

# Mullerian adenosarcoma of the uterine cervix misdiagnosed as an endocervical polyp on magnetic resonance imaging and two preoperative consecutive biopsies: A diagnostic challenge

Eun Hee Yu<sup>1,\*</sup>, Yong Jung Song<sup>1,\*</sup>, Seul Yi Lee<sup>1</sup>, Seo Yoon Hwang<sup>1</sup>, Nam Kyung Lee<sup>2</sup>, Kyung Un Choi<sup>3</sup>,  
Dong Soo Suh<sup>1,4</sup>, Ki Hyung Kim<sup>1,4</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Pusan National University School of Medicine, Busan 49241, Republic of Korea

<sup>2</sup>Department of Radiology, Pusan National University School of Medicine, Busan 49241, Republic of Korea

<sup>3</sup>Department of Pathology, Pusan National University School of Medicine, Busan 49241, Republic of Korea

<sup>4</sup>Biomedical Research Institute, Pusan National University Hospital, Busan 49241, Republic of Korea

## Summary

Mullerian adenosarcoma of the uterine cervix generally displays cervical polyps and can be often misdiagnosed as benign endocervical polyps both clinically and pathologically. A 52-year-old woman presented with a two-month history of postmenopausal bleeding. Pelvic examination revealed a large polyp-like mass protruding from the cervical os. Two preoperative consecutive biopsies showed a histologic diagnosis consistent with an endocervical polyp. Pelvic magnetic resonance imaging (MRI) depicted a lobulated well-enhancing endocervical mass, suggestive of an endocervical polyp based on the apparent diffusion coefficient (ADC) value. The patient was subjected to total hysterectomy with bilateral salpingectomy. Microscopically, the tumor was composed of epithelial and stromal components. The final pathologic diagnosis was Mullerian adenosarcoma of the cervix. The authors presented an unusual case that demonstrated an endocervical polyp on magnetic resonance imaging and two consecutive biopsies preoperatively.

**Key words:** Endocervical polyp; Mullerian adenosarcoma; Uterine cervix.

## Introduction

Mullerian adenosarcoma (MA) is a rare gynecologic tumor with low malignant potential, typically encountered in women with younger age. It mainly involves the endometrium, ovary or pelvis; cervical involvement is exceedingly uncommon [1]. Characteristically, MA consists of benign epithelial and malignant sarcomatous stromal components. The malignant sarcomatous stromal elements are usually low-grade and can either be homologous (such as fibroblast or smooth muscle) or heterologous (such as cartilage, striated muscle or bone) [1]. MAs frequently present as soft polypoidal masses [1]. Notably, MAs present diagnostic challenges because they commonly resemble benign cervical polyps clinically, radiologically and pathologically [2]. Therefore, proper differentiation between both entities, through histologic confirmation, is central to establish the definitive diagnosis [3]. Herein, we present an unusual case of cervical MA that demonstrated a preoperative diagnosis consistent with an endocervical polyp based on magnetic resonance imaging (MRI) and two consecutive preoperative biopsies.

## Case Report

A 52-year-old woman presented with a two-month history of postmenopausal bleeding. Pelvic examination revealed a large polyp-like mass protruding from the cervical os. Two preoperative consecutive biopsies showed a histologic diagnosis consistent with an endocervical polyp. Preoperative serum cancer antigen 125 (CA 125) level was within normal limits. MRI was carried out to further portray the mass and depicted a lobulated well-enhancing endocervical mass with hypointensity on T1-weighted images and slight hyperintensity on T2-weighted images. The mass measured about 60 × 36 mm in the maximum diameter and extended into the vagina. No parametrial invasion or retroperitoneal lymph nodes were identified. Diffusion-weighted imaging (DWI) at b = 1000 s/mm<sup>2</sup> showed hyperintensity and the mean apparent diffusion coefficient (ADC) measured 1.33 × 10<sup>-3</sup> mm<sup>2</sup>/s on the ADC map. The MRI findings were suggestive of an endocervical polyp based on the high mean ADC value (Figure 1).

A differential diagnosis of cervical cancer was contemplated. In consideration of a giant endocervical polyp of more than 4 cm based on two histologic results and MRI findings, the patient underwent total hysterectomy with bilateral salpingectomy. Macroscopically, an exophytic poly-

\*Contributed equally.

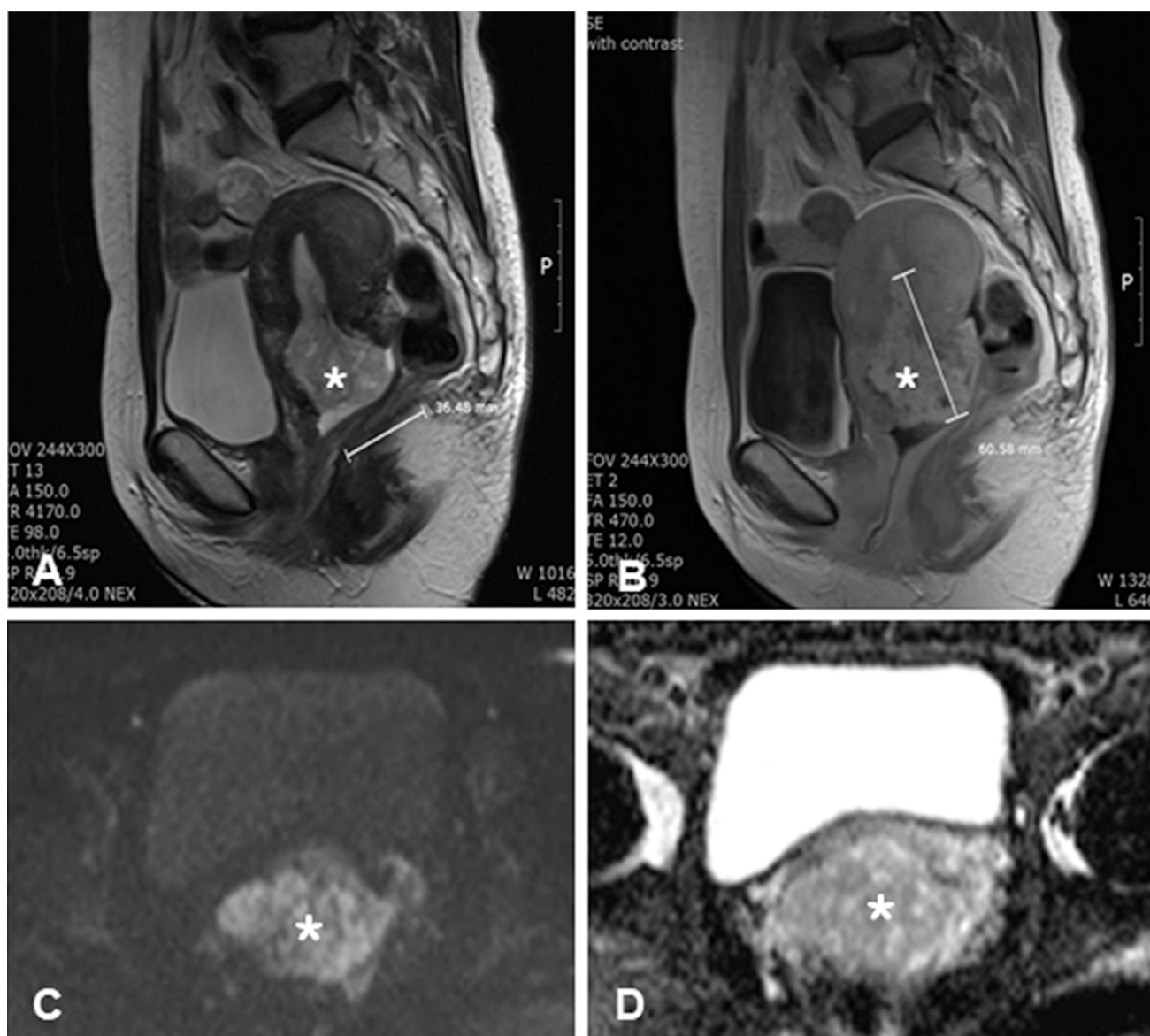


Figure 1. — Magnetic resonance imaging (MRI) features of Mullerian adenosarcoma of the cervix. (A) Sagittal T2-weighted image shows a hyperintense mass (\*) within the endocervical canal. (B) Sagittal contrast-enhanced T1-weighted image shows the enhancement (\*) of the endocervical mass. The tumor (\*) on DWI ( $b = 1000 \text{ s/mm}^2$ ) shows hyperintensity (C), and the ADC value on ADC map is  $1.33 \times 10^{-3} \text{ mm}^2/\text{s}$  (D). ADC: apparent diffusion coefficient; DWI: diffusion-weighted imaging.

roid mass arising from the cervical canal was observed (Figure 2). Microscopically, the tumor displayed a leaf-like architecture and was composed of epithelial and sarcomatous stromal components. The epithelium was bland and the underlying cellular stroma showed mild atypia and periglandular cuffing (Figure 2). No cervical stromal invasion or lymphovascular tumor emboli were identified. Additionally, there were no heterologous elements or sarcomatous overgrowth. The vaginal mucosa, parametrium and both fallopian tubes were tumor-free. The final International Federation of Gynecology and Obstetrics (FIGO) stage was IB. Immunohistochemically, cytokeratin and vimentin highlighted the biphasic epithelial and stromal com-

ponents of the tumor, respectively. Moreover, the tumor stromal component stained positive for estrogen receptor (ER), progesterone receptor (PR) and cluster of differentiation 10 (CD10) cell surface receptors (Figure 3).

Based on the tumor's histologic and immunohistochemical features, the final postoperative diagnosis was consistent with a cervical MA without heterologous elements or sarcomatous overgrowth. The postoperative course was uneventful and the patient received three cycles of adjuvant chemotherapy comprising cisplatin and ifosfamide. At 30 months postoperatively, the patient was disease-free without any proof of recurrence.

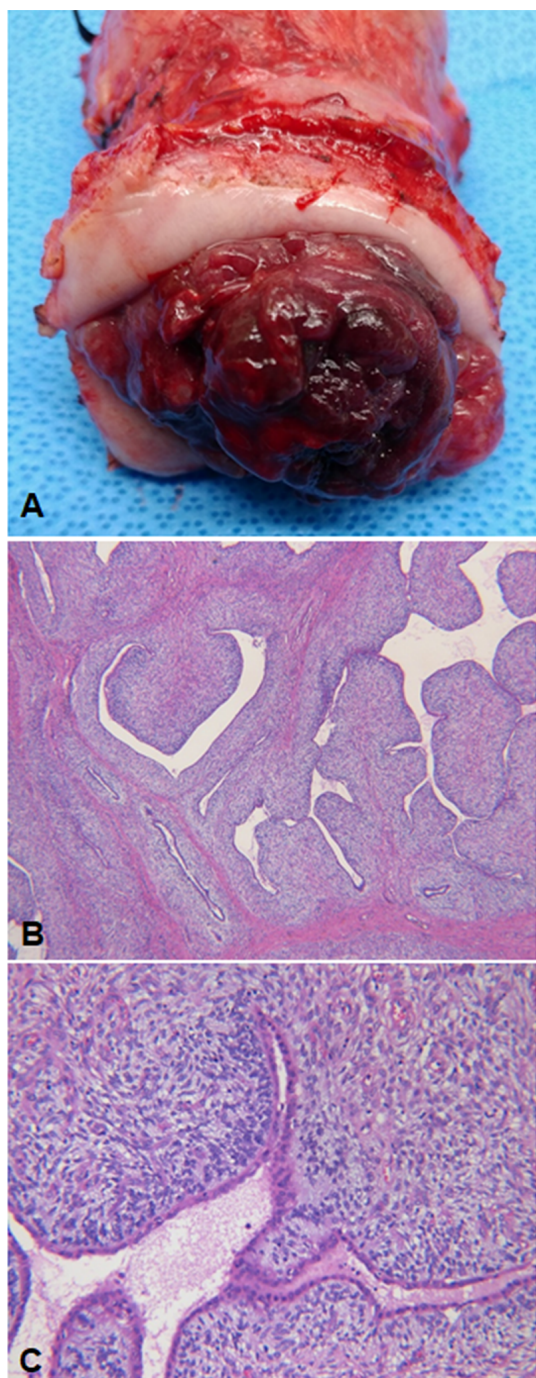


Figure 2. — Gross and microscopic findings of Mullerian adenosarcoma. (A) The cervix shows a large polypoid mass. (B) The tumor displays a leaf-like architecture without heterologous elements or sarcomatous overgrowth (H&E,  $\times 40$ ). (C) The epithelium is bland and the underlying cellular stroma shows mild atypia and periglandular cuffs (H&E,  $\times 100$ ). H&E: hematoxylin and eosin.

## Discussion

Cervical MAs are relatively rare tumors. Overall, 71% of MAs are observed in the endometrium, 15% in the

ovaries, 12% within the pelvis and only 2% in the cervix [3]. Biologically, MAs behave as low-grade malignant tumors and they are capable of recurring locally but distant metastases are rare [1]. The risk of recurrence of cervical MAs without sarcomatous overgrowth is only 10–20%. Although possible risk factors are suggested, the definitive etiologic factors implicated in cervical MA tumorigenesis remain unknown. The most frequently presenting symptom of cervical MAs is abnormal vaginal bleeding, as depicted in our case. Other reported presenting symptoms include abdominopelvic pain, malodorous vaginal discharge and pelvic space-occupying pressure complaints [1]. Pelvic examination usually shows cervical polypoid lesions protruding from the external cervical ostium to the vagina. Cervical MA tends to be observed more often in younger females in the reproductive age compared to endometrial MA in postmenopausal women [3, 4].

The diagnosis of cervical MAs is challenging owing to the commonly shared similarities with benign cervical polyps clinically, radiologically and pathologically. In a large clinicopathologic series of patients with cervical MAs, the clinical impression is frequently benign endocervical polyps based on the most common finding of protruding polypoid or papillary masses from the external cervical ostium [1]. Typically, patients with cervical MAs often report a history of recurrent polyps, clinically and pathologically, before the final cervical MA diagnosis is established [2].

Conventional MRI is an essential radiologic utility with excellent soft tissue contrast resolution. The MRI findings of cervical lesions correlate with the histopathologic features. However, previous literature suggests that the radiologic features of benign and malignant lesions overlap [5].

The DWI values may be helpful in discerning benign and malignant lesions observed in the uterine cavity [6, 7]. Hase *et al.* suggested that most of the DWI signal intensities of endometrial polyps were largely isointense or hypointense [6, 8]. Furthermore, they proposed that the differences of DWI signal intensities might be caused by the tumor cellular density, lesion vascularity or water content in the extracellular space [6]. Similar to the present study, some benign endometrial lesions may persistently show the hyperintensity on high b value DWI due to the T2 shine-through effect [9]. Therefore, DWI values must be interpreted along with the corresponding ADC map.

Previous studies demonstrate that the combined DWI and ADC values can aid in differentiating between normal and cancerous tissues in the cervix and endometrium [6]. In fact, ADC values differ significantly between benign and malignant lesions of the cervix; they usually show lower values in malignant lesions (range:  $0.8\text{--}0.98 \times 10^{-3} \text{ mm}^2/\text{s}$ ) and higher values in benign lesions (range:  $1.27\text{--}1.58 \times 10^{-3} \text{ mm}^2/\text{s}$ ) [6, 7]. McVeigh *et al.* reported that the average median ADC values of cervical cancers were significantly lower than that of normal cervix ( $1.09 \pm 0.20$  versus  $2.09 \pm 0.46 \text{ mm}^2/\text{s}$ , respectively) [10]. Kuang *et al.* reported that the ADC values of cervical cancer, leiomyoma



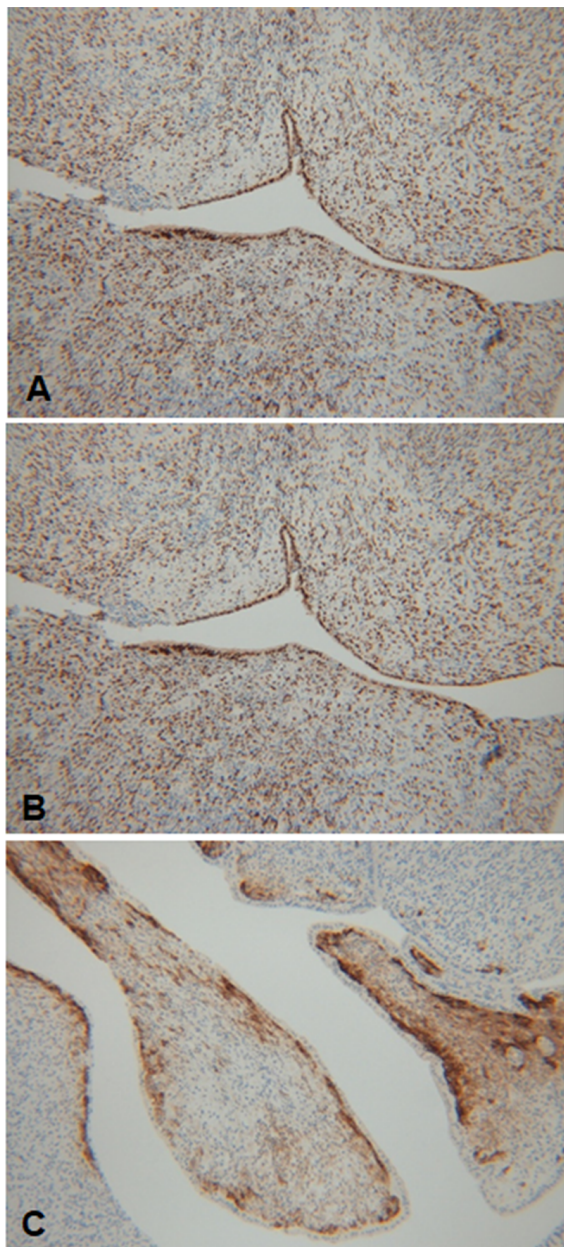


Figure 3. — Immunohistochemical results. The stromal component is positive for ER (A), PR (B) and CD10 (C). CD10: cluster of differentiation 10; ER: estrogen receptor; PR: progesterone receptor.

and cervical polyp were  $0.81 \pm 0.13$ ,  $1.26 \pm 0.13$  and  $1.31 \pm 0.19$  mm<sup>2</sup>/s for the b value = 1000 s/mm<sup>2</sup>, respectively [11]. In the present study, the ADC value was  $1.33 \times 10^{-3}$  mm<sup>2</sup>/s, suggestive of a benign polypoid rather than malignant lesion. Interestingly, the final histopathologic diagnosis of MA was inconsistent with the benign lesion value of the ADC.

Chin *et al.* mentioned that the initial tendency to misdiagnose MAs as benign cervical polyps could be ascribed to the random distribution of the malignant stromal components present in the endocervical curettage material [12].

In cervical lesions with patchy stromal condensations, the endocervical curettage may easily miss the detection of increased cellularity, nuclear atypia and mitotic activity [2]. Moreover, typical histologic features, such as eccentrically shaped glands containing prominent branching, separate periglandular cellular stroma, active mitosis of atypical stromal cells and epithelial lining with altered differentiation, may be unapparent in small biopsy specimens [2]. If the cervical lesion is large, the endocervical biopsy tends to be done superficially. Histologic diagnosis prior to surgery may be vulnerable to sampling errors in large tumors due to tumor heterogeneity. Thus, thorough sampling accompanied by careful pathological examination is critical to establish the definitive diagnosis. MA shares histologic features similar to polyps of benign epithelial glands. In the present case, the initial cervical biopsy was reviewed and there was no evidence of MA findings.

Immunohistochemistry revealed that stromal component of MA was positive for cell differentiation markers, such as ER, PR, and CD10, as in the present case. Such pattern is similar to low-grade endometrial stromal tumors. However, significant differences are noticed in the immunohistochemical profile of MA with sarcomatous overgrowth; ER, PR, and CD10 expressions are negative and the absence of these markers substantially correlate with prognosis [13]. The differential diagnosis of MA includes adenofibroma and endocervical polyp, both of which exhibit benign epithelial and stromal components. They may be difficult to be distinguished microscopically from MA. However, cellular stromal features of phyllodes-like growth, periglandular cuffing and cytologic atypia are often lacking in adenofibromas and endocervical polyps [14, 15].

The optimal management of MA is not determined because of its rarity and lack of evidence that any particular treatment is more beneficial than other therapies. Surgery is the mainstay of treatment for cervical MA. Local resection, such as polypectomy, has been curative in some cases with superficial disease. In the present case, due to the large polypoid mass, easy-touch bleeding and invisible proximal end of the mass, polypectomy alone was not feasible; the patient was subjected to total hysterectomy. There is an inadequate evidence to suggest that adjuvant radiotherapy or chemotherapy improves overall survival for patients with MA [3, 13]. The stromal component of MA is largely responsible for the clinical behavior. MA of the cervix has a low malignant potential and generally carries a good prognosis. A large body of literature highlights unfavorable prognostic factors implicated in MA, such as sarcomatous overgrowth, heterologous elements, high mitotic rate, myometrial invasion, necrosis, extrauterine metastases and tumor size [3, 16, 17]. In the present study, there were no heterologous elements or sarcomatous overgrowth, however, the tumor size was  $\geq 6$  cm in the maximum diameter. At 30 months postoperatively, the patient showed no evidence of recurrence.

## Conclusions

MA of the cervix is an uncommon tumor with a low malignant potential. This case stresses that MA commonly resembles benign cervical polyps clinically and pathologically; thus MA may be easily misdiagnosed. Although extremely rare, however, the differential diagnosis of cervical MA should be considered in postmenopausal patients presenting with abnormal uterine bleeding and large cervical polyps.

## Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Pusan National University Hospital. Informed consent for participation in the study or use of their medical data was obtained from all participants.

## Acknowledgments

KH Kim conceived and designed this study. EH Yu drafted the manuscript. SY Lee and SY Hwang collected and assembled data. YJ Song, NK Lee, and KU Choi performed the data analysis and interpretation. KH Kim and DS Suh participated in the design and coordination of this study in addition to revising and critiquing the manuscript. All authors read and approved the final manuscript.

## Conflict of Interest

The authors declare that they have no competing interests.

Submitted: March 22, 2019

Accepted: June 18, 2019

Published: December 15, 2020

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Corresponding Author:

KI HYUNG KIM, M.D.

Department of Obstetrics and Gynecology,  
Pusan National University School of Medicine,  
179, Gudeok-Ro, Seo-Gu, Busan 49241, Republic of Korea.

e-mail: ghkim@pusan.ac.kr