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Misdiagnosis of Endometrioid Borderline Ovarian Tumors by Intraoperative Frozen Section Pathology: A Case Report and Review of the Literature

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Patient: Female, 55-year-old
Final Diagnosis: Endometrioid borderline ovarian tumors
Symptoms: Endometrioid borderline ovarian tumors
Clinical Procedure: —
Specialty: Surgery

Objective: Rare disease

Background: Endometrioid borderline ovarian tumors (EBOTs) are a rare subtype posing a significant diagnostic challenge on intraoperative frozen section analysis due to their morphological overlap with benign lesions and invasive carcinoma. Misdiagnosis, particularly as adenocarcinoma, can lead to unwarranted extensive surgical staging, resulting in potential overtreatment. This study aims to highlight the diagnostic challenge of a rare bilateral EBOT on intraoperative FS analysis and the consequent risk of surgical overtreatment, through a case report and a review of the literature.

Case Report: A 55-year-old postmenopausal woman presented with a pelvic mass. Intraoperative FS analysis misdiagnosed the tumors as ovarian adenocarcinoma, prompting comprehensive surgical staging, including hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy, omentectomy, and appendectomy. The final histopathological and immunohistochemical examination established the diagnosis of bilateral ovarian borderline endometrioid adenofibroma. A literature review (PubMed, 2006-2026) was conducted, which, after screening, included 6 studies reporting a total of 11 cases of bilateral EBOTs. The review revealed a predominant trend toward radical surgical intervention in these reported cases.

Conclusions: This case and literature review underscores the considerable risk of FS misdiagnosis and subsequent surgical overtreatment for rare bilateral EBOTs. The findings emphasize the critical role of final paraffin pathology in providing a definitive diagnosis for such challenging tumors. They also highlight the need for heightened diagnostic caution, explicit communication of diagnostic uncertainty in FS reports, and management strategies tailored to individual patient profiles rather than relying solely on equivocal intraoperative findings to guide the extent of surgery.

Keywords: Case Reports • Diagnosis • Ovarian Neoplasms • Patients • Gynecology • Endometrioid Tumor • Frozen Sections • Misdiagnosis

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Introduction

Borderline ovarian tumors (BOTs) occupy a unique position in diagnosis and management, accounting for approximately 10% to 15% of all ovarian epithelial tumors [1]. While characterized by the absence of destructive stromal invasion and typically an excellent prognosis, their intraoperative management poses significant clinical challenges [2]. The cornerstone of surgical decision-making lies in the frozen section (FS) diagnosis, which guides surgeons in opting for fertility-sparing surgery or more comprehensive staging procedures [2].

This diagnostic paradigm is particularly stressed for rare BOT subtypes, such as endometrioid BOTs (EBOTs). The histological features of EBOTs can closely mimic benign adenofibromas or, more critically, invasive endometrioid adenocarcinoma [3]. This morphological overlap directly contributes to decreased accuracy of intraoperative FS analysis for this entity. FS misdiagnosis as adenocarcinoma can trigger radical surgical approaches, potentially leading to overtreatment, which is defined as a surgical extent exceeding what is oncologically necessary based on the final diagnosis of BOT. National Comprehensive Cancer Network (NCCN) guidelines recommend that the final diagnosis of this disease should be based on postoperative paraffin pathology assessment, noting the limitations and potential errors of intraoperative FS analysis [4]. For confirmed BOT, standard surgical management, especially in early-stage disease, may involve conservative, fertility-preserving options, while suspected adenocarcinoma usually necessitates comprehensive surgical staging [5,6].

We report a case of a 55-year-old woman with bilateral ovarian tumors initially diagnosed as adenocarcinoma on FS, leading to extensive surgery, with final pathology confirming bilateral borderline endometrioid adenofibroma. We also performed a literature review on bilateral EBOTs to contextualize this case. The aim of this study is to highlight the diagnostic challenges of FS for rare EBOTs and discuss strategies to mitigate the risk of surgical overtreatment.

Case Report

The patient, a 55-year-old woman, gravida 3 para 2, naturally postmenopausal for 3 years, was admitted due to the discovery of a pelvic mass for over 2 months accompanied by weight loss of approximately 5 kg. She reported no postmenopausal bleeding or abnormal vaginal discharge. Gynecological examination revealed a solid-cystic mass about 6×4 cm in size in the right adnexal region, with ill-defined borders, poor mobility, and tenderness; no abnormality was palpated in the left adnexal region. Transvaginal ultrasound showed a heterogeneous echoic mass in the right adnexal region. Pelvic computed tomography (CT) suggested a right adnexal occupying lesion, possibly ovarian in origin, likely epithelial. Tumor marker tests showed cancer antigen 125 (CA-125) at 53.37 U/L and human epididymis protein 4 at 155.11 pmol/L were mildly elevated, while carcinoembryonic antigen, alpha-fetoprotein, and CA19-9 levels were within the reference ranges. Exploratory laparotomy was planned. Intraoperative findings included an ovarian tumor measuring approximately 6×6×4 cm, accompanied by pelvic adhesions and partial adhesions. The tumor was soft and mildly fragile. Intraoperative FS analysis suggested (right) ovarian adenocarcinoma, metastasis not excluded, pending paraffin section and immunohistochemistry. After discussion with the patient's family, comprehensive staging surgery was performed, including extrafascial abdominal total hysterectomy,

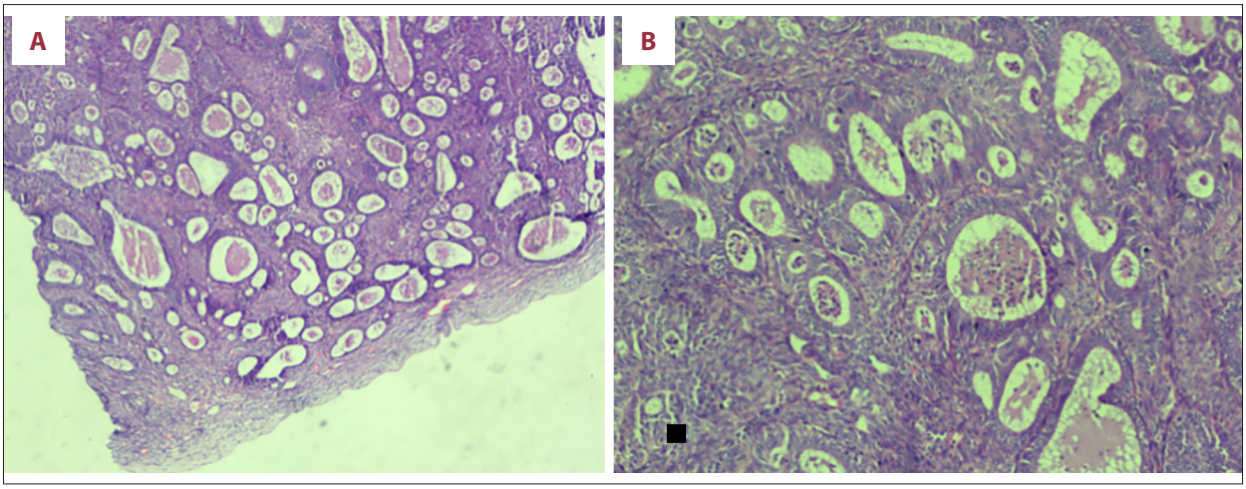

Figure 1. Microscopic view of the ovarian tumor (hematoxylin and eosin stain). (**A**) Ovarian biopsy, ×40: complex architecture with crowded, fused, and cribriform glands, characteristic of a borderline tumor without destructive stromal invasion. (**B**) Ovarian biopsy, ×100: stratified endometrioid epithelium with mild to moderate nuclear atypia and increased mitotic activity, but overall epithelial polarity preserved.

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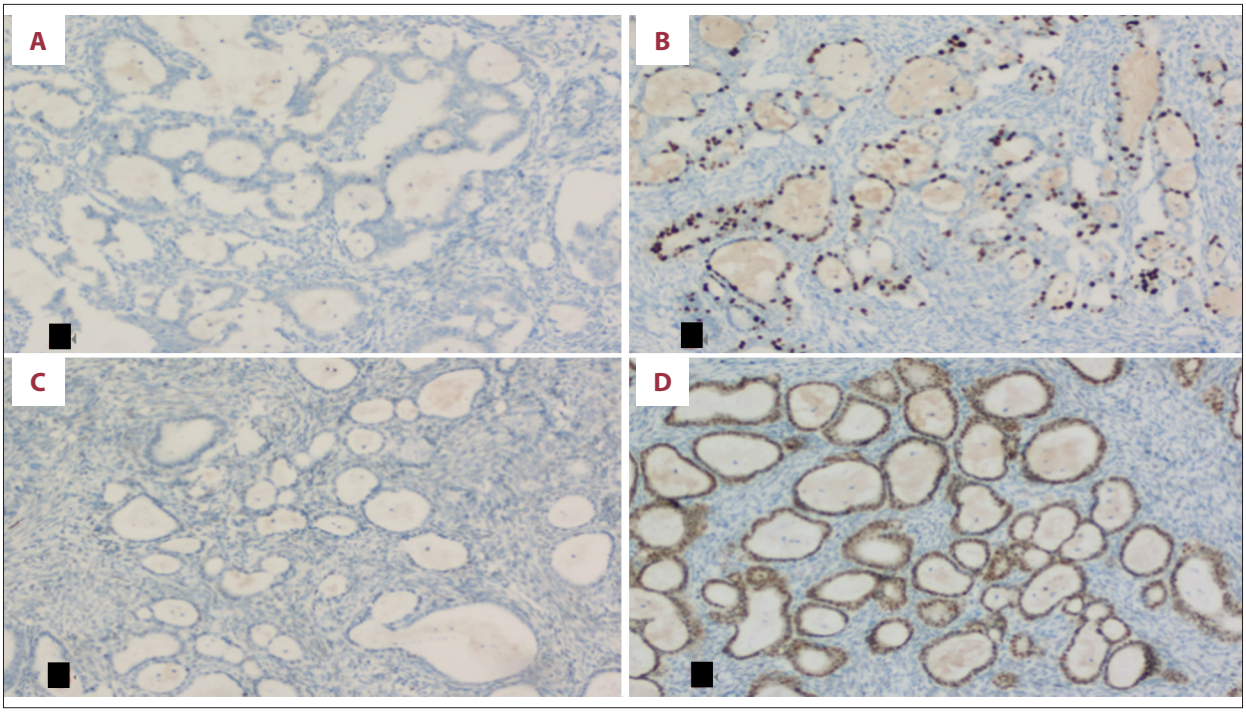

Figure 2. Immunohistochemistry profile. (**A**) Wilms tumor 1, ×200, negative. (**B**) Ki-67, ×200, positive (10-20%). (**C**) Tumor protein p53, ×200, negative. (**D**) Estrogen receptor, ×200, positive.

bilateral salpingo-oophorectomy, pelvic lymph node dissection, para-aortic lymph node dissection, presacral lymph node dissection, omentectomy, and appendectomy.

Postoperative pathological examination (**Figure 1**) and immunohistochemical results showed PAX-8 negative, Vimentin negative, Wilms tumor 1 negative, tumor protein (p)16 negative, p53 negative, estrogen receptor (ER) positive, progesterone receptor (PR) positive, MutL homolog (MLH) 1 positive, MSH2 positive, MSH6 positive, PMS2 positive, CA125 positive, and Ki-67 (approximately 10-20%) (**Figure 2, Table 1**). Final histopathology revealed no destructive stromal invasion. The immunohistochemical profile was consistent with endometrioid borderline ovarian tumor: ER and PR positivity, low Ki 67 proliferation index (10-20%), and negativity for WT 1, PAX 8, p53, and p16. These findings definitively excluded invasive endometrioid carcinoma and confirmed the diagnosis of bilateral ovarian borderline endometrioid adenofibroma.

Postoperative communication with the patient and her family indicated their understanding of the surgical process. During 1 year of follow-up, the patient reported a high quality of life with no related complications or discomfort.

Literature Review Summary

A review of the literature was conducted to contextualize the diagnostic challenge of bilateral EBOTs highlighted in the

Table 1. Immunohistochemical staining results of the bilateral endometrioid borderline ovarian tumor case.

Antibody/marker	Result	Notes
PAX-8	Negative	
Vimentin	Negative	
WT-1	Negative	
p16	Negative	
p53	Negative	
ER	Positive	
PR	Positive	
MLH1	Positive	
MSH2	Positive	
MSH6	Positive	
PMS2	Positive	
CA125	Positive	
Ki-67	Positive	Approximately 10-20%

Abbreviations: CA, cancer antigen; ER, estrogen receptor; PR, progesterone receptor; WT-1, Wilms tumor 1; MLH, MutL homolog; p16, tumor protein 16; p53, tumor protein 53; PMS2, postmeiotic segregation increased 2; PAX-8, paired box gene 8.

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Table 2. Summary of bilateral endometrioid borderline ovarian tumor (EBOT) cases.

Report	n	Surgical approach	Prognosis
Candotti et al (2025) [7]	5	3 Cases: bilateral salpingo-oophorectomy (BSO) + total hysterectomy; 2 cases: BSO	Median follow-up 89 months; no recurrence observed
Ricotta et al (2022) [8]	2	1 Case: abdominal hysterectomy + BSO + comprehensive staging; 1 case: unilateral salpingo-oophorectomy + contralateral ovarian cystectomy + comprehensive staging	Both patients showed no recurrence during long-term follow-up (72 months and 126 months)
El Hajj et al (2022) [9]	1	Intramucosal low-grade endometrioid adenocarcinoma found in one side; underwent comprehensive staging surgery	Patient prognosis not mentioned
Yüksel et al (2018) [10]	1	Total hysterectomy + BSO	Postoperative follow-up 72 months; no tumor recurrence observed
Jia et al (2018) [11]	1	Surgical approach not specified	No recurrence; specific follow-up time not mentioned.
Uzan et al (2012) [12]	1	Surgical approach not specified	Postoperative follow-up 24 months; no tumor recurrence observed

present case. The PubMed database was searched for studies published between 2006 and 2026 using the terms "endometrioid AND borderline". Titles and abstracts were first screened, followed by full-text evaluation. Studies were included if they reported pathologically confirmed bilateral EBOTs; reviews, non–English-language papers, and studies without detailed clinical data were excluded. After screening titles, abstracts, and full texts, 6 studies reporting on bilateral EBOTs were included for analysis, which collectively described a total of 11 cases of the disease [7-12]. No relevant reports on FS misdiagnosis were identified in the initially retrieved literature, either for bilateral or unilateral EBOTs. None of the included studies documented the intraoperative FS diagnostic results of these bilateral EBOT cases, nor was there any description of diagnostic discordance between FS and final paraffin pathology for this rare entity. The surgical approaches and clinical outcomes of these 11 bilateral EBOT cases are summarized in **Table 2**. Although the primary focus of the reviewed literature was on the surgical management and clinical prognosis of bilateral EBOTs, no included studies contained any documentation of FS diagnostic accuracy.

Discussion

EBOTs are a rare subtype of borderline ovarian tumors BOTs with distinctive histological features that pose substantial challenges for intraoperative FS diagnosis [13]. As a unique category of ovarian neoplasms without destructive stromal invasion, EBOTs exhibit morphological overlap with both benign endometrioid adenofibromas and invasive endometrioid adenocarcinoma, a characteristic that has been consistently identified as the primary cause of reduced FS diagnostic accuracy for unilateral EBOTs in existing clinical studies [3,14-16]. Despite the established diagnostic challenges of unilateral EBOTs, the intraoperative diagnostic landscape of bilateral EBOTs remains poorly characterized. A comprehensive literature review (2006-2026) identified only 6 studies reporting 11 cases of bilateral EBOTs, with no documented FS results or misdiagnosis-related data available for this rare entity [7-12]. The present case, detailing the misdiagnosis of bilateral EBOTs as ovarian adenocarcinoma on intraoperative FS and the subsequent radical surgical intervention, thus provides rare clinical documentation of FS diagnostic discordance in this tumor subtype, filling a critical gap in the evidence base for intraoperative management. Furthermore, the predominance of radical surgical interventions among the previously reported bilateral EBOT cases underscores the potential for overtreatment arising from intraoperative diagnostic uncertainty [7-12].

The misdiagnosis of bilateral ovarian borderline endometrioid adenofibroma as ovarian adenocarcinoma in the present case on intraoperative FS analysis is a multifaceted event driven by both the intrinsic pathological characteristics of bilateral EBOTs and the contextual clinical biases inherent to intraoperative diagnostic assessment [15,16]. At the pathological level, EBOTs exhibit a spectrum of cytological atypia ranging from mild to moderate, a feature that blurs the morphological boundary between benign hyperplasia and invasive carcinoma and has been identified as a primary contributor to FS diagnostic uncertainty for EBOTs [15]. For bilateral lesions in particular, the absence of definitive morphological evidence of stromal invasion, which is the key diagnostic criterion distinguishing BOTs from carcinoma, is easily overlooked under

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the time constraints of intraoperative FS evaluation, as pathologists are tasked with providing a rapid diagnostic conclusion [16]. Compounding this pathological ambiguity is the clinical bias associated with bilateral ovarian tumors: the presence of bilateral lesions inherently elevates clinical suspicion for metastatic carcinoma or dual primary malignant tumors, a subconscious inclination that may influence pathological judgment and lead to the overinterpretation of borderline cytological atypia as definitive adenocarcinoma [16]. In the present case, the mild elevation of CA-125 and the presence of pelvic adhesions further reinforced this clinical suspicion, creating a diagnostic context that predisposed to the overdiagnosis of the bilateral EBOTs as malignant disease, a scenario that aligns with the broader clinical challenges of FS diagnosis for rare ovarian tumor subtypes reported in existing literature [15,16].

In the present case, the surgical management can be analyzed in terms of necessity and potential overtreatment driven by the FS misdiagnosis. For this 55-year-old postmenopausal patient, total hysterectomy and bilateral salpingo-oophorectomy were appropriate and necessary given her age, absence of fertility desire, and risk of synchronous endometrial pathology [11,13]. By contrast, pelvic lymphadenectomy, para-aortic lymphadenectomy, presacral lymphadenectomy, omentectomy, and appendectomy were additional procedures prompted solely by the FS misdiagnosis of adenocarcinoma. These extended staging procedures are not routinely indicated for borderline tumors and therefore constitute overtreatment [2,5]. This distinction underscores that surgical decision-making for rare tumors should be rooted in individualized patient factors and an accurate diagnosis. The present case illustrates how FS diagnostic error can lead to unnecessary procedures that confer no additional clinical benefit for borderline disease [2,5].

The clinical dilemma observed in the present case is further reflected in the 11 cases of bilateral EBOTs identified in the present literature review [7-12], in which a predominance of radical surgical interventions was noted despite the absence of documented FS diagnostic results for these cases. While the reviewed studies do not report FS misdiagnosis for bilateral EBOTs (a critical research gap highlighted in the case report section), the routine use of hysterectomy and bilateral salpingo-oophorectomy even for select patients suggests that clinical uncertainty regarding the malignant potential of bilateral EBOTs is a pervasive issue in clinical practice. Notably, 1 case in the Ricotta et al (2022) study underwent fertility-preserving surgery with no subsequent recurrence during long-term follow-up, demonstrating that conservative surgical management is a feasible option for young patients with bilateral EBOTs when the diagnosis is clarified [8]. This finding, in conjunction with the present case, underscores that the primary challenge in the management of bilateral EBOTs is not the lack of effective surgical strategies, but rather the absence of reliable intraoperative diagnostic evidence to guide appropriate surgical decision-making.

Beyond the general diagnostic challenges of EBOTs, bilateral disease presents unique barriers to accurate FS analysis that further reduce diagnostic accuracy [15,16]. Unlike unilateral EBOTs, in which pathologists may prioritize the identification of stromal invasion in a single lesion, bilateral EBOTs require concurrent evaluation of 2 ovarian masses. This increases the cognitive and time pressure of intraoperative FS assessment, a factor identified by Shen et al (2021) as a key contributor to diagnostic discordance between FS and final paraffin pathology [16]. Additionally, bilateral EBOTs may coexist with benign ovarian lesions or exhibit heterogeneous cytological atypia between the 2 adnexal masses, a morphological complexity that further complicates rapid intraoperative diagnosis [12,17]. In the present case, the presence of pelvic adhesions and a soft, fragile tumor texture—nonspecific morphological features—further blurred the pathological distinction between borderline and malignant disease, as these features are often associated with ovarian adenocarcinoma in clinical practice. Collectively, these factors create a diagnostic "perfect storm" for bilateral EBOTs, in which the rarity of the entity, morphological ambiguity, and intraoperative constraints converge to increase the risk of FS misdiagnosis.

The lessons derived from the present case and the associated literature review inform a pragmatic approach to the intraoperative diagnosis and management of bilateral EBOTs, with the overarching goal of mitigating the risk of FS misdiagnosis and unnecessary surgical intervention. Central to this approach is the explicit communication of diagnostic uncertainty in FS reports for atypical ovarian lesions suspicious for EBOTs, as binary diagnoses of benign or malignant disease are often not feasible given the morphological overlap of these tumors [15,16]. This report provides surgeons with the critical decision-making buffer needed to avoid immediate radical staging and instead prioritize confirmatory paraffin pathology and immunohistochemistry—the gold standard for EBOT diagnosis according to NCCN guidelines [4]. Equally important is routine intraoperative endometrial sampling for all patients with suspected EBOTs, a practice mandated by multiple studies due to the high risk of synchronous endometrial carcinoma or atypical hyperplasia [11,14]. This step was performed in the present case and ruled out concurrent endometrial pathology, a key finding for post-surgical follow-up and prognosis assessment. Finally, stratified surgical decision-making based on patient age, fertility desire, and clinical context, rather than sole reliance on FS results, is essential: fertility-preserving surgery may be cautiously considered for young patients with clear borderline features, while definitive radical surgery for postmenopausal patients should be justified by clinical factors alone, not diagnostic uncertainty [5,6]. These strategies

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address the core diagnostic and management challenges of bilateral EBOTs, aligning clinical practice with the available evidence for this rare tumor subtype [18-21].

Conclusions

In conclusion, this case report with literature review illustrates the diagnostic challenges associated with rare EBOTs on intraoperative FS. These challenges can contribute to extensive surgical interventions. The literature indicates that radical surgery is frequently performed for bilateral EBOTs, driven by multiple clinical considerations. To address this, enhancing pathological accuracy, routinely performing endometrial evaluation, and tailoring surgical management to individual patient profiles are important considerations for optimizing care of these rare tumors.

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Patient Permission

Informed consent was obtained from the patient for publication of this case report and any accompanying images.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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