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GYNECOLOGIC ONCOLOGY

Successful treatment of a very rare case: locally treated cervical rhabdomyosarcoma

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Abstract
Aim To study the local treatment of uterine cervical rhabdomyosarcoma in which fertility-sparing surgery is done.
Methods We report an embryonal rhabdomyosarcoma of the uterine cervix which presented as a cervical polyp in a 22-year-old nulliparous woman.
Results The tumor was composed of rhabdomyoblasts of varying differentiation dispersed within a loose, myxoid stroma, and formed a distinct cambium layer beneath the epithelium. The patient was successfully treated with fertility-sparing surgery and adjuvant chemotherapy.
Conclusion The treatment modality should be done according to the patients individually. Treatment has recently inclined toward conservative therapy. Patients with favorable prognostic factors such as localized disease, single polyp and embryonal histologic subtype and without deep invasion can be treated with minimal invasive surgery.

Keywords Rhabdomyosarcoma · Uterine cervix rhabdomyosarcoma

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Introduction

Rhabdomyosarcoma (RMS) is the most common soft-tissue sarcoma in children and young adults and accounts for 4–6% of malignancies in this age group [1, 2]. RMS, a tumor of skeletal muscle, originates from embryonic mesenchyme. RMS is primarily located in the head and neck region, but approximately 20% of primary lesions are localized in the genitourinary tract [2, 3]. Histologically, RMS has been classified into three subtypes by the Intergroup RMS Study Group (IRS): embryonal, alveolar, and undifferentiated. Embryonal RMS has a special variant called sarcoma botryoides (SB), which means "grape-like"; it is so named because of a layer of spindle cells that pushes up beneath the mucosa in polypoid masses. SB typically occurs as a vaginal tumor in female infants and rarely occurs in the cervix or uterine fundus. In contrast to vaginal lesions, which are mostly seen before the age of 4 years, cervical RMS is usually seen in the second decade of life. Microscopically, it is characterized by a submucosal cellular zone of primitive rhabdomyoblasts. Early diagnosis is possible if irregular bleeding is the first symptom. Outcome depends on tumor size, extent, and histological subtype. The traditional treatment of SB, whether occurring in the vagina, cervix, or uterine fundus, has historically been radical fertility-compromising surgery. However, the recent literature suggests that SB of the cervix behaves less aggressively than does SB of the vagina and uterus, and conservative surgery combined with adjuvant chemotherapy is now the treatment of choice to preserve future fertility [4].

Case

A 22-year-old null-gravid woman was admitted to our hospital with a complaint of irregular vaginal bleeding.

Cervicovaginal inspection revealed a 3 × 2 cm polypoid mass, protruding from the cervical os. Further physical examination showed no pathologic findings. Vaginal sonography revealed no uterine or adnexal abnormalities.

When we checked her detailed medical history, we found that she had a cervical polypectomy which was performed in another hospital nearly 6 months ago. Report of pathological examination of that polyp was cervical polyp without malignancy. There was no other speciality on her medical history.

We decided to perform polypectomy again. We took the polypoid mass visually and sent it for pathological examination. Histological examination revealed the diagnosis of cervical embryonal rhabdomyosarcoma. A polypoid mass covered with pink, smooth and glistening mucosa was removed and no distinct stalk was identified. Histologically, a zone of increased cellularity composed of undifferentiated rhabdomyoblasts (cambium layer) was identified (Fig. 1). A cambium layer adjacent to the surface epithelium and surrounding endocervical glands with and without cross-striations and small foci of immature cartilage were also present (Fig. 2). Immunohistochemistry remains the current ancillary method of choice in the pathologic evaluation of small blue round-cell tumors. In at least 20% of cases of rhabdomyosarcoma (RMS), it is considered an essential factor in the final and/or differential diagnosis of the malignancy. In cases where histological diagnosis of rhabdomyosarcoma is difficult, immunostaining with monoclonal antibodies against the intranuclear myogenic transcription factors MyoD1 and myogenin, and a polyclonal antibody preparation against desmin (P-DES) is suggested. Nearly all RMS tumors are positive for P-DES, myogenin. In our case, Immunohistochemical staining within the tumor cells showed cytoplasmic filaments in an alternating pattern of thick and thin filaments. The rhabdomyoblasts stained with desmin and vimentin positive, but negative with S100 CD99, CK. In conclusion, sarcoma botryoides with disease-free surgical margins was found (Fig. 2).

After this diagnosis, we suspected that underdiagnosis of embryonal rhabdomyosarcoma on the first polyp which was taken at the district hospital. The histological re-examination of the first polyp also showed a small area of sarcomatous tissue.

For the staging of the tumor, subsequent chest X-ray, intravenous pyelogram, cystoscopy, barium enema, rectoscopy, and computed tomography of the abdomen and pelvis were performed. There were no abnormal findings on these tests.

Histopathologic staging was group IA (localized to the cervix) embryonal RMS of the uterine cervix according to the IRS Clinical Grouping Classification.

Due to patient's fertility desire and early stage disease, we performed loop electrical excision procedure conization (LEEP) for further local treatment and diagnosis of local residual tumor on cervix instead of abdominal hysterectomy. Histology of surgical specimen of LEEP conisation revealed a disease-free surgical margin.

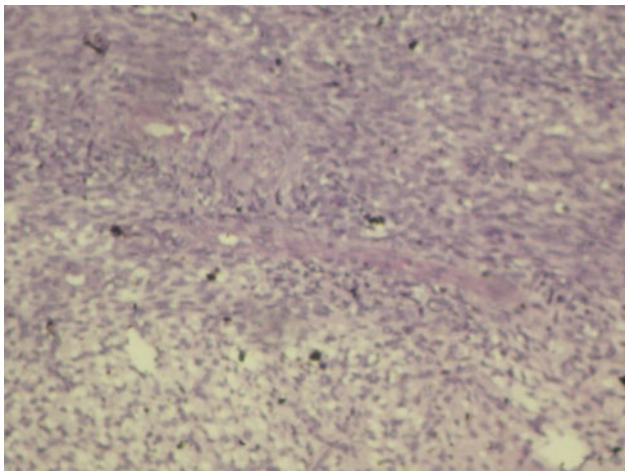

Fig. 1 A zone of increased cellularity composed of undifferentiated rhabdomyoblasts (cambium layer)

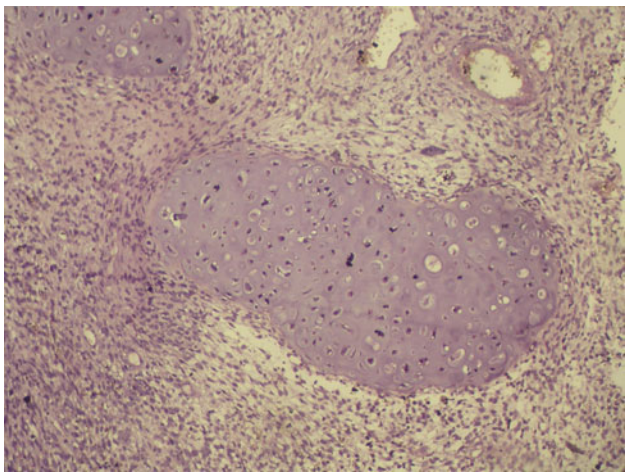

Fig. 2 A cambium layer adjacent to the surface epithelium and surrounding endocervical glands with small foci of immature cartilage

The patient underwent adjuvant chemotherapy according to the protocols by IRS-III. The patient received treatment with chemotherapy consisting of vincristine 1.5 mg/m^2, actinomycin D 0.5 mg/m^2, and cyclophosphamide 500 mg/m^2 (VAC) every 3 weeks for six courses**.** She was free of disease during 18 months follow-up period.

Discussion

The World Health Organization classification of soft-tissue tumors defines the botryoid type of RMS as a tumor of skeletal muscle differentiation arising beneath a mucosal epithelial surface [5]. It is known to occur in almost any mucosa-lined organ. In the female genital tract, the most

common site is the vagina, and it occurs most frequently in infants or young children.

SB in the cervix is rare, and most of the presently available information is based on individual case reports. SB tumors of uterine origin tend to develop approximately one decade later than those of vaginal origin. The botryoid type is generally found in the vagina during early childhood, in the cervix during adolescence and the reproductive period, or in the corpus uteri during the postmenopausal years.

Botyroid RMS (a variant of embryonal RMS) presents in children and adolescents as a myxoid polypoid mass covered by attenuated epithelium. The appearance is generally similar to that of homonymous vaginal tumors. However, some cervical tumors in older patients may contain cartilage, which is associated with a better prognosis [6]. Most patients present with vaginal bleeding or a feeling of a mass in the introitus. Like SBs occurring at other mucosal sites, the tumor may form soft, grape-like clusters and may present as single or multiple polyps. In many cases reported in the literature, including our case, the tumor initially appears as a benign intracervical or endometrial polyp that protrudes through the vaginal introitus. This typical presentation of SB was observed in all cases reported by Daya and Scully and Bernal et al. [7, 8].

Diagnosis is difficult because of the rarity of embryonal RMS. The differential diagnoses are adenosarcoma, edematous cervical mesodermal polyp (pseudosarcoma botryoides), rhabdomyoma, and other small round blue-cell tumors. Adenosarcomas can also be found in young women but can be histologically distinguished from SB by their fibrous stroma and leaf-like gland pattern. Edematous cervical mesodermal polyps (pseudosarcoma botryoides) may resemble SB because of their edematous stroma but tend to occur in older women, are usually small, and lack both a cambium layer and rhabdomyoblasts. Rhabdomyoma is a benign tumor that displays skeletal muscle differentiation, but lacks a cambium layer, and has uniformly distinct skeletal muscle differentiation of the tumor cells. It also tends to occur in older age groups. Other small round blue-cell tumors, such as small-cell carcinoma and lymphoma, can also have similarities to SB of the cervix. Alveolar RMS shows recurrent translocation of t(2;13)(q35;q14); however, molecular studies of embryonal RMS have not found a recurrent genetic abnormality that may aid in diagnosis. Only one case of SB of the cervix has been cytogenetically studied; deletion of the short arm of chromosome 1 and trisomy 13 and 18 were demonstrated [10]. Semcuzk et al. reported that p53, but not K-ras, gene alterations play a role in the development and progression of SB of the uterine cervix [9]. The prognosis of cervical SB is more favorable than that of other genital RMS types, particularly when the tumor arises as a single polypoid lesion and the polyp is completely removed. The proper treatment of cervical SB has not been well assessed, and it continues as a subject of investigation. Before 1970, radical surgery involving pelvic lymphadenectomy was considered to be the treatment of choice, although no significant improvement in survival has yet been proven. According to the IRS, chemotherapy increases the survival rate and radiotherapy is ineffective for stage I disease [15, 16]. The main treatment is surgery with or without adjuvant chemotherapy and radiotherapy. Surgical strategies range from simple local excision to complete hysterectomy [11]. Recent data show satisfying results with cervical SB in which local fertility-sparing surgery and chemotherapy were performed [8].

Brand et al. reported 21 patients with SB, 80% of whom were disease free after 68 months of follow-up. They reported that the survival rates increased significantly with adjuvant chemotherapy. Stankovic et al. [11] reported a patient treated by fertility-preserving surgery in combination with adjuvant chemotherapy; complete preservation of the bladder, rectum, uterus, and vagina was achieved. Lin et al. reported a patient who underwent initial cone biopsy in which the endocervical resection margin showed tumor involvement. After chemotherapy, cone biopsy was performed. Histology failed to reveal any evidence of a tumor, and the patient remained disease free for 36 months after the initial diagnosis [12]. Hays et al. reported eight patients with cervical RMS: all patients in group I ($n = 5$) and one patient in group III ($n = 3$) survived for >24 months. Local fertility-sparing surgery stands as the main treatment for patients with local disease, followed by chemotherapy [13]. In one reported patient in whom adjuvant chemotherapy was not used after adequate surgical excision, death occurred 4 months after surgery [14]. This case emphasizes the importance of adjuvant chemotherapy in the treatment of this tumor.

Conclusion

Although SB rarely seen in cervix, it should be in the differential diagnosis list of a young woman with vaginal bleeding. In case of favorable outcomes such as localized disease to the cervix without deep myometrial invasion (without extension to the corpus uteri and vagina) and embryonal histologic subtype, fertility-sparing surgery can be performed successfully.

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

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