Mullerian adenosarcoma of the cervix with heterologous elements and sarcomatous overgrowth

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Cervical adenosarcomas are exceedingly infrequent tumors that occur most often in women of reproductive age. Adenosarcomas comprise benign epithelial elements and malignant stromal elements. The malignant stromal elements can either be homologous, such as fibroblasts or smooth muscle, or heterologous, like cartilage, striated muscle, or bone. We report a case of adenosarcoma of the cervix with heterologous elements and sarcomatous overgrowth in a 38-year-old woman.

Adenosarcomas are rare malignant mixed mullerian tumors that are composed of benign epithelial and malignant stromal components. These entities occur most often in the endometrium, ovary, or pelvis and less often in the cervix. The presence of sarcomatous overgrowth and heterologous elements are two histopathologic features associated with a worse prognosis. Sarcomatous overgrowth is diagnosed when the pure sarcomatous portion of the neoplasm constitutes >25% of the primary tumor. Heterologous elements are features present in the tumor that are not native to the primary site and include cartilage, skeletal muscle, or bone. Adenosarcomas rarely have distant metastases, but they have a propensity for local recurrence (1, 2). We present the findings in a young woman with a cervical mullerian adenosarcoma with sarcomatous overgrowth and heterologous elements.

CASE REPORT

A 38-year-old G3, P3, white woman with genital herpes presented to her gynecologist with postcoital spotting and light brown discharge. Examination found a cervical polyp, which was subsequently biopsied. Microscopically, it consisted of polypoid fragments of endocervical mucosa and squamous mucosa on the surface. Small blue cells with scant cytoplasm, ovoid nuclei, and bundles of spindled cells were underneath the surface epithelium, resembling a cambium layer (*Figure 1a*), and within the endocervical stroma (*Figure 1b*). There was a section of dense proliferation of blue cells around small vessels (*Figure 1c*). Numerous mitotic figures and apoptotic cells were present. A focus of striated muscle cells consistent with rhabdomyoblasts was also identified (*Figure 1d*). The biopsy had up to 4 mitotic figures per 10 high-power fields in hypercellular areas. Scattered groups of stromal cells were strongly immunohistochemically

reactive for estrogen and progesterone receptors, myogenin, and desmin. The stromal cells were immunohistochemically negative for WT1. On biopsy, an embryonal rhabdomyosarcoma, botryoid type, was diagnosed. The patient underwent three cycles of chemotherapy with cyclophosphamide, vincristine, and actinomycin D. Three months later, she underwent a radical hysterectomy, bilateral salpingectomy, and bilateral pelvic lymph node dissection.

The uterus measured 8.5 × 6.0 × 3.5 cm and weighed 92 g. The ectocervix was remarkable for a protuberant, red-brown endocervical mass measuring 2.3 × 2.3 × 1.8 cm located at the 1:00 to 4:00 position. Microscopically, the tumor had dilated benign glands with focal periglandular stromal cuffing (*Figure 2a*) and stromal condensation underneath the surface epithelium (*Figure 2b*). Heterologous elements included foci of benign cartilage (*Figure 2c*) and elongated strap cells with muscle striations consistent with rhabdomyoblasts (*Figure 2d*). Sarcomatous overgrowth was also present. The stromal cells were immunohistochemically reactive for estrogen receptor, progesterone receptor, and CD10. No myometrial invasion was present. The vaginal mucosa, parametrium, and the 21 lymph nodes were not involved by tumor.

DISCUSSION

In our case, the diagnosis of embryonal rhabdomyosarcoma was based on the morphology and immunohistochemical staining pattern, in particular the positive desmin stain. After assessing the entire lesion in the main resection specimen and the immunohistochemical stains, the lesion was best diagnosed as an adenosarcoma.

Clement and Scully (1) first described mullerian adenosarcoma as an uncommon variant of malignant mixed mullerian tumors that were composed of benign epithelial elements and malignant stromal elements. The malignant stromal elements may be homologous (fibroblasts or smooth muscle) or heterologous (cartilage, striated muscle, or bone) (1). A review disclosed few reported cases of cervical adenosarcoma with heterologous

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Figure 1. (a) Stromal condensation underneath the endocervical surface epithelium (hematoxylin and eosin [H&E] 100×). (b) Small round blue cells within the endocervical stroma (H&E 400×). (c) Small round blue cells surrounding vessels (H&E 400×). (d) Foci of skeletal muscle consistent with rhabdomyoblasts (H&E 100×).

Figure 2. (a) Periglandular cuffing of stromal cells (hematoxylin and eosin [H&E], 200×). (b) Stromal overgrowth underneath the surface epithelium (H&E 200×). (c) Foci of benign cartilage (H&E 200×). (d) Foci of rhabdomyoblasts present within the main resection specimen (H&E 400×).

elements or sarcomatous overgrowth (1–16). Even fewer cases have both sarcomatous overgrowth and heterologous elements. Cervical adenocarcinomas have been reported in a wide age range of women (11–67 years of age), but in a study of 12 cases, the

of rhabdomyosarcomatous adenocarcinoma of the uterine cervix (6). It is now believed that these two entities are distinct. In 2013, Fanghong et al discussed the morphologic and immunohistochemical clues to differentiate between the two. Adenocarcinomas

average age was 31 years, with one-third of patients presenting before age 15 (11). The most common presentation is abnormal vaginal bleeding. Examination usually shows a polypoid lesion protruding through the external cervical os. Distant metastases are rare (1), but these tumors can recur locally.

The histopathologic diagnosis of an adenocarcinoma includes the following: the formation of periglandular cuffing and intraglandular protrusions of cellular stroma; noninvasive glands lined by benign-appearing müllerian epithelium of various types showing mild to marked nuclear atypia; an average of ≥ 2 mitotic figures per 10 high-power fields in the stromal component; and more than mild nuclear atypia of the stromal cells (1, 11).

Factors indicating a poor prognosis include cytologic atypia, high proliferation rate, sarcomatous overgrowth, presence of heterologous elements, deep myometrial invasion, necrosis, and extrauterine spread (9, 11). Of the aforementioned factors, sarcomatous overgrowth and myometrial invasion are consistently associated with poor prognosis and recurrence (1, 11). Sarcomatous overgrowth is present when it accounts for at least 25% of the tumor area (16).

The differential diagnosis of an adenocarcinoma of the cervix includes benign lesions such as adenofibroma, atypical endocervical polyp, and adenomyoma of the cervix and malignant neoplasms including uterine adenocarcinoma with secondary involvement of the cervix, carcinosarcoma, and embryonal rhabdomyosarcoma (17).

As evidenced by this case, adenocarcinomas with rhabdomyoblastic differentiation and/or those with areas of sarcomatous overgrowth are sometimes difficult to distinguish from embryonal rhabdomyosarcomas. In 1985, Chen reported a case

should exhibit foci with intraluminal polypoid projections and a phyllodes-like growth pattern (18). Intraluminal polypoid projections can be focally present in an embryonal rhabdomyosarcoma; however, a phyllodes-like growth pattern should be absent (18). Immunohistochemical stains are also very helpful in differentiating between an adenosarcoma and an embryonal rhabdomyosarcoma. Adenosarcomas exhibit estrogen and progesterone receptor reactivity, but embryonal rhabdomyosarcomas should be negative for hormone receptors (18).

Treatment and clinical management of patients with cervical adenosarcomas is not well defined and continues to be under intense investigation. No radiation or chemotherapy guidelines exist for cervical adenosarcomas due to lack of evidence that any one treatment is more advantageous than other therapies (19–21). Much of the clinical management of cervical adenosarcomas is based on experience with uterine adenosarcomas (17). At 10 months postoperatively, our patient remains free of disease.

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