

Uterine Cervical Adenosarcoma Showing an Endophytic Growth Pattern

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Abstract

Adenosarcomas are biphasic neoplasms that usually originate in the uterine corpus and comprise a benign epithelial component and a malignant stromal component. Uterine adenosarcomas typically present with abnormal genital bleeding, an enlarged uterus, and a tumor that protrudes into the endometrial cavity. These tumors rarely protrude through the cervical os and are often misdiagnosed as cervical polyps. We present the case of a patient with cervical adenosarcoma with characteristics different from those reported in previous cases. This tumor showed endophytic growth, which is rare in cervical adenosarcomas. No watery discharge or obvious genital bleeding was noted. Although the tumor measured 4 cm, vaginal bleeding was noted only once at 6 months before diagnosis and was in the form of faint brown discharge.

Keywords: Adenosarcoma; Uterine cervix; Endophytic growth

Introduction

Uterine adenosarcomas are mixed tumors comprising benign Mullerian epithelium and malignant mesenchymal cells. Uterine sarcomas account for 7-9% of all malignant tumors of the uterus [1, 2], and uterine adenosarcomas account for only 8% of these uterine sarcomas [3]. Primary adenosarcomas of the cervix are extremely rare and account for only 2% of all uterine adenosarcomas [4].

Typical clinical presentation of uterine adenosarcomas includes vaginal bleeding from a protruding mass, which can be observed during pelvic examination. Adenosarcomas rarely

show an endophytic growth pattern. Moreover, cervical adenosarcomas usually present with abnormal discharge or evident genital bleeding [5].

Herein, we report a case of cervical adenosarcoma showing an endophytic growth pattern wherein faint brown discharge appeared only once despite the tumor reaching 4 cm in diameter.

Case Report

Investigations

A 51-year-old woman, who was 4 years postmenopausal, underwent radiation therapy after bilateral breast-conserving surgery for breast ductal carcinoma *in situ* at 41 years old. She had no history of tamoxifen use during breast cancer treatment. She underwent fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) as part of the routine follow-up for breast cancer, and results revealed increased uptake in the cervix (Fig. 1). She subsequently presented to our hospital for further gynecological evaluation.

Diagnosis

Gynecological examination revealed that the 4-cm long cervix

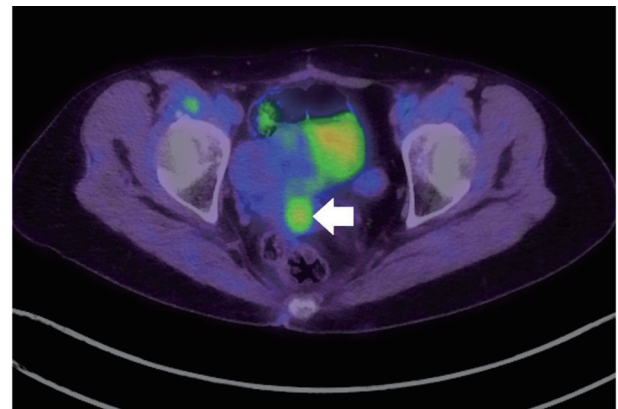


Figure 1. Fluorodeoxyglucose positron emission tomography-computed tomography indicating increased uptake in the cervix (arrow: cervical tumor).

Manuscript submitted June 19, 2022, accepted August 5, 2022
Published online August 19, 2022

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doi: <https://doi.org/10.14740/jmc3952>

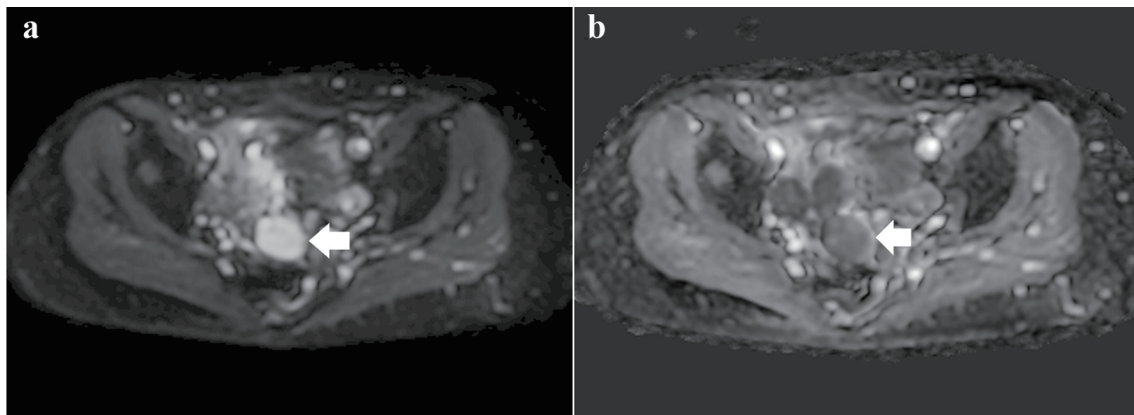


Figure 2. (a) Diffusion-weighted image showing a heterogeneous high-intensity tumor (arrow). (b) Apparent diffusion coefficient image showing a tumor with mild diffusion restriction (arrow).

had been replaced by a gray-white tumor with no vaginal or bilateral parametrial involvement. Magnetic resonance imaging (MRI) indicated that the tumor was 4 cm in size, contained small cysts, and had entirely replaced the cervix, similar to gross findings. The cervical mass exhibited heterogeneously high attenuation on diffusion-weighted imaging (DWI) and mild diffusion restriction on apparent diffusion coefficient (ADC) (Fig. 2a, b). These MRI findings suggested a degenerated adenomyoma; however, the possibility of a rare invasive tumor could not be ruled out. Multiple hyperintense small cysts were found inside the tumor on T2-weighted imaging (T2WI) (Fig. 3). There was no evidence of ascites or pelvic lymphadenopathy. Contrast-enhanced chest and abdominal computed tomography showed no evidence of distant metastases. Cervical biopsy revealed a mesenchymal tumor; however, the biopsy result was inconclusive as the amount of biopsied tissue was small.

Treatment

We decided to further evaluate all lesions in the cervix through hysterectomy and accordingly performed total ab-

dominal hysterectomy with bilateral salpingo-oophorectomy. Gross examination of the cervix revealed that the cut surface of the tumor was white and that the cervix had been completely replaced by the tumor (Fig. 4). Histologically, the surface of the tumor had a leaf-like papillary appearance, with a benign-appearing glandular epithelium (Fig. 5a, b). There was also a distinctive band of hypercellular stroma surround-

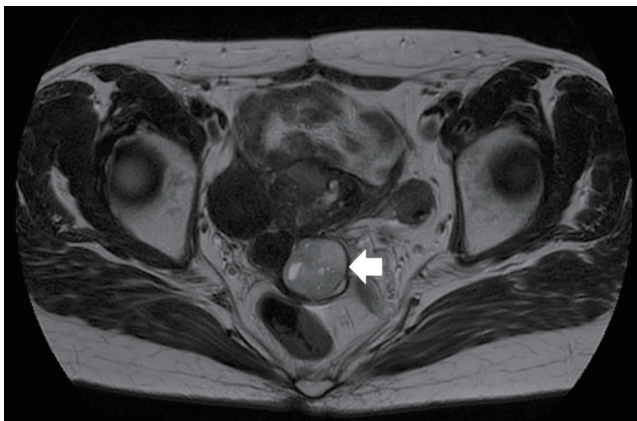


Figure 3. Multiple hyperintense small cysts inside the tumor on T2-weighted imaging (arrow).

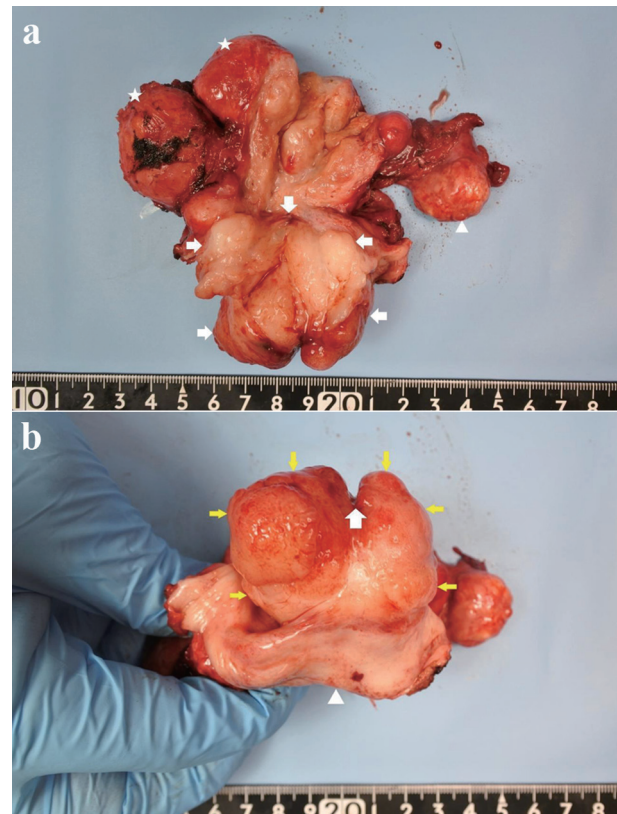


Figure 4. (a) Gross pathological specimen showing a mass occupying the entire cervix (arrowhead: ovary, star: leiomyoma, arrow: cervical tumor). (b) Cervix replaced by the tumor, as seen from the vaginal side (arrow: external os with an incision at 12 o'clock; yellow arrow: cervix; arrowhead: vaginal wall).

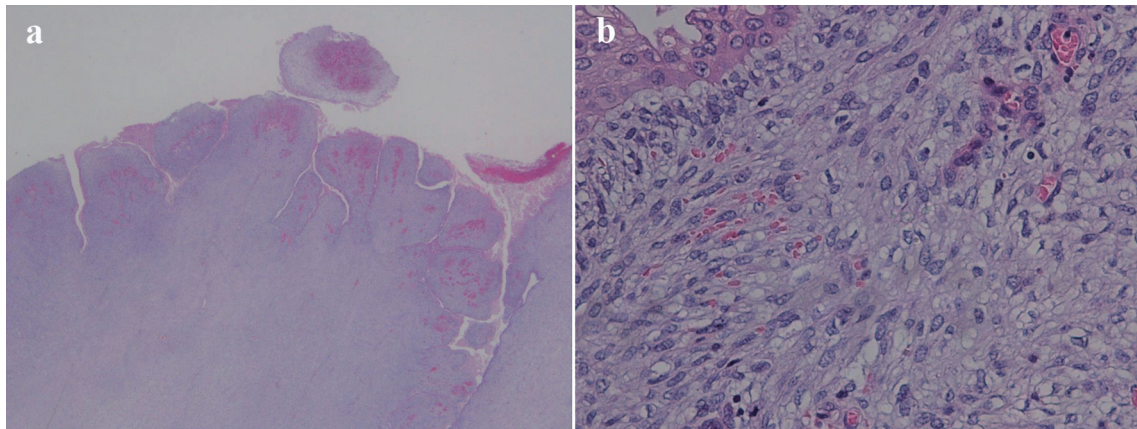


Figure 5. (a) Low-power field showing characteristic leaf-like architecture (hematoxylin and eosin staining, magnification × 10). (b) Papillary stromal fronds lined by benign epithelium accompanied with squamous metaplasia. The stromal cells show mild nuclear atypia and mild pleomorphism (hematoxylin and eosin staining, magnification × 200).

ing the glandular epithelium, known as periglandular cuffing (Fig. 6a, b). The mean mitotic count of the tumor was 2 per 10 high-power fields (Fig. 7). These findings confirmed cer-

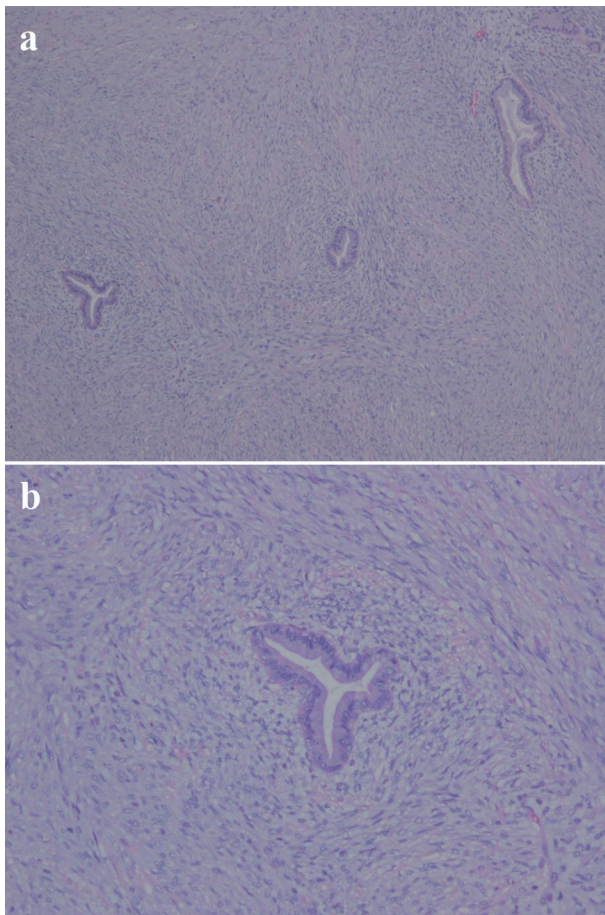


Figure 6. (a) Subepithelial condensation of the stroma; periglandular cuffing (hematoxylin and eosin staining, magnification × 40). (b) Hypercellular stroma and high cellularity beneath the epithelium (hematoxylin and eosin staining, magnification × 100).

vical adenosarcoma from the removed uterus. Adenosarcoma has been associated with endometriosis, although only few reports support this association [6, 7]; however, there were no findings of endometriosis in the excised uterus and bilateral adnexa.

No immunostaining is specifically positive for adenosarcoma. However, the cytoplasm in adenosarcoma stromal cells is often positive for CD10, and the nucleus is often positive for estrogen receptors, progesterone receptors, and P53 [8]. In the present case, the stromal cell cytoplasm was positive for CD10, and the glandular epithelium nuclei were positive for estrogen receptors but negative for progesterone receptors. Nonspecific nuclear staining for P53 was noted, which was interpreted as wild-type (Fig. 8).

Follow-up and outcomes

She has been followed up for the last 10 months without any adjuvant therapy after the surgery.

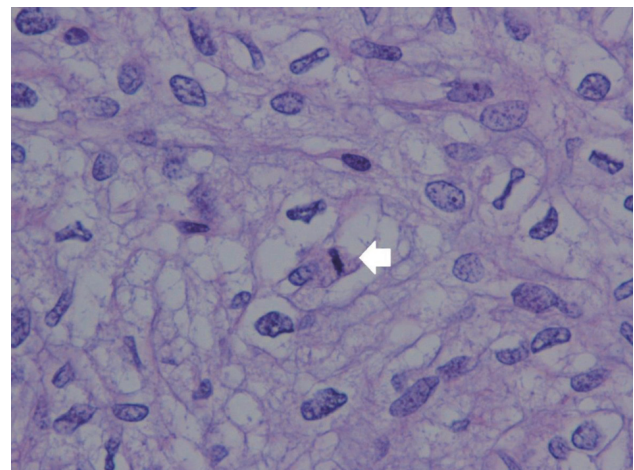


Figure 7. Stromal atypia with mitosis in the stromal element (arrow) (hematoxylin and eosin staining, magnification × 400).

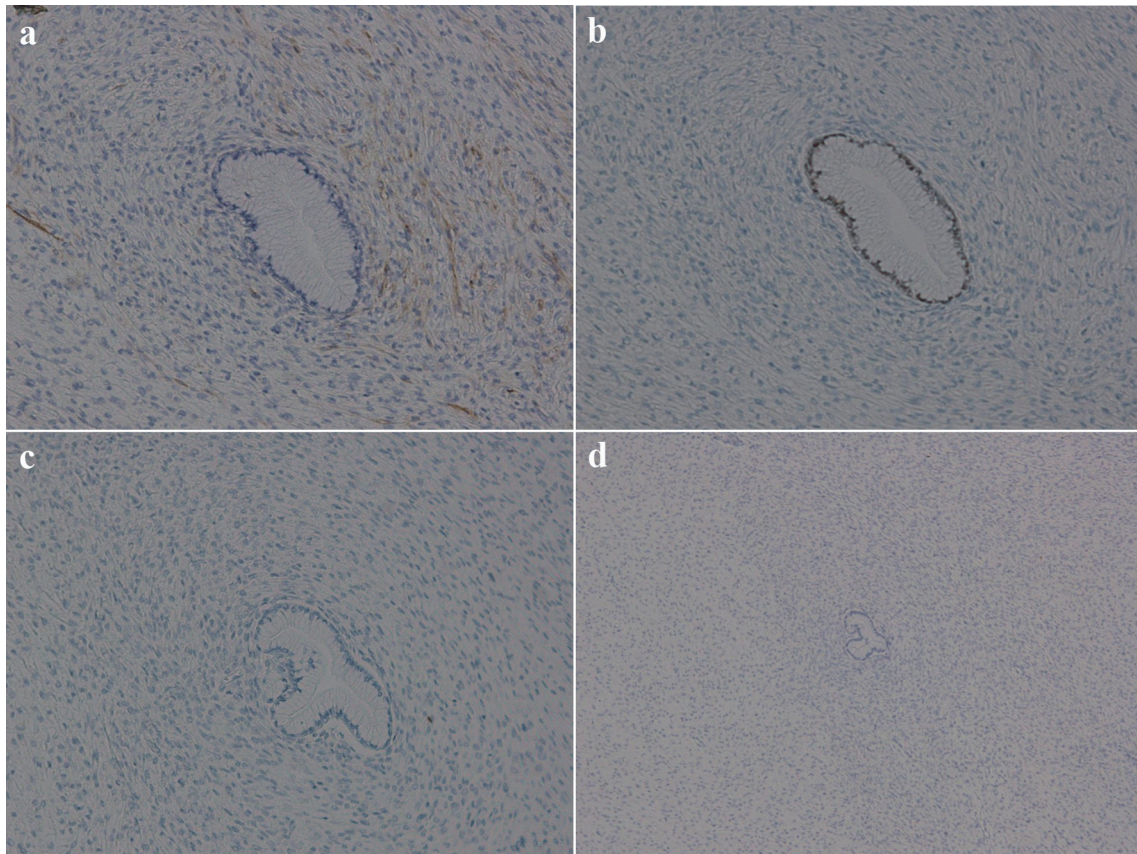


Figure 8. Immunohistochemical findings of the tumor. (a) Stromal cell cytoplasm positive for CD10 (magnification, $\times 100$); (b) glandular epithelia nuclei positive but stromal cell nuclei negative for estrogen receptors (magnification, $\times 100$); (c) both glandular epithelia nuclei and stromal cell nuclei negative for progesterone receptors (magnification, $\times 100$); (d) stromal cell showing wild-type pattern for P53 (magnification, $\times 40$).

Discussion

An accurate diagnosis of adenosarcoma solely on the basis of preoperative imaging, clinical symptoms, and pathological biopsy findings without surgery is difficult. This may be because of the following three reasons.

First, in diagnostic imaging for adenosarcoma, several studies have reported cysts in polypoid lesions that appear hypo- and hyperintense on T1-weighted images and T2WI, respectively [9, 10]. However, this finding is not unique to adenosarcomas; it is also observed in adenomyomas or atypical polypoid adenomyomas with intimal glands within the myometrium [11]. In our case, the tumor had high attenuation with hyperintense cysts on T2WI and moderately low ADC. In sarcomas, ADC restriction is known to demonstrate high attenuation on DWI; however, our case demonstrated high attenuation on DWI and mild diffusion restriction on ADC. These findings are similar to those of cystic/myxoid degeneration, which is difficult to distinguish from sarcomas [12]. In addition, the cervix in our case was found to have moderately increased uptake by PET, which prompted further examination. Although a negative FDG image may exclude the possibility of uterine sarcoma, even benign uterine tu-

mors can be FDG-positive, which is said to be related to age and inflammation [13].

Second, cervical adenosarcomas are often extroverted and appear as polypoid tumors. Therefore, cervical adenosarcomas protrude into the vagina and are often misdiagnosed as cervical polyps [14, 15]. However, in our case, the tumor developed such that it replaced the cervix and exhibited an endophytic growth pattern. Tumors showing an exophytic growth pattern can often be biopsied as sufficient tissue samples are available for pathological diagnosis. In contrast, tumors showing endophytic growth pattern may not be diagnosed even with adenosarcoma as the amount of tumor tissue available for a biopsy is small. In our case, the biopsy did not indicate adenosarcoma as mitosis, phyllodes-like architecture, and periglandular cuffing were not observed in the tumor cells. However, pathological analysis of the resected uterus revealed mitosis of stromal cells, phyllodes-like architecture, and periglandular cuffing, leading to the diagnosis of cervical adenosarcoma.

Despite the tumor measuring 4 cm, vaginal bleeding was noted only once at 6 months before diagnosis as faint brown discharge. This may be attributed to the tumor's growth pattern; tumors showing an exophytic growth pattern usually appear polypoid or papillary. Such tumors then grow into the

vaginal cavity and cause vaginal bleeding. In contrast, tumors showing an endophytic growth pattern infiltrate and eventually replace the cervix without any visible surface growth [16]. Therefore, the squamous epithelium of the cervix may remain intact even if the diameter of the tumor exceeds 4 cm. As the squamous epithelium is intact, bleeding may not occur. The tumor in the present case exhibited an endophytic growth pattern; therefore, no bleeding occurred despite the entire cervix being replaced by the tumor.

Third, although we performed a biopsy on the tumor, no definitive pathological diagnosis was made. In this case, cervical adenosarcoma was pathologically diagnosed after hysterectomy. If biopsy results indicate a mesenchymal tumor, the presence of adenosarcoma should still be considered even in the absence of mitosis or other malignancy characteristics on imaging. Hence, it is necessary to completely excise the tumor and evaluate it pathologically.

A well-established poor prognostic factor of uterine adenosarcoma is the surgical stage, which primarily indicates deep muscle infiltration and extrauterine extension [17]. Although the examination of pathological factors is limited to single-center data, an examination of previous cases of uterine adenosarcoma indicates that sarcomatous overgrowth or heterologous elements, such as pathological factors, indicate a poor prognosis [18, 19]. Systemic anticancer drug treatment is the best option for patients with relapse or distant metastasis. However, the optimal first-line treatment remains unclear because of the lack of large-scale, multicenter, prospective studies. Our case did not present with sarcomatous overgrowth or heterologous elements; however, the prognosis was poor as the tumor had replaced the cervix entirely. Moreover, the efficacy of adjuvant therapy for patients with a poor prognosis has not been established; therefore, we decided to follow-up the patient without adjuvant therapy.

Conclusions

Adenosarcomas are low-grade stromal tumors with benign epithelium. Therefore, nuclear mitosis or atypia of tumor cells may be overlooked depending on the amount of tissue collected. As a result, several reports have indicated that recurring cervical polyps are finally diagnosed as adenosarcoma [14, 15].

If cervical biopsy reveals a mesenchymal tumor, the presence of an adenosarcoma should be considered. Tumor resection, including hysterectomy, should be performed, and the whole tumor should be pathologically evaluated even if the biopsied specimen does not show mitosis and there is no evidence of malignancy on imaging.

Learning points

Adenosarcomas can originate in the cervix. Although adenosarcomas usually cause genital bleeding, cervical adenosarcoma showing an endophytic growth pattern may not lead to vaginal bleeding. Even if the cervical biopsy results reveal a mesenchymal tumor and there is no evidence of malignancy

on imaging, the presence of adenosarcoma should be considered.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Informed consent was obtained from the patient prior to completing the case report.

Author Contributions

ELS and SiI contributed to the writing of the manuscript. TK, RK, MM, and YS reviewed and adjusted the manuscript prior to submission.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

MRI: magnetic resonance imaging; DWI: diffusion-weighted imaging; ADC: apparent diffusion coefficient; T2WI: T2-weighted imaging

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