Vaginal Tumors in the Pediatric Age Group: The Children's Cancer Hospital Egypt (CCHE)-57357 Experience

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Abstract

Background: Primary vaginal malignancies are rare in children. Their management has evolved during the last decades from radical surgery to neoadjuvant chemotherapy followed by local control with conservative surgery or radiotherapy.

Aim: To describe the presentation, management, and outcome of pediatric vaginal malignancies.

Methods: Retrospective review of the medical records of children with 1st vaginal malignancies who had been treated at the Children’s Cancer Hospital Egypt (CCHE)-57357 from June 2007 till December 2018.

Results: During the 11 years, 34 pediatric patients with 1st vaginal malignancies were identified. The histopathology was rhabdomyosarcoma (RMS) in 19 (55.9%) patients, germ cell tumor (GCT) in 13 (38.2%), and clear cell adenocarcinoma (CCA) in two (5.9%). Vaginal bleeding was the presenting symptom in 65% of the patients. The 5-year overall survival and event-free survival rates were 73.7% and 77.8%, respectively, in RMS patients. In GCT patients, the 5-year overall survival and event-free survival rates were 84.6% and 61.5%, respectively. One of the two CCA patients died because of disease progression and the other was alive with progressive disease.

Conclusions: Primary vaginal tumors are rare in children and generally have a good prognosis. Treatment with chemotherapy only or with either conservative surgery or radiotherapy may achieve an excellent outcome in pediatric primary vaginal RMS and GCT.

Keywords: Clear cell adenocarcinoma, Germ cell tumor, Pediatric, Rhabdomyosarcoma, Vagina

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Introduction

Genital tract tumors are rare in children 1. They constitute <5% of all pediatric cancers. The three most common malignancies of the vagina are rhabdomyosarcoma (RMS), germ cell tumors (GCT), mainly yolk sac tumor (YST), and clear cell adenocarcinoma (CCA) 1. Gynecological squamous cell carcinoma and adenocarcinoma types are more common in adults. Vaginal tumors may present with abdominal pain, abdominal mass, or mass protruding from the vagina, and bloody discharge 1.
The management of pediatric vaginal tumors has changed from radical surgery in the 1970s and early 1980s to upfront chemotherapy followed by local control with surgery or radiotherapy.

The differentiation between RMS, YST, and CCA by histopathological examination is often difficult, that is why histopathology and immunohistochemistry are needed. Rhabdomyosarcomas express myogenin and myoD1 which are highly sensitive and specific. The clear cells of YST are of different patterns with Schiller-Duval bodies and hyaline globules, which are PAS-positive, diastase-resistant, alpha-fetoprotein (AFP) positive, and LeuM1 negative. On the other hand, the hyaline globules in CCA are PAS-positive, diastase-sensitive (glycogen), AFP negative, and LeuM1 positive.

Rhabdomyosarcoma of the female genital tract, including the vagina, uterus, and cervix, comprises 4% of RMS cases. The tumors also rarely occur in the cervix or uterine fundus and are often described in another term as a “cluster of grapes.” Vaginal RMS in infants is usually described as sarcoma botryoides. Vaginal RMS is considered a favorable site with a 5-year overall survival (OS) rate greater than 90%, but, because of its specific location, it poses unique challenges for local tumor control.

Malignant germ-cell tumors (GCTs) are rare tumors of childhood, accounting for less than 3% of pediatric malignancies. Endodermal sinus tumor (EST) is the most common histologic subtype of malignant GCTs. The vagina is a rare site for GCTs. Partial vaginectomy with combination chemotherapy is the most recommended line of treatment. The surgery eradicates local tumor cells and makes subsequent chemotherapy more effective, and simple tumor excision is not sufficient. Serum AFP level is a valuable marker for diagnosis and monitoring the recurrence of vaginal EST in infants.

Mesonephric adenocarcinoma of the cervix and vagina is very rare in childhood, with a median age at presentation of 15 years. Patients usually present with vaginal bleeding. Adenocarcinoma of the cervix or vagina in adults usually presents with stage I/II disease. There is a high incidence (24%) of advanced disease (stage III/IV) in children and adolescents. The treatment of choice for vaginal adenocarcinoma is surgical resection. This is followed by radiation therapy for residual microscopic disease or lymph node spread. The role of chemotherapy in the management of CCA is debatable and drugs such as carboplatin and paclitaxel, have been used.

In this study, we describe the clinical presentation, treatment modality, and outcome of vaginal tumors in pediatric patients treated at the Children's Cancer Hospital Egypt (CCHE)-57357.

Methods

A retrospective review of the electronic medical records of children with vaginal tumors treated at the CCHE-57357 over 11 years from June 2007 to June 2018. Patients were followed up until March 2019.

The data retrieved included: age at diagnosis, presenting symptoms, histological findings, stage and risk stratification, systemic chemotherapy given, local control intervention, and outcome.

The initial workup at the presentation included a computerized tomography scan or magnetic resonance imaging and vaginoscopy to assess local disease (tumor size and invasiveness). Computerized tomography scans of the chest and bone scans were done for evaluation of metastatic disease. Bone marrow aspirate and biopsy were performed for cases of vaginal RMS and tumor markers (AFP and beta-human chorionic gonadotropin [BHCG]) were measured in GCT cases. Alpha-fetoprotein half-life (AFP T1/2) was calculated and defined as the time required for the AFP amount in the body to be reduced by one-half. Rhabdomyosarcoma was staged according to the TNM system of the International Union against Cancer (UICC) and the Intergroup Rhabdomyosarcoma Study Group (IRSG) clinical grouping system. Vaginal GCT cases were stratified according to the Children Oncology Group (COG) staging and risk stratification system for extragonadal GCT (8th edition of AJCC/UICC, 2016).

A biopsy was taken for pathological diagnosis. Rhabdomyosarcoma usually embryonal or botryoid subtype (sarcoma botryoides) is positive to desmin with or without myogenin. Yolk sac tumors (or endodermal sinus tumors), which may form histologic patterns that resemble embryonal structures, are positive for AFP, cytokeratin (in almost all cases), vimentin (in spindle cell patterns), and placental alkaline phosphatase (P LAP) in approximately 40-80% of YSTs. The diagnosis of CCA was based on morphology (sheets of clear cells due to the decay of glycogen) and immunophenotyping. Clear cell adenocarcinoma was positive for GATA...
binding protein 3 (GATA3), paired box 2 (PAX2), and CD10; and negative for hormonal receptors and all germ cell markers.

**Statistical methods**

Statistical analysis was done using SPSS Statistics for Windows, Version 17.0. (Chicago: SPSS Inc.). Tumor objective response outcomes were defined as responders (complete remission [CR], partial response [PR], and stable disease [SD]) and non-responders (no response [NR] and progressive disease [PD]). The Kaplan-Meier method was used to estimate event-free survival (EFS) which was defined as the time from the initial diagnosis to the date of disease progression/recurrence or death due to any cause. Overall survival (OS) was defined as the time from the initial diagnosis to death. A p-value <0.05 was considered significant.

**Results**

During the specified 11-year period, 34 children with vaginal tumors had been treated at CCHE-57357. The most common pathology was RMS (19/34, 55.9%) followed by GCT (13/34, 38.2%) and CCA (2/34, 5.9%). Vaginal bleeding was the most common presenting symptom (65% of patients).

**Treatment and outcome of vaginal rhabdomyosarcoma**

The characteristics of 19 RMS patients are illustrated in Table 1. The median age of RMS patients was 2.7 years (range: 0.72–12.15) and the most common presenting symptom was vaginal bleeding/discharge (65%) followed by a protruding mass and one case presented with urinary obstruction and constipation. The majority had an embryonal pathology (73.7%) and stage I disease (89.5%).

All RMS patients were treated using the Children’s Oncology Group (COG) Intergroup Rhabdomyosarcoma Study (IRS)-V ARST0331 and ARST0531 protocols for low and intermediate-risk patients, respectively, which are based on (VAC)\(^{11,12}\). The roadmap for the treatment of the intermediate-risk group is illustrated in Figure 1.

**Table 1: Characteristics of 19 children with vaginal rhabdomyosarcoma (RMS)**

| Characteristic              | n | %  |
|----------------------------|---|----|
| **Age (years)**            |   |    |
| ≤ 1                        | 3 | 15.8 |
| > 1 to < 10                | 12| 63.2 |
| ≥ 10                       | 4 | 21.1 |
| **Size (cm)**              |   |    |
| ≤ 5                        | 3 | 15.8 |
| > 5                        | 12| 63.2 |
| Unknown                    | 4 | 21.1 |
| **Pathology**              |   |    |
| Embryonal                  | 14| 73.7 |
| Botryoid                   | 5 | 26.3 |
| **Risk group**             |   |    |
| Intermediate               | 13| 68.4 |
| Low                        | 6 | 31.6 |
| **Local control**          |   |    |
| Radiotherapy               | 16| 84.2 |
| Surgery                    | 2 | 10.5 |
| None                       | 1 | 5.3  |
| **Stage**                  |   |    |
| I                          | 17| 89.5 |
| III                        | 2 | 10.5 |
| **Group**                  |   |    |
| 1                          | 1 | 5.3  |
| 3                          | 18| 94.7 |
| **Regional lymph nodes**   |   |    |
| Not clinically involved    | 17| 89.5 |
| Clinically involved        | 1 | 5.3  |
| Unknown                    | 1 | 5.3  |

Most of the vaginal RMS tumors had a conservative approach for local control. The majority (16/19, 84.2%) received radiotherapy in time of local control aiming to preserve the genital organs. Patients received radiotherapy as a method of local control according to the stage and clinical grouping. Only clinical group I (apart from alveolar pathology cases) did not receive radiotherapy. The radiotherapy total dose was 36 Gy for stage I alveolar type/stage II node -ve, 41.4 Gy for stage II node +ve, 45 Gy for stage III alveolar/orbital, and 50.4 Gy for all other stage III. Only two patients underwent surgery. Upfront conservative surgery by colposcopy was done for one case, while total hysterectomy was done at relapse for another case.

Fifteen out of 19 cases (78%) were in remission with a median follow-up of 116 months (range, 23.3 – 116.7). The median OS of RMS cases was not reached, the mean was 105.3 months (95%CI: 79.7-130.9) and the 5-year OS rate was 73.7% (Figure 2).
The median EFS of RMS was not reached as well, the mean was 107 months (95% CI: 83-131.1) and the 5-year EFS rate was 77.8% (Figure 3). Four cases relapsed and the same cases died.

The four relapsed RMS patients received a second-line (ifosfamide, carboplatin, and etoposide [ICE] regimen). Two patients died after one and two cycles of ICE due to central nervous system and renal toxicities. The 3rd patient had progressive disease after 8 cycles of salvage chemotherapy and radiotherapy. The 4th patient had progressive disease after 8 cycles of salvage chemotherapy plus panhysterectomy and radiotherapy.

**Figure 1: Roadmap for the treatment of intermediate-risk rhabdomyosarcoma**

The four relapsed RMS patients received a second-line (ifosfamide, carboplatin, and etoposide [ICE] regimen). Two patients died after one and two cycles of ICE due to central nervous system and renal toxicities. The 3rd patient had progressive disease after 8 cycles of salvage chemotherapy and radiotherapy. The 4th patient had progressive disease after 8 cycles of salvage chemotherapy plus panhysterectomy and radiotherapy.

**Figure 2: Kaplan-Meier curve of overall survival of 19 children with vaginal rhabdomyosarcoma**

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**Figure 3: Kaplan-Meier curve of event-free survival of 19 children with vaginal rhabdomyosarcoma**
**Treatment and outcome of vaginal germ cell tumors**

Among the 13 patients with GCT, the yolk sac tumor (YST) subtype was the most common pathology (10/13, 76.9%). The details of GCT patients are shown in Table 2. All cases presented below three years of age and the mean age was 1.3 years (range: 0.66 – 2.8). Vaginal bleeding was a presenting symptom in all patients. All patients received the neoadjuvant platinum-based chemotherapy regimen C-PEB (cyclophosphamide, cisplatin, etoposide, and bleomycin) for 4 cycles except 3 patients who received PEB without cyclophosphamide for 6 cycles. Colposcopic excisional biopsies were done post neoadjuvant treatment mainly to assess the viability of any residual disease. All patients had near-total therapy effect except the 1st patient who subsequently underwent a total hysterectomy.

Events were reported in 3 patients. Patient # 2 who developed local recurrence after two months of follow-up, was successfully salvaged by a TIP (paclitaxel, ifosfamide, cisplatin) regimen. Patient # 3 lost to follow-up after 2 cycles of chemotherapy despite normalization of markers then she presented four months later with a progressive rise in AFP where chemotherapy was reinitiated. Still, she lost to follow up again after 6 cycles of chemotherapy and normalization of AFP. Patient # 7 died after the end of chemotherapy at home for an unknown cause despite marker normalization after 2nd chemotherapy cycle.

Regarding local controls, colposcopic excision of residual vaginal GCTs was performed following 4-6 cycles of chemotherapy. Only one case had a total hysterectomy due to the persistent viability of the residual.

Patients with GCT were followed up for a median of 36 months (IQR: 15.6-55.5). The median OS of GCT patients was not reached, the mean was 82.7 months (95%CI: 64.6-100.9) and the 5-year OS rate was 84.6% (Figure 4). The median EFS was not reached, the mean was 59.3 months (95%CI: 36.7-81.9) and the 5-year EFS rate was 61.5% (Figure 5).

**Treatment and outcome of mesonephric adenocarcinoma**

Mesonephric adenocarcinoma was found in 2 of 34 patients. The first case presented vaginal bleeding at the age of 11 years. She underwent a marginal resection via partial vaginectomy and received postoperative radiotherapy 60 Gy. Six months later, she had a local recurrence for which a total hysterectomy was done with sparing of the ovaries. The disease progressed and the patient lost to follow up in a poor general condition and anuria.

The second one had a cervical mass encroaching on the vagina and lower part of the uterus with metastasis to the iliac and paraaortic lymph nodes. Being unresectable, she received 4 cycles of neoadjuvant chemotherapy (paclitaxel/carboplatin).

**Figure 4:** Kaplan-Meier curve of overall survival of 13 children with vaginal germ cell tumors

**Figure 5:** Kaplan-Meier curve of event-free survival of 13 children with vaginal germ cell tumors
Table 2: Details of 13 pediatric patients with germ cell tumor

| Pt. # | Initial complaint          | Pathology     | Stage | Initial AFP | AFP T1/2 (days) | AFP normalization | Chemo-therapy | Surgery | Last Status |
|-------|---------------------------|---------------|-------|-------------|-----------------|-------------------|---------------|---------|-------------|
| 1     | Vaginal bleeding / discharge | Mixed GCT    | III   | 1547        | NA              | NA                | PEB           | Total hysterectomy | Alive       |
| 2     | Vaginal bleeding           | Mixed GCT    | III   | 9112        | 7               | Post 2nd cycle    | C-PEB & TIP   | Excisional biopsy | Alive in relapse |
| 3     | Vaginal bleeding           | YST          | IV    | 7667        | 8               | Post 2nd cycle    | C-PEB         | NA      | Progression & loss to FU |
| 4     | Vaginal bleeding           | YST          | III   | 3127        | 5               | Post 2nd cycle    | C-PEB         | Excisional biopsy | Alive       |
| 5     | Vaginal bleeding / mass    | YST          | III   | 2864        | 5               | Post 2nd cycle    | C-PEB         | Excisional biopsy | Alive       |
| 6     | Vaginal bleeding           | YST          | III   | 5877        | 8               | Post 2nd cycle    | C-PEB         | Excisional biopsy | Alive       |
| 7     | Vaginal bleeding           | YST          | III   | 1820        | 7               | Post 2nd cycle    | C-PEB         | NA      | Alive       |
| 8     | Vaginal bleeding           | YST          | III   | 3572        | 5               | Post 3rd cycle    | C-PEB         | Excisional biopsy | Alive       |
| 9     | Vaginal bleeding           | YST          | III   | 1334        | 9               | Post 2nd cycle    | C-PEB         | NA      | Alive       |
| 10    | Vaginal bleeding, hematuria| YST          | III   | 3565        | 7               | Post 2nd cycle    | C-PEB         | NA      | Died        |
| 11    | Vaginal bleeding           | YST          | III   | 5804        | >10             | Post 3rd cycle    | C-PEB         | Excisional biopsy | Alive       |
| 12    | Vaginal bleeding           | YST          | III   | 15962       | 7               | Post 4th cycle    | PEB & TIP     | Excisional biopsy | Alive in relapse |
| 13    | Vaginal bleeding           | Immature teratoma | II   | 1           | NA              | NA                | PEB           | Excisional biopsy | Alive       |

**AFP:** Alpha-fetoprotein, **GCT:** Germ cell tumor, **NA:** Not applicable, **PEB:** Cisplatin, etoposide & bleomycin, **C-PEB:** Cyclophosphamide, cisplatin, etoposide & bleomycin, **TIP:** Topotecan, ifosfamide & cisplatin

She then received external beam radiotherapy (total dose = 60 Gy) to the primary tumor and involved lymph nodes with concomitant cisplatin as a radiosensitizer. One year later, she presented with local disease progression and pulmonary metastasis and was under supportive/palliative care at the last assessment.

**Discussion**

Primary vaginal tumors are very rare in the pediatric age group. Over 39 years, only 18 patients <21 years of age out of 4485 (0.4%) treated at St. Jude Children’s Research Hospital had primary vaginal tumors. In the current study, RMS was the commonest pathology followed by GCTs which agrees with the study from St Jude Children’s Research Hospital in which 13/18 (72%) of reviewed primary pediatric vaginal neoplasms were RMS. On the contrary, another study reported that endodermal sinus tumor is more common (17/24, 71%) in the current study, RMS was the commonest pathology followed by GCTs and was mostly diagnosed in children younger than six years of age.

In our study, 12 cases out of 19 (63%) were between 1-10 years. In young and adolescent patients, the cervix and uterus are more prevalent, whereas, in infants, vaginal lesions are common. The survival of adolescent and adult patients with RMS is significantly lower than that of children.
trials are ongoing to improve its outcome, standard treatment protocols are still lacking. In the past, treatment protocols for primary vaginal EST and RMS were very aggressive and led to serious sequelae such as loss of the reproductive function due to radical surgery (ranging from vaginectomy to total pelvic exenteration) or external radiation and vaginal brachytherapy \(^\text{13}\). The development of chemotherapy allowed a conservative strategy to maintain sexual and reproductive function for the future in this group of patients \(^\text{13}\). Protocols are currently trying to reduce the intensity of treatment and alleviate treatment-related complications, especially in patients in the low-risk group \(^\text{15}\).

Management of vaginal tumors has progressed from radical surgery to neoadjuvant chemotherapy followed by surgery or radiotherapy. Radical surgical resection was reserved for truly persistent or recurrent disease \(^\text{16}\). Local control by radiotherapy is associated with significant late effects \(^\text{17}\). In our study, most RMS cases had radiotherapy as a measure of local control (16 out of the 19 patients). In the International Society of Pediatric Oncology (SIOP) Malignant Mesenchymal Tumor Group (MMT) studies patients who achieved complete remission with primary chemotherapy did not receive local treatment \(^\text{8}\). Management may also include radical surgery with or without external-beam radiotherapy. Another conservative approach was also adopted to do a limited surgical intervention and, when feasible, with intracavitary brachytherapy \(^\text{8}\). The conservative approach resulted in a local failure of around 18% and a 5-year OS of 91%. The European pediatric Soft tissue sarcoma Study Group (EpSSG) protocol and COG initially adopted the conservative approach early in 1997. But COG reported local recurrence in patients with partially resected vaginal RMS as they used a response-related approach that could delay or eliminate radiotherapy \(^\text{8}\).

Chemotherapy in RMS is used to decrease tumor size and eliminate micrometastases. VAC (vincristine, actinomycin-d, and cyclophosphamide) and IVA (ifosfamide, vincristine, and doxorubicin) were the chemotherapy regimens mostly used in the COG and European studies, respectively. In our study, cases were treated according to COG protocols and received chemotherapy in the form of VAC. Sixteen cases out of 19 in our study had radiotherapy as a method of local control and initial partial resection was done in only one case. As a salvage treatment, radical total hysterectomy was done in a recurrent RMS case and another one mesonephric adenocarcinoma. The current findings confirm that of Fernandez-Pineda et al, who reported that RMS arising in the vagina has an excellent prognosis and the importance of a local therapy that leads to a high rate of cure \(^\text{1}\). In the present study, 15 out of 19 RMS patients are alive in CR.

GCT represents around 3% of all malignancies in children and extragonadal GCT, especially in the vagina is rare and usually presents by vaginal bleeding in girls below 3 years. In our cases, the age ranged from 8 months to 2.8 years and vaginal bleeding was the main presentation. Yolk sac tumor was the most common GCT pathology in our study (9/13 GCT patients). Alpha-fetoprotein is considered an important marker for the diagnosis and assessment of treatment response of GCTs \(^\text{18}\). In our group of patients, all GCT cases presented with elevated AFP with a half-life (T1/2) <10 days which indicates a good response to chemotherapy, with normalization of markers post 2\(^{nd}\) cycle of chemotherapy in all cases except in one. The progressive rise of AFP after normalization is an indicator of relapse or progression.

Upfront surgery followed by VAC chemotherapy was the usual management in the past, and only a few cases with small tumors had surgery with organ preservation \(^\text{19, 20}\). Regimens including platinum drugs have a superior response rate and higher survival in pediatric GCT in general, with the current 2-year survival for vaginal GCT reaching 70% \(^\text{21}\). A biopsy followed by chemotherapy and vaginal preservation in patients showing a complete tumor response including AFP normalization is the current approach for vaginal malignant GCT \(^\text{1}\). This approach is what we followed in our patients as 9/13 of them underwent excisional biopsy by colposcopy after 4 PEB cycles. Only one patient underwent a total hysterectomy. Radical surgery for vaginal YST is unwarranted but may be required for tumors infiltrating into surrounding structures \(^\text{3}\). Others recommended partial vaginectomy / local tumor excision for better tumor eradication and lower risk of local recurrence \(^\text{22}\).

Vaginal CCA usually occurs in adolescence and has been very rarely reported under the age of 6 years \(^\text{23}\). Both cases in the current study were above ten years old at presentation. The aggressive pattern is often seen in young children with higher survival rates for patients who undergo tumor resection with pelvic and para-aortic nodal dissections, even in
patients with early-stage disease. Post-operative radiotherapy is reserved for microscopic residual or nodal metastasis.

The current study is limited by the small number of patients and being from a single institution. Prospective multi-institutional studies are needed to optimize the management of these rare tumors.

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Authors' contribution
Conception or design: All authors; Acquisition, analysis, or interpretation of data: All authors; Drafting or revising the manuscript: All authors; Approval of the manuscript version to be published: All authors; Agreement to be accountable for all aspects of the work: All authors.

Conflict of interest
The authors declare that they have no conflict of interest to disclose.

Data availability
The deidentified datasets used and/or analyzed during the current study are available from the corresponding author (EE) on reasonable request.

Ethical considerations
This study was approved by the Institutional Review Board of Children's Cancer Hospital Egypt (CCHE-57357).

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Study registration
Not applicable.

References
1. Fernandez-Pineda I, Spunt SL, Parida L, Krasin MJ, Davidoff AM, Rao BN. Vaginal tumors in childhood: the experience of St. Jude Children’s Research Hospital. J Pediatr Surg. 2011; 46(11): 2071-2075.
2. Arndt CA, Donaldson SS, Anderson JR, et al. What constitutes optimal therapy for patients with rhabdomyosarcoma of the female genital tract? Cancer. 2001; 91(12):2454–2468.
3. Ishi K, Suzuki F, Saito A, Komatsu J, Kubota T. Cytodiagnosis of vaginal endodermal sinus tumor: A case report. Acta Cytol. 1998; 42(2): 399–402.
4. Sebire NJ, Malone M. Myogenin and MyoD1 expression in pediatric rhabdomyosarcomas. J Clin Pathol. 2003; 56(6): 412–416.
5. Lacy J, Capra M, Allen L. Endodermal sinus tumor of the infant vagina treated exclusively with chemotherapy. J Pediatr Hematol Oncol. 2006; 28(11): 768–771.
6. Aboud MJ. Vaginal parts of sarcoma botryoides in children: A case report. Acta Scientific Paediatrics. 2019; 2: 100-104.
7. Arora M, Shrivastav RK, Jaiprakash MP. A rare germ-cell tumor site: vaginal endodermal sinus tumor. Pediatr Surg Int. 2002; 18(5-6): 521-523.
8. Minard-Colin V, Walterhouse D, Bisogno G, et al. Localized vaginal/uterine Rhabdomyosarcoma - results of a pooled analysis of four international cooperative groups. Pediatr Blood Cancer. 2018; 65(9): e27096.
9. Smith MA, Seibel NL, Altekruse SF, et al. Outcomes for children and adolescents with cancer: challenges for the twenty-first century. J Clin Oncol. 2010; 28 (15): 2625-2634.
10. Lawrence W Jr, Anderson JR, Gehan EA, Maurer H. Pretreatment TNM staging of childhood rhabdomyosarcoma: a report of the Intergroup Rhabdomyosarcoma Study Group. Children’s Cancer Study Group. Pediatric Oncology Group. Cancer. 1997; 80(6): 1165-1170.
11. Walterhouse DO, Pappo AS, Meza JL, et al. Shorter-duration therapy using vincristine, daunomycin, and lower-dose cyclophosphamide with or without radiotherapy for patients with newly diagnosed low-risk rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children’s Oncology Group. J Clin Oncol. 2014; 32(31): 3547-3552.
12. Hawkins DS, Chi YY, Anderson JR, et al. Addition of vincristine and irinotecan to vincristine, daunomycin, and cyclophosphamide does not improve outcome for intermediate-risk rhabdomyosarcoma: A report from the Children’s Oncology Group. J Clin Oncol. 2018; 36(27): 2770-2777.
13. Xie W, Shen K, Yang J, Cao D, Yu M, Wang Y. Conservative management of primary vaginal endodermal sinus tumor and rhabdomyosarcoma. Oncotarget. 2017; 8(38): 63453-63460.
14. Yuan G, Yao H, Li X, Li H, Wu L. Stage 1 embryonal rhabdomyosarcoma of the female genital tract: A retrospective clinical study of nine cases. World J Surg Oncol. 2017; 15(1): 42.
15. Chauhan RS, Singhi DK, Guha B, Kumar I, Verma A. Multimodality imaging of vaginal rhabdomyosarcoma. Indian J Radiol Imaging. 2017; 27(2): 148–151.
16. Newton WA Jr, Gehan EA, Webber BL, et al. Classification of rhabdomyosarcomas and related sarcomas. Pathologic aspects and proposal for a new classification-an Intergroup Rhabdomyosarcoma Study. Cancer. 1995; 76(6): 1073–1085.
17. Spunt SL, Sweeney TA, Hudson MM, Billups CA, Krasin MJ, Hester AL. Late effects of pelvic rhabdomyosarcoma and its treatment in female survivors. J Clin Oncol. 2005; 23(28): 7143-7151.
18. Davidoff AM, Hebra A, Bunin N, Shochat SJ, Schnauffer L. Endodermal sinus tumor in children. J Pediatr Surg. 1996; 31(8): 1075–1078; discussion 1078-1079.
19. Copeland LJ, Sneige N, Ordonez NG, et al. Endodermal sinus tumor of the vagina and cervix. Cancer. 1985; 55(11): 2558–2565.

20. Hwang EH, Han SJ, Lee MK, Lyu CJ, Kim BS. Clinical experience with conservative surgery for vaginal endodermal sinus tumor. J Pediatr Surg. 1996; 31(2): 219–222.

21. Rescorla F, Billmire D, Vinocur C, et al. The effect of neoadjuvant chemotherapy and surgery in children with malignant germ cell tumors of the genital region: a pediatric intergroup trial. J Pediatr Surg. 2003; 38(6): 910–912.

22. Tao T, Yang J, Cao D, et al. Conservative treatment and long-term follow-up of endodermal sinus tumor of the vagina. Gynecol Oncol 2012; 125(2): 358–361.

23. McNall RY, Nowicki PD, Miller B, Billups CA, Liu T, Daw NC. Adenocarcinoma of the cervix and vagina in pediatric patients. Pediatr Blood Cancer. 2004; 43(3): 289–294.