

# Endometrial Adenocarcinoma with Pattern of Invasion Resembling Adenoma Malignum

Case Report  
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## Author Details

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## Abstract

Endometrial adenocarcinoma with a glandular invasion pattern resembling adenoma malignum of cervix is a deceptively benign and highly differentiated form of endometrioid adenocarcinoma which can be resistant to radiation therapy and exhibit a deep invasion pattern. We report a 57-year-old female who was a biopsy-proven case of FIGO grade 2 endometrial adenocarcinoma with 4 cm cervical involvement, who underwent whole pelvic radiation therapy followed by hysterectomy. Her hysterectomy sections revealed conventional endometrioid adenocarcinoma with a deceptively bland pattern of well-spaced, branching glands with myometrial invasion up to 90%. Extensive lymphovascular space invasion was identified and cervical stroma was involved. Immunohistochemistry was consistent with an endometrial origin. The final diagnosis was endometrial adenocarcinoma with adenoma malignum pattern of invasion. It is not clear whether the gland morphology was due to radiation treatment however, the widespread and extensive invasion makes it imperative to recognize that these patients need to be vigilantly followed up. It is important to recognize this entity because these deeply invasive and benign appearing glands can be resistant to the conventional approach of radiation treatment and highlights the fact that the patient needs to be cautiously staged and accordingly treated.

**Keywords:** Endometrial adenocarcinoma; Minimal deviation; Adenoma malignum; Uterus; Pelvic radiotherapy

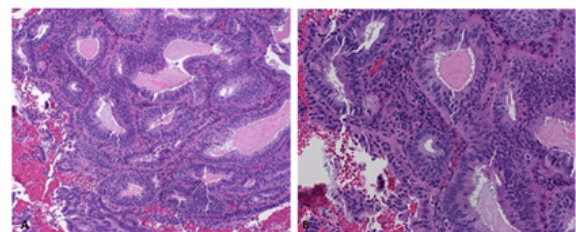
## Introduction

Adenoma Malignum (AM) or Minimal Deviation Adenocarcinoma (MDA) of the cervix has been described in the literature as a highly deceptive form of mucinous adenocarcinoma of endocervix with benign morphology of glands and an extremely invasive pattern [1,2]. A similar entity has been described for well-differentiated endometrial adenocarcinoma in which the glands are extremely well-differentiated and exhibit deep myometrial invasion [3]. Here, we present a case of an endometrial adenocarcinoma with an invasion pattern resembling minimal deviation adenocarcinoma of the cervix and will be discussing associated pitfalls and treatment challenges.

## Case Presentation

We present a 57-year-old postmenopausal female, known case of hypertension, diabetes, and morbid obesity (Body mass index of 45) who presented with a single episode of heavy vaginal bleeding. The patient did not have any prior reportable gynecological or surgical history. Her transvaginal ultrasound revealed a heterogeneous uterus and a left adnexal cystic mass which was noted to be 13.5 x 6.5 x 6.8 cm. The patient was taken to the operating room for examination under

anesthesia due to vaginal bleeding where a large cervical mass (up to 4 cm) was seen and biopsied (Figure 1). Results showed the mass was an adenocarcinoma of endometrial origin grade 1.

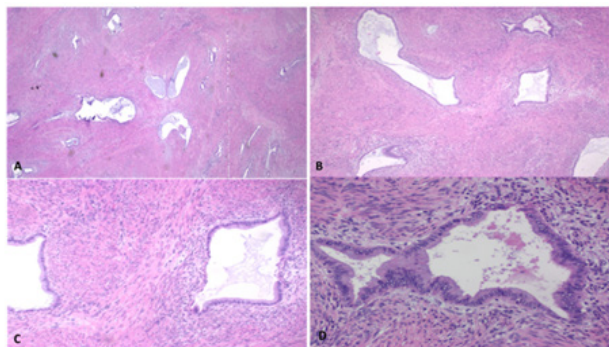


**Figure 1:** Hematoxylin and eosin-stained sections (A: 10x and B: 20x) of initial cervix biopsy showed conventional FIGO grade 1 endometrial carcinoma, endometrioid type.

A left salpingo-oophorectomy and biopsy was also performed, showing the adnexal mass to be a fibrothecoma. The patient was reviewed to be a stage 2 endometrial cancer with 4 cm cervical involvement. She was counseled to receive radiation therapy followed by surgery.

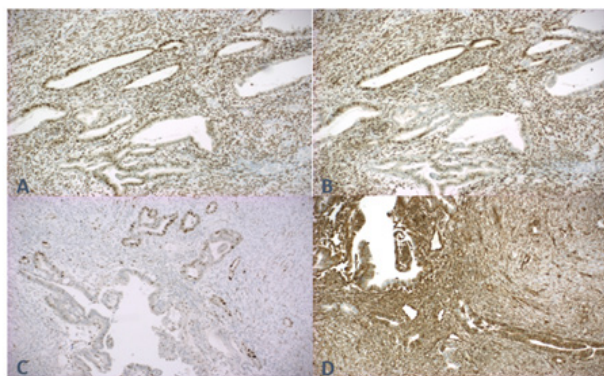
The patient completed whole pelvic radiation therapy (4500cgy, 2 brachytherapy doses (1200cgy). Two months later, she had a laparoscopic hysterectomy and right salpingo-oophorectomy.

Hematoxylin and eosin staining of sections of the uterus (Figure 2) revealed endometrioid adenocarcinoma with a deceptively bland pattern of well-spaced, branching glands with myometrial invasion up to 90%. The glands were lined by uniform columnar cells and benign morphology. No atypical features were identified in the deeply invading glands. Extensive lymphovascular space invasion was present and the cervical stroma was also involved.



**Figure 2:** Hematoxylin and eosin staining of subsequent hysterectomy sections (A: 10x, B-C: 20 x, and D: 40x) revealed a benign pattern of well-spaced deeply invasive branching glands lined with uniform columnar cells and minimal atypia.

Immunohistochemistry (IHC) was performed to confirm endometrial origin; the invasive glands were positive for estrogen and progesterone receptors (Figure 3A & 3B respectively). The p53 was positive for some tumor cells (around 5-8%) consistent with wild type (Figure 3C); vimentin was positive (Figure 3D). CDX2 and CEA were negative and ruled out intestinal origin of these glands whereas mucicarmine and p16 were patchy positive.



**Figure 3:** Immunohistochemistry of hysterectomy sections confirmed that the invasive glands were positive for estrogen and progesterone receptors (A and B respectively). p53 (Figure C) was positive (wild type) and vimentin (Figure D) was diffusely positive.

The overall morphological and immunohistochemical features were consistent with endometrioid adenocarcinoma with adenoma malignum invasion pattern. Mismatch repair IHC showed intact nuclear expression of MLH1, MSH2, MSH6, and PMS2; which ruled out Lynch syndrome associated malignancy. Other molecular studies and gene sequencing (e.g., for POLE mutation status) were not performed. The patient was discharged on a close follow-up schedule by Gynecology/Oncology. The patient survived and is currently doing well.

## Discussion

Initially, Minimal Deviation Adenocarcinoma (MDA) of the cervix was initially described as a highly differentiated form of mucinous adenocarcinoma of the endocervix, with benign morphology of glands and an extremely invasive pattern [1,2]. Endometrioid adenocarcinoma with an adenoma malignum pattern of myometrial invasion has not been clearly described in the literature. Only a few cases have been reported and most of them were associated with conventional endometrioid adenocarcinoma [3-6].

Most of the uterine corpus cases are linked to the well-established cases of minimal deviation adenocarcinoma of cervix however, we noted key differences between them, leading us to believe they are most likely to be two separate entities [3,4]. Our patient did not present with the most common presentation for MDA of the cervix, a complaint of copious, mucinous vaginal discharge; instead she had an episode of heavy vaginal bleeding and was found to have endometrial adenocarcinoma. Our patient didn't respond to radiation therapy and deeply invading glands with minimal treatment response were identified in her post-radiation hysterectomy specimen.

Immunohistochemistry ruled out a cervical origin and our case was confirmed to be a primary endometrial tumor. This can be a challenging diagnosis considering the deceptively benign appearance of these glands and no surrounding stromal response [3-6]. The main differential diagnosis in such circumstances is adenomyosis due to similar appearance of glands. Another possibility which needs to be considered is the post-radiation changes in the appearance and morphology of these glands and further studies and follow-up is needed to establish the etiology of these deceptively benign looking but deeply invasive glands [7,8].

Radiography has limited role and identification of these glands as the reported cases of MDS cervix showed mixed solid and cystic patterns [9-14]. Guo et al [10] described multiple cervical cysts in the Magnetic Resonance Imaging (MRI) of a more conventional case of MD cervix [10]. Oguri et al [11] described similar findings of a cervical cyst in the MRI of a case of MDA cervix [11]. The cyst appeared to be high T2WI and low T1W1 with an irregular septum along with fine and rough granules [11].

Nonspecific features like a heterogeneously enlarged uterus might be helpful but the reliance is on a pathologist to better identify and characterize those deeply invasive glands. Kaminski et al [12] described that the conventional MDA cervix usually grows slowly and the glands appear distorted with an irregular outline and deep stromal invasion [12]. Ding et al [13] reported ultrasound findings of a hypoechoic lesion surrounded by a echogenic ring [13]. Takatsu et al [14] reported a predominantly solid pattern of MDA cervix on MRI [14]. It is therefore postulated that the diagnosis of MDS cervix should be made more reliably on histopathologic analysis rather than radiology. Li et al [15] have emphasized the importance of early diagnosis and appropriate treatment of MDS cervix to improve prognosis [15]. Similar criteria can be applied to cases of endometrial carcinoma with invasion pattern resembling MDA cervix however, more studies are needed to appropriately identify those cases.

## Conclusion

This interesting case shows that endometrial adenocarcinoma with adenoma malignum invasion pattern may present with a deceptively benign appearance of widely spaced and deeply invasive glands with no mitosis and minimal atypia. Despite its benign-looking appearance, endometrial adenocarcinoma with this pattern can be resistant to radiation therapy. Increased awareness of this phenomenon is needed to appropriately treat these patients and a more vigilant follow-up



is required. It is also suggested to report this pattern separately in the pathology report. It is important to realize the existence of this pattern in the uterine corpus (in addition to MDA of the cervix) and more studies are needed to determine any possible correlation between radiation treatment and conventional endometrial adenocarcinoma.

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