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Case series

Fertility-sparing surgery for the management of young women with embryonal rhabdomyosarcoma of the cervix: A case series

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ABSTRACT

Objective: To report three cases of embryonal rhabdomyosarcoma (ERMS) of the cervix in young women successfully treated with fertility-sparing surgery and chemotherapy.
Methods: Between January 2014 and December 2015, three cases of ERMS of the cervix were confirmed in young women at a single tertiary cancer center. All cases were managed by a pediatric oncologist and a gynecologic oncologist with a combination of surgery and chemotherapy. Fertility-sparing surgeries (cervical conization or robotic-assisted radical trachelectomy) were offered to patients depending on the tumor size.
Results: All patients were nulliparous and aged 14, 20 and 21 years and all presented with abnormal uterine bleeding. The first patient was managed with radical trachelectomy followed by adjuvant chemotherapy. The second patient underwent primary hysteroscopic resection of the tumor followed by completion cervical conization and adjuvant chemotherapy. The third patient received neoadjuvant chemotherapy followed by loop electrosurgical excision procedure (LEEP) with positive residual margins. She then underwent completion radical trachelectomy. None of the patients experienced perioperative complications. None of the women received radiation. All patients are alive with no evidence of disease.
Conclusion: Fertility-sparing surgery and chemotherapy in well-selected patients with ERMS of the cervix result in low complication rates and excellent oncologic outcomes. This treatment option may be considered in young patients who wish to preserve fertility by avoiding hysterectomy. A collaborative effort between pediatric oncologists and gynecologic oncologists is imperative to facilitate innovative approaches to these rare tumors in young adults.

1. Introduction

Rhabdomyosarcomas (RMS) are soft tissue sarcomas arising from primitive mesenchymal cells. RMS can arise from any part of the body, with head and neck region and genitourinary tract being the most common sites (Dehner et al., 2012). These tumors are uncommon in adults but account for over half of soft tissue sarcomas in children (Pastore et al., 2006). The Intergroup Rhabdomyosarcoma Study Group (IRSG) identified three histologic subtypes including embryonal, alveolar, and undifferentiated (Kriseman et al., 2012). The embryonal subtype is further divided into classic, botryoid, and spindle cell (Kriseman et al., 2012). Botryoid variant is responsible for the majority of cases of embryonal RMS (ERMS) of the cervix.

Cervical RMS are rare and usually affect young women in the first or second decades of life (Bernal et al., 2004). In the adult literature, there are no standard treatments for the management of ERMS of the cervix as only small case series and case reports are available. Often multimodality treatments with a combination of surgery or RT and systemic chemotherapy are utilized. The 5-year overall survival for locoregional disease is excellent ranging from 80 to 90% (Ferguson et al., 2007; Arndt et al., 2001). Significantly, the cost of cure often includes infertility secondary to pelvic RT and/or hysterectomy.

Through collaboration with our pediatric oncology colleagues, we treated 3 patients with ERMS of the cervix with fertility-sparing surgery and chemotherapy, and herein report their outcome. In our study, cervical conization was performed in the management of one patient, while robotic-assisted radical trachelectomy was performed in the other two cases. To our knowledge, only one other case report is available in the literature describing the use of radical trachelectomy in the management of cervical ERMS (Kayton et al., 2009).

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2. Methods

Between January 2014 and December 2015, three cases of ERMS of the cervix were confirmed in young women at a single tertiary cancer center. All cases were managed by a multidisciplinary team including a pediatric oncologist, a gynecologic oncologist and a gynecologic pathologist. A combination of minimally invasive fertility-sparing surgery and systemic chemotherapy was offered to all patients. Fertility-sparing surgery included cervical conization or robotic-assisted radical trachelectomy depending on the tumor size. All patients underwent pre-operative imaging including pelvic MRI to assess tumor size and local spread as well as CT scans of the chest, abdomen and pelvis to rule out metastatic disease. A frozen section of the cervical cone or trachelectomy specimen was performed intraoperatively to evaluate surgical margin. The chemotherapy regimen included a combination of vincristine, actinomycin-D and cyclophosphamide (VAC). Patients were referred for genetic counseling for consideration of *DICER1* molecular genetic analysis. A written informed consent was obtained from all patients included in the study.

3. Results

3.1. Case #1

A 14 year-old gravida 0 adolescent girl was experiencing dysfunctional uterine bleeding after menarche. A year later, she noticed a mass protruding through the vagina. A pelvic MRI confirmed a large exophytic mass measuring 5.3 × 2.9 × 6.7 cm and involving the lower aspect of the cervix. She had no evidence of vaginal, parametrial or uterine invasion. Pelvic MRI and CT scans showed no evidence of extra-cervical disease. Pathological confirmation of the tumor histology was performed pre-operatively. Robotic-assisted radical trachelectomy with placement of abdominal cerclage was performed without complications (Fig. 1). She was discharged home on post-operative day 1. Final pathology confirmed ERMS with diffuse anaplastic features and heterologous (cartilage) differentiation. Surgical margins were negative for malignancy (4.8 mm from radial margin, 18 mm from endocervical margin, 14 mm from vaginal margin). Patient was referred for molecular genetic analysis of *DICER1*. She was enrolled in Children's Oncology Group ARST 0531 clinical trial and received 43 weeks of VAC alternating with vincristine and irinotecan. Her menses have resumed and are regular. She has no evidence of disease 10 months following diagnosis.

3.2. Case #2

A 20 year-old gravida 0 woman presented with heavy vaginal bleeding and a mass protruding through the vaginal introitus. On exam, she was found to have a 5 cm polypoid mass with pedunculated narrow stalk arising from the posterior lip of the cervix. Ultrasound confirmed a 5.9 × 3.9 × 2.9 cm polypoid cervical mass. She was taken to the operating room at an outside institution for an examination under anesthesia. At that time, the mass had detached from the posterior aspect of the cervix with only the stalk remaining. Pathological assessment confirmed ERMS of the cervix. Postoperatively a pelvic MRI showed no evidence of residual disease and CT scans were negative for distant disease. She underwent a hysteroscopic assessment of the cervical canal and uterine cavity followed by a cervical conization to remove potential residual disease. Frozen section assessment showed negative margins and identified the site of the previous tumor stalk. Final pathology showed no residual tumor. She then received adjuvant chemotherapy with 4 cycles of VAC followed by 4 cycles of VA. Molecular genetic analysis of *DICER1* is underway. Her menses have resumed and are regular. She has no evidence of disease 25 months from diagnosis.

3.3. Case #3

A 21 year-old gravida 0 woman presented with a one-year history of abnormal uterine bleeding. Pelvic examination revealed a large polypoid cervical mass which was confirmed to be an embryonal RMS on biopsy. Pelvic MRI demonstrated a 3.3 × 1.7 × 2.8 cm polypoid mass involving the cervix and extending into the endocervical canal. The mass appeared to be involving the vaginal fornices and upper vagina. Considering the size of the cervical lesion and the vaginal involvement, neoadjuvant chemotherapy was recommended and she received 6 cycles of VAC. She had a near complete response and underwent a diagnostic LEEP at an outside institution. Pathological assessment indicated that the deep resection margin was positive for residual RMS. She was counseled regarding management options which included a cold knife cone versus a trachelectomy and she elected to proceed with a completion trachelectomy. She underwent an uncomplicated

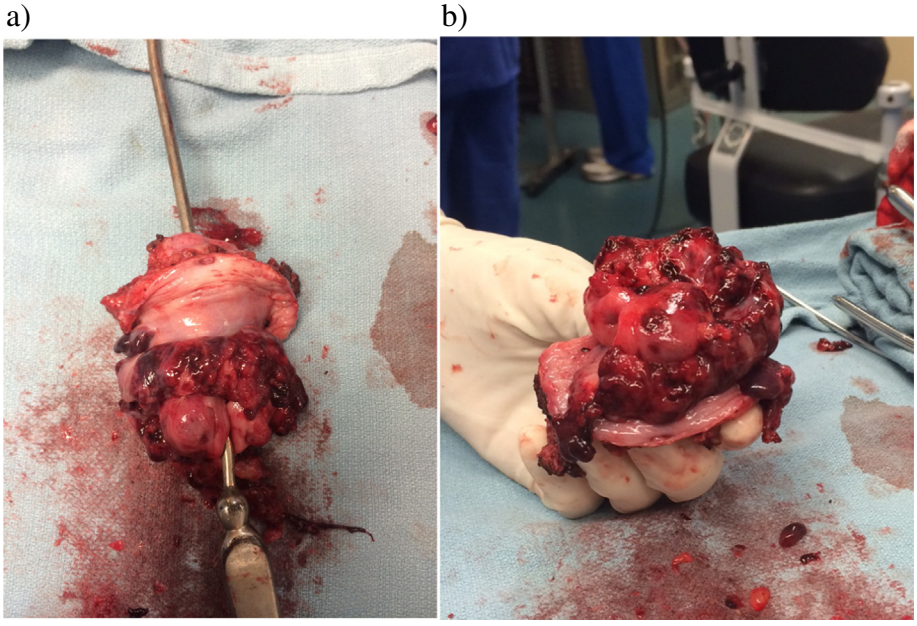

Fig. 1. a - Radical trachelectomy specimen of case # 1 with 5.3 × 2.9 × 6.7 cm cervical RMS involving the lower aspect of the cervix. b - The completely excised embryonal rhabdomyosarcoma is observed in the trachelectomy specimen with negative vaginal, uterine and parametrial margins.