Case Report

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Endometrial Carcinoma Arising in Adenomyosis in the Myometrium with Uninvolved Endometrium: A Case Report

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ABSTRACT

Endometrial carcinoma arising in adenomyosis (EC-AIA) is a rare entity that originates deep within the myometrium and often spares the endometrial lining. We report a 53-year-old woman who presented with a vascularized uterine mass invading the bladder (International Federation of Gynecology and Obstetrics [FIGO] stage $\text{III}B_2$). Despite imaging findings suggesting malignancy, endometrial curettage yielded only atrophic cells, and hysterectomy confirmed a histologically normal endometrial cavity. Final pathology revealed endometrioid adenocarcinoma confined to adenomyotic lesions with lymph node involvement. This case underscores a critical diagnostic pitfall: negative endometrial sampling does not exclude EC-AIA. Moreover, applying current FIGO staging systems, designed for endometrial-origin tumors, to EC-AIA presents significant limitations, risking either underestimation of deep invasion or artificial upstaging.

Key words: endometrial cancer arising in adenomyosis; adenomyosis; endometrial neoplasm

INTRODUCTION

Adenomyosis, characterized by the ectopic presence of endometrial glands and stroma within the myometrium, is a common benign condition affecting women of reproductive age[1], yet it harbors a rare potential for malignant transformation into endometrial carcinoma arising in adenomyosis (EC-AIA)[2]. While adenomyosis is frequently found coexisting with endometrial cancer (EC) in hysterectomy specimens[1], EC-AIA represents a distinct and exceptionally rare entity (<1% of EC cases) where the malignancy originates exclusively from the adenomyotic focus, sparing the superficial endometrium[3]. This unique origin poses a significant diagnostic challenge, as the tumor often grows centrifugally toward the serosa rather than the uterine cavity, leading to false-negative endometrial biopsies and delayed diagnosis until advanced local invasion or metastasis occurs[1]. Consequently, patients may present with non-specific symptoms such as abdominal pain rather than the hallmark postmenopausal bleeding, causing EC-AIA to be frequently misdiagnosed as complex adenomyosis or other pelvic malignancies.

Our present report details an exceptionally rare case of EC-AIA in a postmenopausal woman who presented with persistent lower abdominal pain and a negative endometrial biopsy, defying the typical clinical presentation of EC. The uniqueness of this case lies not only in its diagnostic elusiveness due to the intact endometrial lining but also in the aggressive behavior of the tumor, which breached the uterine serosa to invade the bladder and demonstrated the rare finding of ectopic endometrial glands within lymph nodes. Unlike standard EC cases diagnosed *via* abnormal bleeding and positive curettage[1], this case underscores the critical limitation of relying solely on endometrial sampling for patients with a history of adenomyosis. By highlighting the pivotal role of advanced imaging (e. g., magnetic resonance imaging [MRI]) and the necessity of maintaining a high index of suspi-

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cion for EC-AIA in patients with unexplained pelvic pain and elevated CA125[4], this report aims to refine the diagnostic approach and prevent the underestimation of this elusive malignancy.

CASE PRESENTATION

Clinical presentation

A 53-year-old woman (body mass index [BMI] 22.0 kg/m^2, $G_3P_0A_3$), seven years postmenopausal, presented with a six-month history of lower abdominal pain. Initially intermittent and dull, the pain was attributed by the patient to a history of dysmenorrhea, delaying medical consultation. One month prior to admission, the pain became persistent and severe enough to disrupt sleep, with no relief from self-medicated non-steroidal anti-inflammatory drugs (NSAIDs). Notably, she denied any vaginal bleeding, discharge, urinary urgency, dysuria, or constipation. Her past surgical history included a transabdominal adenomyomectomy at age 46. She had no history of diabetes, hypertension, or significant comorbidities, and reported no family history of malignancy. Upon admission, physical examinations (abdominal, bimanual pelvic, and rectal digital) were unremarkable, revealing no tenderness, rebound tenderness, or palpable masses.

Diagnostic workup

Diagnostic evaluation revealed a significant discrepancy between imaging findings and endometrial sampling results. Imaging studies were highly suspicious for malignancy: transvaginal ultrasound identified a 4.1 cm × 2.4 cm hyperechoic mass in the anterior lower uterine segment with rich vascularity (**Fig. 1A** and **B**), while pelvic MRI confirmed a 25 mm × 16 mm × 16 mm solid-cystic mass of myometrial origin protruding from the right uterine corpus (**Fig. 1C** and **D**). Laboratory tests showed an isolated elevation in cancer antigen 125 (CA125) (62.20 U/mL), with other markers (carbohydrate antigen 19-9 [CA19-9], carcinoembryonic antigen [CEA], and alpha-fetoprotein [AFP]) within normal limits. Despite these findings, a diagnostic dilation and curettage (D&C) performed on the next day revealed no endometrial abnormalities. This negative histopathology, combined with the absence of vaginal bleeding, created a diagnostic dilemma that strongly suggested an extra-

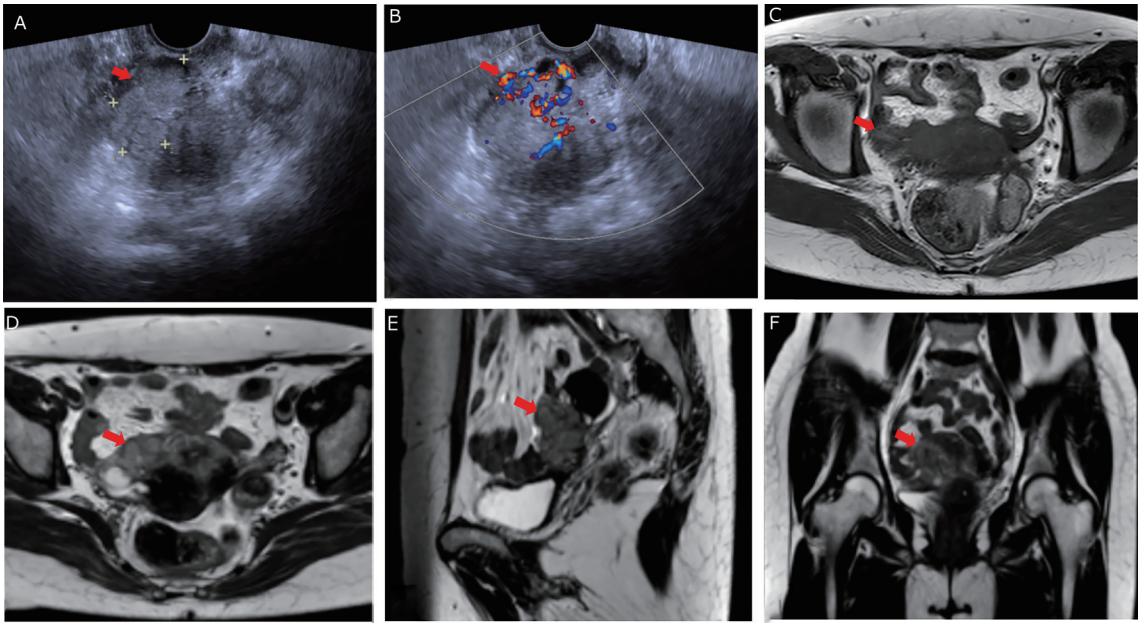

Figure 1. Imaging findings of a 53-year-old woman with uterine mass of endometrial carcinoma arising in adenomyosis.
(**A**) Transvaginal sonography revealed a slightly hyperechoic mass with irregular borders and focal peripheral hypoechoic areas suggestive of liquefactive necrosis (red arrow). (**B**) Color Doppler ultrasound imaging demonstrates abundant and disordered intralesional blood flow signals (red arrow), consistent with a hypervascular tumor. (**C**) MRI T1WI image shows heterogeneous hypo-intensity mass relative to myometrium (red arrow) indicating solid components. (**D**) Pelvic MRI T2WI image shows the mass originates from the uterine corpus, extending through serosa into pelvic cavity (red arrow), with internal heterogeneity suggesting necrosis or hemorrhage. (**E**) Sagittal T2WI image of pelvic MRI: a large, heterogeneous hyper-intensity mass with irregular margins, indistinct interface with the posterior bladder wall (red arrow), suggesting invasion or adhesion; uterine zonal anatomy is disrupted. (**F**) Coronal T2WI image of pelvic MRI: the infiltration involving the right parametrium and approaching the pelvic sidewall (red arrow).

endometrial origin, such as a primary myometrial carcinoma arising from adenomyosis.

Surgical management and pathological findings

Operative course

On day 4, an exploratory laparotomy revealed ascites and a 2-cm cauliflower-like nodule arising from the right anterior myometrium, breaching the serosa and directly invading the bladder neck. Concurrent adenomyosis and a right ovarian endometrioma were also noted. Intraoperative frozen section analysis of the uterine and bladder lesions confirmed endometrioid adenocarcinoma. Based on this finding, the surgical scope was escalated to comprehensive staging, comprising total hysterectomy, bilateral salpingo-oophorectomy (THBSO), resection of the bladder metastasis, and pelvic lymphadenectomy. The procedure was completed successfully despite dense pelvic adhesions.

Pathological diagnosis

Final histopathology confirmed endometrioid adenocarcinoma originating from the myometrium with direct bladder invasion. Notably, the endometrium remained uninvolved (thin and smooth), supporting a diagnosis of primary myometrial carcinoma associated with adenomyosis (**Fig. 2A** and **B**). While the right ovarian lesion was confirmed as an endometrioma, a notable finding in the lymph nodes was the presence of endometrial glandular structures lacking cellular atypia. These structures expressed Pan-CK and Pax-8, an immunoprofile that supports a diagnosis of lymph node endometriosis rather than metastatic carcinoma (**Fig. 2C** and **D**).

Postoperative course and follow-up

Postoperatively, the patient received intraperitoneal chemotherapy *via* an abdominal drain (carboplatin 400 mg). After discharge, she underwent six cycles of systemic combination chemotherapy with paclitaxel and carboplatin. The patient tolerated the regimen well with no grade 3/4 adverse events reported. During intermittent follow-up to date, clinical examinations and imaging have demonstrated no evidence of disease progression or recurrence, indicating a favorable response to the multimodal treatment.

DISCUSSION

Strengths and limitations

The primary strength of this case report lies in its detailed documentation of a rare entity, EC-AIA, presenting with an atypical clinical trajectory that challenges standard diagnostic algorithms. Specifically, we highlight a nulliparous, postmenopausal patient whose tumor exhibited a unique exophytic growth pattern toward the serosa, sparing the endometrial cavity until late stages. This presentation resulted in a false-negative endometrial biopsy, providing a critical teaching point on the limitations of superficial sampling in

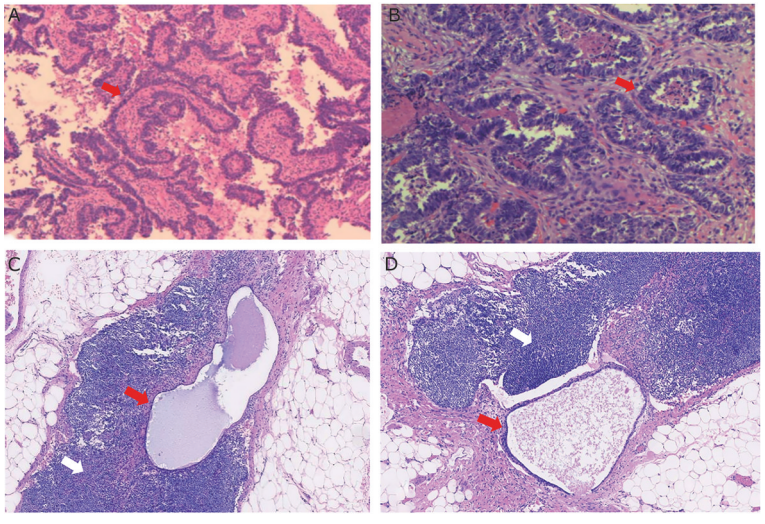

Figure 2. Histopathological finding of a primary myometrial carcinoma associated with adenomyosis in a 53-year-old woman.
(**A** and **B**) Nests of endometrioid adenocarcinoma infiltrating the myometrium. The malignant glands exhibit architectural complexity and cytologic atypia and are embedded within smooth muscle bundles (red arrows). These findings are consistent with a primary myometrial carcinoma arising in the setting of adenomyosis (HE staining, magnification ×100, scale bar = 200 μm). In the left (**C**) and right (**D**) pelvic lymph nodes, ectopic endometrial tissues are observed within the lymph node parenchyma. Red arrows indicate endometrial-type glands with surrounding stroma; white arrows denote the background lymphoid tissue (HE staining, magnification ×100, scale bar = 200 μm).

deep myometrial lesions. Furthermore, the histological discovery of ectopic, non-atypical endometrial glands within the lymph nodes offers rare empirical evidence supporting the hypothesis of lymphatic dissemination of adenomyotic tissue, suggesting a potential metastatic route distinct from frank carcinoma. However, this report is limited by its nature as a single-case observation, which precludes statistical generalization regarding incidence or survival outcomes. Additionally, while molecular profiling was discussed in the context of existing literature, comprehensive genomic sequencing of this specific tumor was not performed[5], limiting our ability to definitively map its mutational landscape against known EC-AIA drivers.

Review of literature and clinical context

EC is classically associated with postmenopausal women and typically presents with abnormal uterine bleeding, while adenomyosis typically affects women in their late reproductive years[6]. Our patient, a nulliparous woman presenting with vague abdominal pain seven years post-menopause, defies these classic epidemiological profiles. The absence of early bleeding is a hallmark of EC-AIA; because the malignancy originates within isolated adenomyotic foci deep in the myometrium, it often does not communicate with the uterine lumen until significant progression occurs[7]. This anatomical disconnect explains the high rate of false-negative biopsies and the frequent underestimation of EC-AIA incidence[2,8]. As noted in recent studies, reliance on endometrial sampling alone is insufficient when clinical suspicion persists, particularly in patients with a history of adenomyosis presenting with non-specific symptoms such as abdominal pain, hematuria, or unexplained intra-abdominal hemorrhage[7,9].

Diagnostic evaluation in this case underscores the complementary roles of imaging and biomarkers. While transvaginal ultrasound (TVUS) remains the first-line tool with high sensitivity for endometrial thickness, its specificity in differentiating benign adenomyosis from EC-AIA is limited[10,11]. In our patient, elevated CA125 served as a crucial "red flag". Although CA125 can be elevated in active adenomyosis, its significant rise in a postmenopausal woman warrants concern for deep myometrial invasion or extrauterine spread[12]. Consequently, MRI proved indispensable. Unlike TVUS, MRI provided high-resolution tissue differentiation, revealing serosal extension of the lesion and guiding the decision to proceed with laparotomy despite negative biopsy results[4]. This aligns with emerging consensus that MRI should be prioritized in cases where deep myometrial involvement is suspected but not confirmed by superficial sampling[13].

Pathological and mechanistic rationale

The definitive diagnosis of EC-AIA rests on rigorous pathological criteria: (1) exclusion of tumor in the superficial endometrium; (2) confirmation of origin exclusively from adenomyotic epithelium; and (3) presence of abnormal glands enveloped by endometrial stroma[2,14]. Our case met these criteria, revealing an endometrioid histology, the most common subtype, though serous and clear-cell variants exist. A pivotal finding was the presence of benign-appearing endometrial glands in the lymph nodes. While lymph node endometriosis is exceptionally rare, its presence here supports the theory that adenomyosis possesses inherent invasive and metastatic potential *via* the lymphatic system[5].

The pathogenesis of EC-AIA likely involves a synergistic interplay of hyperestrogenism, chronic inflammation, and shared genetic alterations[5,15]. Both conditions share mutations that drive cell proliferation, such as *PTEN* loss and *PIK3CA* mutations, alongside epigenetic dysregulation[16]. The inflammatory microenvironment of adenomyosis, rich in cytokines and oxidative stress, may facilitate malignant transformation[17]. Furthermore, alterations in the TSC2-mTOR pathway and hormonal imbalances contribute to this complex biology[15]. These shared mechanisms suggest that EC-AIA is not merely a coincidental co-occurrence but a distinct biological entity driven by specific molecular evolution.

Therapeutic implications and prognosis

Currently, no unified consensus exists for EC-AIA treatment due to scarce large-scale data. Clinical management largely extrapolates from standard EC protocols, involving total hysterectomy, bilateral salpingo-oophorectomy, and staging lymphadenectomy[18,19]. However, application of the International Federation of Gynecology and Obstetrics (FIGO) staging system to EC-AIA is problematic; tumors originating deep in the myometrium may be understaged if criteria based on endometrial origin are strictly applied. The patient underwent compre-

hensive surgical staging followed by adjuvant intraperitoneal and systemic chemotherapy, achieving a favorable response. While some literature suggests that EC co-occurring with adenomyosis may have a better prognosis due to earlier detection or biological factors[14,20], the aggressive growth pattern (serosal extension) and potential for lymphatic spread observed in our case argue for treating EC-AIA as a high-risk disease requiring vigilant monitoring and potentially intensified multimodal therapy[21].

SUMMARY

This case illustrates that EC-AIA is a diagnostically elusive entity that demands a high index of suspicion, particularly in postmenopausal women with a history of adenomyosis who present with non-specific pelvic pain and elevated CA125, even in the absence of abnormal uterine bleeding. The primary lesson for clinicians is that a negative endometrial biopsy does not rule out malignancy in this context; advanced imaging, specifically MRI, is essential to evaluate deep myometrial architecture and guide surgical decision-making. Furthermore, the finding of ectopic endometrial glands in lymph nodes highlights the potential for lymphatic dissemination of adenomyotic tissue, warranting thorough pathological examination of nodal specimens. Future research must focus on defining specific molecular signatures and imaging biomarkers for EC-AIA to facilitate early diagnosis and to develop individualized, mechanism-based therapeutic strategies that address its unique biological behavior, ultimately improving outcomes of patients with this rare and complex disease.

ARTICLE INFORMATION

Patient consent

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Wang ZQ performed case data collection, patient follow-up, literature search, and manuscript writing. Zhang C supervised the manuscript preparation and revised the final draft. All authors reviewed and approved the final manuscript.

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