patients, the prognosis of botryoid sarcomas has dramatically improved in recent years through the combination of chemotherapy, radiotherapy, and/or surgery. Likewise most other cancers, the prognosis depends on the tumor size, histological variant, and

the depth to which the disease has spread to adjacent structures at the time of diagnosis. It appears that there is a more favorable prognosis for the tumors arising from the cervix compared with the ones arising from other parts of the female genital tract.⁶¹

Generally, the 5-year survival rate for sarcoma botryoides is 83%,70%,52%, and 25% for clinical stages I-IV respectively. Unfortunately, despite the advances in therapeutic modalities, there are several reports of tumor recurrences with the pelvis being the most common region for primary recurrence.

Conclusion

According to the literature, this tumor can be treated in a variety of ways, ranging from extreme exenterative procedures to more conservative management techniques.

Because botryoid rhabdomyosarcoma of the cervix is a juvenile malignancy that must be treated immediately, the therapeutic approach is critical. The most crucial thing is to organize each patient's treatment plan. The initial considerations in therapy are staging and fertility preservation, but it is also critical to complete excision of the tumor so that there is no recurring disease and no chance of recurrence.

If the tumor is excisable, surgical treatment is the first and best option. The scope of surgery is determined by the tumor's location, its expansion into nearby or distant tissues, and the need to preserve fertility. Surgery, chemotherapy, and radiation therapy are commonly used to treat sarcoma botryoides. Treatment options will vary depending on the tumor's location and stage, as well as the patient's overall health and preferences. Despite the tumor's aggressiveness, sarcoma botryoides have a better prognosis than other kinds of rhabdomyosarcoma.

Wide excision with a safe margin of 1-2 cm is the most successful treatment for sarcoma botryoides, followed by 6-12 rounds of vincristine, actinomycin D, and cyclophosphamide (VAC) as adjuvant chemo-

therapy. The treatment strategy must be understood by the family to obtain the intended results. Even with minimal resources, this cancer can be treated effectively.

Overall, sarcomas have a dismal prognosis, with a high recurrence rate of 45–73 percent for all stages (40 percent recurrence in the lung, 13 percent in the pelvic area). Furthermore, the majority of individuals who have recurrence do so within two years of finishing their first treatment. The myometrium, pelvic blood arteries and lymphatics, adjacent pelvic and abdomen structures, and lung metastases are all part of the tumor's metastatic pathway. Cervical sarcoma botryoides, on the other hand, have a considerably better prognosis than other genital RMS, especially when the tumor appears as a single polypoid lesion and is excised.

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