Advanced embryonal rhabdomyosarcoma of the uterine cervix: a case report

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Summary

Background: Primary embryonal rhabdomyosarcoma (RMS) arising from the uterine cervix is a rare and extremely malignant entity. Young women aged 12-26 years are mostly affected. Before the introduction of effective adjuvant chemotherapy, the prognosis of these lesions was poor. *Case:* A 16-year-old girl presented with vaginal bleeding. The histological examination revealed embryonal RMS of the uterine cervix. The patient was treated with a combination of surgery, chemotherapy and radiotherapy. The patient was alive and free of disease five years after the operation. *Conclusion:* A combined modality approach to treating RMS using surgery, multidrug chemotherapy, and radiotherapy has significantly improved survival. The medical community should keep in mind that embryonal RMS of the uterine cervix, despite its malignancy and rarity, can be cured if timely and adequate treatment is given.

Key words: Advanced; Embryonal rhabdomyosarcoma; Uterine cervix.

Introduction

Embryonal rhabdomyosarcoma (RMS) is a tumor composed of embryonal rhabdomyoblasts, the origin of which is the stromal mesenchyme in the lamina propria. Its former name, "sarcoma botryoides", reflects the gross appearance of the neoplasm as multiple "grape-like" polyps [1]. Primary embryonal RMS arising from the uterine cervix is a rare and extremely malignant entity. Mostly young women aged 12-26 years are affected [1, 2].

The most common symptom is vaginal bleeding, which in infants is often detected because of intermittent bloody discharge on the diaper. If large, the tumor may distend the lumen of the vagina and protrude through the introitus as soft, polypoid, grape-like masses.

Microscopically, embryonal RMS has a "cambium layer", represented by a subepithelial condensation of tumor cells. The neoplastic cells are reactive for desmin, myo-D1, and myogenin [1].

Before the introduction of effective adjuvant chemotherapy, the prognosis of these lesions was poor. A combined modality approach to treating RMS using surgery, multidrug chemotherapy, and radiotherapy has significantly improved survival [3, 4]. With treatment, the overall survival rate nears 80% [5].

We have treated a very young woman suffering from advanced embryonal RMS using a combination of surgery, chemotherapy and radiation therapy with excellent results.

Case Report

A 16-year-old girl presented to a gynecologist with one-month history of abnormal vaginal bleeding and abdominal pain. Her past medical history was unremarkable. Physical examination revealed a decaying lobulate necrotic tumor, filling the vagina and whole pelvis. Pelvic computed tomography (CT) scan revealed an anechogenic tumorous mass originating from the uterus and filling the whole pelvis. Chest X-ray was normal.

Histology of the vaginal tumor biopsy showed rhabdomyosarcoma botryoides with micro foci of cartillage (Figure 1). Immunohistochemically tumor cells were positive for the skeletal muscle markers: sarcomeric actin, myoglobin, myo-D1 and desmin, which confirmed the diagnosis of embrional RMS (Figure 2).

At laparotomy, it was clearly that the tumor originates from the cervical part of the uterus, with normal appearance of the uterine corpus. There were no signs of dissemination of disease in the abdominal cavity. Lymphatic glands were without palpable signs of disease. We performed total abdominal hysterectomy, upper vaginectomy and bilateral pelvic and paraaortic lymphadenectomy. The ovaries showed no signs of disease and were preserved.

The surgical resected specimen measured 13 x 17 x 8 cm, and was partially necrotic. Tumor was present within the cervical canal and infiltrated into the uterine cavity in multiple grape-like shaped masses. Tumor infiltrated the cervical and uterine wall with multiple overgrowths beneath the serosa. The microscopically resected specimen showed embrional RMS including cartilaginous neoplastic elements. Metastases were present in the vaginal cuff, obturatory and iliac lymph nodes. The tumor was classified as group II C by the Intergroup Rhabdomyosarcoma Study Group (IRSG) clinical grouping classification (Table 1) [3].

After surgery, the patient received treatment with adjuvant chemotherapy consisting of vincristin, actinomycin D and cyclophosphamide (VAC regimen) every three weeks for six courses. After six courses of chemotherapy, she was treated with radiotherapy. She was followed up closely (every 2-3 months) after completing the therapy.

The patient was alive and well with no evidence of disease five years after the surgery.

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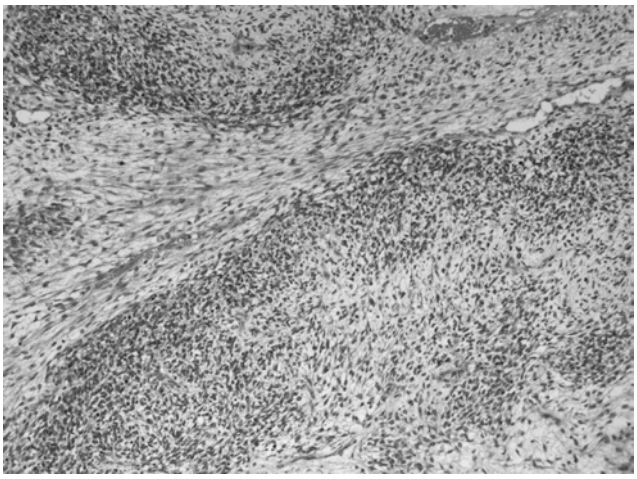
Fig. 1



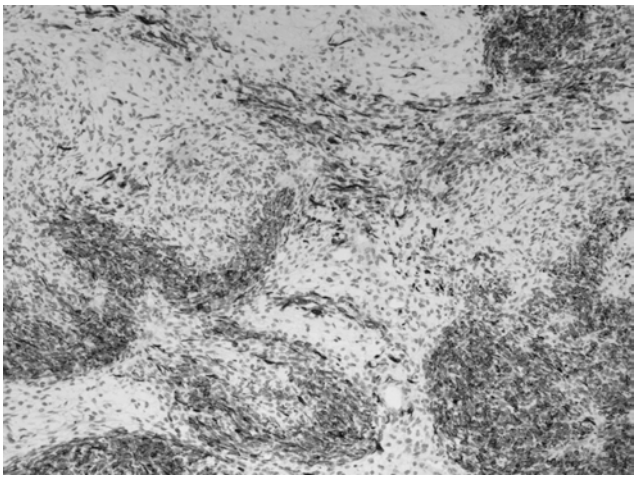


Fig. 2

Figure 1. — Islands of immature cartilage are present within the rhabdomyosarcomatous component.
Figure 2. — Nuclear immunoreactivity of rhabdomyosarcomatous elements with desmin.

Table 1. — *IRS clinical grouping classification*.

GROUP I
Localized disease, completely resected.
A) Confined to organ or muscle of origin.
B) Infiltration outside organ or muscle origin; regional nodes no involved.
GROUP II
Compromised or original resections of three types including.
A) Grossly resected tumors with microscopic residual.
B) Regional disease, completely resected, in which nodes may be involved and/or extension of tumor into an adjacent organ present.
C) Regional disease with involved nodes, grossly resected, but with evidence of microscopic residual.
GROUP III
Incomplete resection or biopsy with gross residual disease.
GROUP IV
Distant metastasis, present at onset.

Discussion

RMS is a highly malignant tumor arising from embryonal mesenchyma, and is the most common soft tissue sarcoma in childhood and in young adults accounting for 4-6% of all malignancies in this age group [2].

Embryonal RMS occurs primarily in three regions – the head and neck, the genitourinary tract, and the infantile vagina is the most common site, but this cancer may also occur in the uterine cervix. This neoplasm frequently has a vaginal location in children younger than four years, whereas cervical onset has a peak incidence in the first or second decade of life [6]. Some recently published studies suggested that, in contrast to embryonal RMS occurring in the vagina, cervical embryonal RMS has a favorable outlook [7].

The IRS group has reported a new classification of RMS recognizing three major histological subtypes: embryonal, alveolar, and undifferentiated. The botryoid type is a variant of embryonal RMS [1], which accounts for no more than 5-10% of all RMS. A distinct "cambium layer" beneath the epithelium is characteristic. Several cases, including ours, have shown metaplastic cartilaginous differentiation, which is a positive prognostic factor. Histopathologic factors that appear to correlate with an adverse prognosis include deep myometrial invasion, lymphatic invasion, and a focal alveolar pattern [8].

At the time of presentation, the embryonal subtypes are often localized with a favorable prognosis, in contrast to alveolar subtypes which present with distant metastasis and less favorable prognosis [8].

Pathologically the tumor may be misdiagnosed as malignant mixed müllerian tumor, because both conditions are characterized by malignant epithelial and supportive tissue. Absence of malignant epithelial tissue is the critical point for the differential diagnosis between carcinosarcoma and RMS [9]. Immunohistochemistry is extremly useful for confirming the diagnosis of RMS. Myogenin and myo-D1 are relatively new antibodies generated against intranuclear myogenic transcription factors and are considered to be relatively specific markers of skeletal muscle differentiation, although occasional myogenin-positive nuclei may be seen in reactive lymph nodes [9, 10]. These markers are more commonly positive in alveolar than embryonal RMS. They are considered the best available markers for confirmation of RMS. In our case the tumor cells were positive for sarcomeric actin, myoglobin, myo-D1 and desmin, which confirmed the diagnosis of embrional RMS.

The mainstay of primary therapy consists of local or radical surgery with or without adjuvant postoperative chemotherapy and radiotherapy [11, 12]. Prior to the introduction of multiple chemotherapeutic agents in the 1960s, surgery played a principal role in the treatment of patients with RMS. In the past, these lesions were treated with extensive surgery, including exenteration, with poor results. The addition of chemotherapeutics as an adjuvant

to surgery has markedly improved the overall prognosis for RMS. The IRS Group was formed under the auspices of the National Cancer Institute in 1972 to investigate the therapy and biology of RMS and undifferentiated sarcoma, thus the treatment of RMS has been extrapolated from this group, so that optimal management may be achieved. As a result, the five-year survival rates for patients in clinical groups I-IV reported by the IRSG were 83%, 70%, 52% and 25%, respectively [3]. For cervical sarcoma botryoides, Brand *et al*. [5] reported an overall survival of 80%. Approximately 75% of cervical RMS patients present with group I disease.

The surgical procedures range from tumorectomy, wide local excision, and trachelectomy up to radical hysterectomy and pelvic lymph node dissection in cases with more advanced disease or large or deeply infiltrating neoplasms [4, 13]. Patients with embryonal RMS with favorable prognostic parameters, such as localized disease without deep myometrial invasion, a single polyp and embryonal histologic subtype, can effectively be treated by surgery. In early disease, also with the aim of preserving the reproductive potential, a conservative surgical approach consisting of local excision of the neoplasm has been reported [4, 13, 14]. This type of treatment is reserved only for patients with Stage I disease (Table 1) and neoplasm confined to the cervix. Patients with unfavorable prognostic parameters seem to benefit from a multimodality approach including surgery, adjuvant chemotherapy and radiotherapy.

The most widely used chemotherapy regimen includes VAC. One important result of the IRSG Study II for group I patients (Table 1) was that cyclophosphamide did not contribute to the success of treatment, but significantly reduced treatment toxicity [12]. A report by Gordon and Montag suggested that between six and 12 VAC cycles would allow a reasonable probability for return of menstruation and reproductive function [15].

The most important prognostic factors appear to be extent of disease at diagnosis and site of primary tumor, with sites that produce symptoms earlier having a better prognosis [2, 12].

In the present case the necessity of complementary chemotherapy and radiotherapy was chosen according to the locally advanced disease infiltrating also the upper vaginal vault and both obturatory and iliac lymph nodes.

This case represents another example of a successful multimodality approach to treatment of advanced RMS with excellent results.

Conclusions

Patients with embryonal RMS with favorable prognostic parameters, such as localized disease without deep myometrial invasion, a single polyp and embryonal histologic subtype, can effectively be treated by surgery. Patients with unfavorable prognostic parameters seem to benefit from a multimodality approach including surgery, adjuvant chemotherapy and radiotherapy. The medical community should keep in mind that embryonal RMS of the uterine cervix, despite its malignancy and rarity, can be cured if adequate and timely treatment is given.

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