

## Adenomyosis involved by endometrial adenocarcinoma is a significant risk factor for deep myometrial invasion

Nadia Ismiil, MD, FRCPC<sup>a,\*</sup>, Golnar Rasty, MD<sup>a</sup>, Zeina Ghorab, MD<sup>a</sup>, Sharon Nofech-Mozes, MD<sup>a</sup>, Marcus Bernardini, MD<sup>b</sup>, Ida Ackerman, MD<sup>c</sup>, Gillian Thomas, MD<sup>c</sup>, Allan Covens, MD<sup>b</sup>, Mahmoud A. Khalifa, MD, PhD<sup>a</sup>

<sup>a</sup>Department of Pathology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada M4N 3M5

<sup>b</sup>Division of Gynecologic Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada M4N 3M5

<sup>c</sup>Radiation Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada M4N 3M5

### Abstract

Adenomyosis is commonly seen in association with endometrial adenocarcinoma where it may or may not be involved by malignancy. This study of grade 1 endometrioid adenocarcinoma investigates whether patients with cancer-positive adenomyosis are at a different risk for deep myometrial invasion compared with those with cancer-negative adenomyosis. Ninety-three hysterectomy specimens with FIGO (International Federation of Gynecologists and Obstetricians) grade 1 endometrial endometrioid adenocarcinoma associated with adenomyosis were studied. Four experienced gynecologic pathologists retrospectively reviewed all hematoxylin and eosin-stained sections. Myometrial invasion was confirmed by CD10-negative staining around glands with jagged outline surrounded by inflamed desmoplastic stroma. Adenomyosis was involved by adenocarcinoma in 46 cases, whereas it was carcinoma-negative in 47 cases. Myometrial invasion was found in significantly more carcinoma-positive adenomyosis cases ( $n = 42, 91.3\%$ ) than with carcinoma-negative adenomyosis cases ( $n = 30, 63.8\%$ ) ( $\chi^2 = 12.10; P = .0005$ ). Moreover, myometrial invasion in the outer half was also seen in significantly more carcinoma-positive adenomyosis cases ( $n = 16, 34.8\%$ ) than with carcinoma-negative adenomyosis cases ( $n = 3, 6.4\%$ ) ( $\chi^2 = 11.53; P = .0007$ ). Among all cases of FIGO grade 1 endometrial endometrioid adenocarcinoma associated with adenomyosis, the ones that extend in the adenomyosis gain more invasive advantage, probably through increasing the surface area of its interface with the adjacent myometrium. When compared with tumors that do not involve adenomyosis, these tumors are not only more likely to invade the myometrium but are significantly more prone to achieve deep invasion into the outer half.

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### Keywords:

Adenomyosis; Endometrial adenocarcinoma; Myometrial invasion; CD10

### 1. Introduction

Endometrial adenocarcinoma is the most common invasive gynecologic malignancy. The depth of myometrial invasion by endometrial carcinoma closely correlates with lymph node metastasis and prognosis. It also predicts the risk for hematogenous recurrence [1]. It is believed that tumors with high FIGO grades are more likely to invade the

myometrium and to extend deep into its outer half [2]. Other tumor factors that have also been claimed to influence myometrial invasion included the nondendometrioid histology [2], oncogene overexpression [3,4], ploidy [5,6], and proliferative activity [6,7]. Given the lack of definitive data regarding the effectiveness of adjuvant therapy in patients with uterine-confined disease, adjuvant therapy is recommended only in selected cases. In grade 1 endometrioid adenocarcinoma, deep myometrial invasion is a key factor in selecting patients for adjuvant treatment. For example, patients with stage IC may be given pelvic radiotherapy or vaginal brachytherapy if adverse risk factors are present.

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\* Corresponding author. Tel.: +1 416 480 4278; fax: +1 416 480 4271.  
E-mail address: [nadia.ismiil@sw.ca](mailto:nadia.ismiil@sw.ca) (N. Ismiil).

Several reports have documented the coexistence of adenomyosis and endometrial adenocarcinoma in hysterectomy specimens with incidences ranging from 16% to 34% [8–12]. When adenomyosis is positive for adenocarcinoma, the tumor may remain within its confines or may progress to invade the adjacent myometrium. Tumor foci limited to adenomyosis have round, smooth contour and are usually surrounded by endometrial stroma and sometimes even benign endometrial glands. The presence of these foci does not affect tumor stage or outcome [9]. However, when the tumor appears to extend from these foci to invade the surrounding myometrium, true myometrial invasion is documented, which might upstage the tumor and confer a worse prognosis.

In this study, we reported on hysterectomy specimens harboring grade 1 endometrial endometrioid adenocarcinoma with coexistent adenomyosis. This work investigates whether patients with cancer-positive adenomyosis are at a different risk for deep myometrial invasion compared with those with cancer-negative adenomyosis.

## 2. Materials and methods

To eliminate the confounding effect of varying tumor grades on myometrial invasion and because most endometrial adenocarcinomas are well differentiated, we limited our analysis to FIGO grade 1 tumors. Patients with FIGO grade 1 endometrial, endometrioid adenocarcinoma treated by hysterectomy with or without bilateral salpingo-oophorec-

tomy were retrieved from pathology files of Sunnybrook and Women's College Health Sciences Center. These cases were accessioned during the period from July 1999 to June 2004. Four experienced gynecologic pathologists retrospectively reviewed all hematoxylin and eosin-stained sections from the hysterectomy specimens and entered their findings in a shared Microsoft Access 2000 database.

Adenomyosis was defined as the presence of endometrial glands and stroma in the myometrium, disconnected from the native endometrium, deeper than one half of a low-powered field, or 2.1 mm [11]. Involvement of adenomyosis by endometrial adenocarcinoma was defined by the presence of neoplastic glands, fulfilling the qualitative and quantitative adenocarcinoma criteria, within the confines of these foci. Myometrial invasion arising from these areas was recorded when irregular clusters or glands with ragged outlines extended into neighboring myometrium surrounded by desmoplastic stromal response in the absence of endometrial stroma (Fig. 1). These areas typically exhibited edema and chronic inflammation [13]. Invasive cells typically acquired eosinophilic cytoplasm. Cancer-positive adenomyosis was only reported in cases where clear evidence of adenomyosis was present elsewhere in the uterus. This criterion was used to eliminate the possibility of overcalling in cases where the adenocarcinoma directly invaded the myometrium in a geographic pattern mimicking that of those extending into adenomyosis.

In cancer-positive adenomyosis with myometrial invasion, immunostaining for CD10 was performed using clone

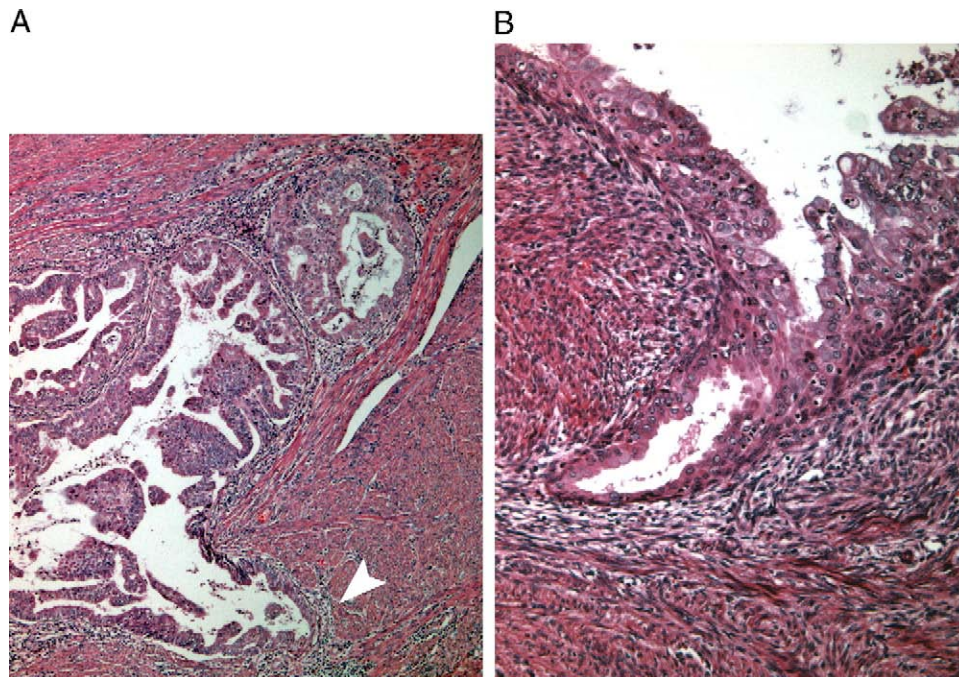


Fig. 1. Cancer-positive adenomyosis showing myometrial invasion. (A) Low-power view of irregular glands directly extending into adjacent myometrium (arrowhead) surrounded by desmoplastic stromal response in the absence of endometrial stroma. (B) High-power view of another focus of pointed invasive gland with eosinophilic malignant cells.

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