International Journal of Women's Health

Dovepress
Taylor & Francis Group

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CASE REPORT

Contrast-Enhanced Ultrasound Findings of Peritoneal Polypoid Endometriosis: A Case Report and Literature Review

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Abstract: Polypoid endometriosis (PEM) is a rare and distinctive variant of endometriosis, with ectopic endometrium presenting as a polypoid appearance. Due to the irregular shape of the mass on imaging, accompanied by obvious blood flow signals and often with elevated tumor marker CA125, it is prone to be misdiagnosed as a malignant tumor. We report a 43-year-old female with a history of ovarian endometriosis, in whom a heterogeneous echo mass was found in the pelvic cavity. The mass, located on the peritoneum and adhered to the omentum majus, had an irregular shape and prominent blood flow signals, complicating the imaging findings. Both contrast-enhanced computed tomography and magnetic resonance examinations identified the mass as a malignant ovarian tumor, whereas conventional ultrasound failed to determine its nature. However, venous contrast-enhanced ultrasound (CEUS) revealed benign characteristics, such as uniform enhancement of the solid portion and slow, consistent regression. The postoperative pathology confirmed that it was PEM. PEM is difficult to diagnose preoperatively due to its rarity, non-specific symptoms, and complex imaging features. This case, by summarizing and analyzing the CEUS image characteristics of peritoneal PEM, fills the gap in this new technology of CEUS, expands the possibilities of non-invasive imaging diagnosis, and reviews the relevant literature published to emphasize its features, pathogenesis, diagnostic methods, and treatment approaches, thereby enhancing the understanding and management of this condition.

Keywords: endometriosis, polypoid endometriosis, ovarian malignancy, venous contrast-enhanced ultrasound

Introduction

Endometriosis is a complex syndrome characterized by the abnormal implantation of endometrial glands and stroma outside the uterine cavity, often driven by an estrogen-dependent chronic inflammatory process. Studies have demonstrated that 10–15% of women of reproductive age are affected by pelvic endometriosis, and 30–50% of these patients experience symptoms of chronic pelvic pain and/or infertility.[1–3] The American Society for Reproductive Medicine (rASRM) classification stages endometriosis (I–IV) via surgical scoring of lesion location, size, depth, and adhesions, categorizing subtypes as peritoneal, ovarian, or deep infiltrating.[4] When endometriotic tissues undergo somatic mutations, accompanied by alterations in the microenvironment of the peritoneal cavity such as estrogen/progesterone hormonal imbalance, inflammation, immune evasion, and neoangiogenesis,[5] it can eventually lead to various macroscopic manifestations.[1] Polypoid endometriosis (PEM) is a rare variant of endometriosis, characterized by polyp-like masses with pedicles or broad bases. Microscopically, it consists of endometriotic glands and stroma, accounting for less than 1–2% of all endometriosis cases.[6] PEM was often misdiagnosed as ovarian carcinoma due to its polypoid morphology, complex imaging features, and hypervascularity-mimicking malignancy. Currently, systematic research on this subtype is still very limited on a global scale. As of 2024, PubMed has indexed less than 100 articles related to PEM,

Received: 3 December 2024
Accepted: 21 May 2025
Published: 30 May 2025

most of which are case reports or small-sample retrospective analyses.[6] This evidence gap makes clinical decision-making highly dependent on individual experience, and there is an urgent need for multi-center collaboration to clarify its natural course, molecular typing, and prognostic markers.

Herein, we reported a case of peritoneal PEM. Through literature review and detailed case analysis, combined with histopathological, immunophenotypic, and molecular testing results, we systematically investigated its diagnostic pitfalls, clonal evolution characteristics, and personalized treatment strategies. Our aim is to develop improved imaging-based diagnostic methods, enhance diagnostic accuracy, deepen clinicians' and pathologists' understanding of this disease, minimize misdiagnosis and inappropriate treatment, and provide direction for future research to optimize follow-up protocols for recurrence or malignant transformation.

Case Presentation

The patient, a 43-year-old woman, presented to our hospital for cervical cancer screening. During routine ultrasound examination, an uneven echo mass was detected in the lower abdomen, with no obvious symptoms of abdominal pain. On examination, the uterus was slightly firm with no obvious tenderness. Both adnexa were palpable, soft, with clear borders and acceptable mobility. The patient had a history of ovarian endometriosis cysts but no family history of tumors. The patient denied experiencing significant abdominal pain, weight loss, or fatigue. Ultrasonography revealed a heterogeneous echo mass, measuring approximately 116×67 × 92 mm, extending from the posterior uterine fundus to about 3 cm below the umbilicus. The mass had clear boundaries and a slightly irregular shape with an uneven internal echo, consisting of hypoechoic, medium echo, and multiple oval anechoic fusions (Figure 1A). Color doppler flow imaging (CDFI) showed a coarse, branched blood flow signal around the mass (Figure 1B). The mass was clearly demarcated from the bilateral ovaries, and no obvious free fluid was detected in the pelvic or abdominal cavities.

Further investigation with venous contrast-enhanced ultrasound (CEUS) (SonoVue 2.4 mL injected through the right elbow vein) showed centrifugal "vesicle-shaped" enhancement of the mass 12 seconds after injection (Figure 1C). The mass reached peak enhancement at 25 seconds, revealing multiple regular oval non-perfusion areas, while the residual parenchymal tissue showed uniform enhancement. The enhancement gradually subsided at 44 seconds and became equal to that of the surrounding intestine by two minutes and 14 seconds. A distinct "black margin" of very low perfusion area surrounded the mass (Figure 1D). In the regression phase, thick, straight branched vessels were still visible in some solid

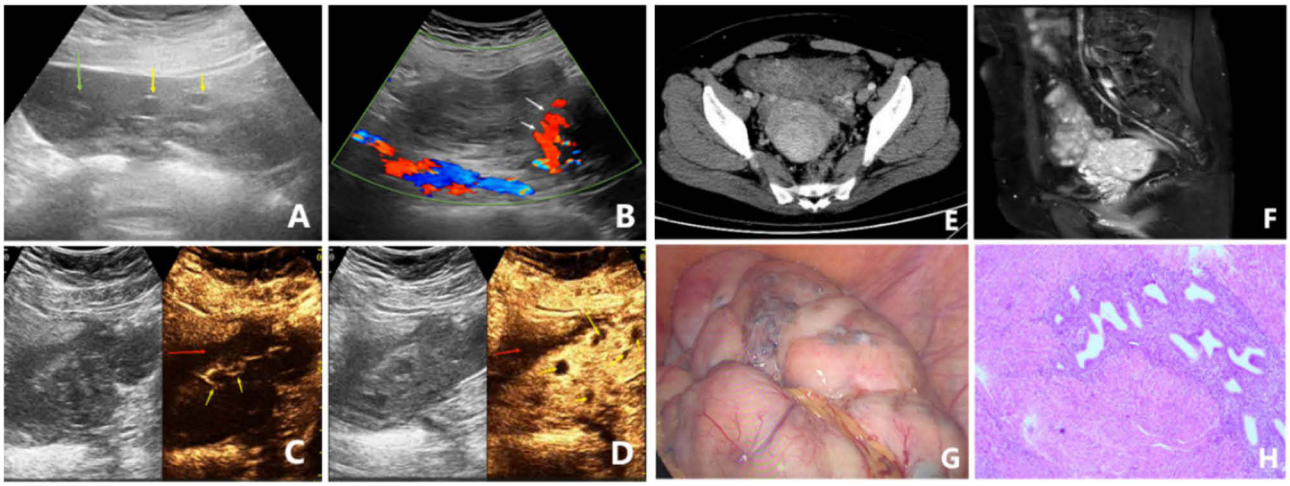

Figure 1 (**A**) Multiple circular anechoic areas (yellow arrows) are observed within the lump, with hypoechoic areas seen around the periphery (green arrows); (**B**) Coarse, branch-like blood flow signals are visible both around and within the mass (white arrows); (**C** and **D**) Following the injection of contrast medium, the mass enhances in a "vesicle-like" pattern from the center (yellow arrow). The remaining parenchyma shows uniform and equal enhancement, peaking at 25 seconds. Numerous regular, circular non-perfusion areas are visible inside, and a "black margin" of fibrosis (red arrow) is seen at the periphery. Enhancement gradually subsides evenly and slowly by two minutes and 14 seconds. At two minutes and 30 seconds during the regression phase, thick, straight blood vessels are visible at the edge of the mass; (**E**) CT imaging reveals multiple pelvic masses and nodules; (**F**) MRI shows an intrapelvic cystic solid mass; (**G**) Intraoperative view of a pinkish-white mass with multiple purple-blue nodules on the surface; (**H**) Intraoperative pathology reveals a variety of endometrial glands, endometrial stromal cell proliferation, and disordered arrangement.
Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

echoes. Overall, CEUS showed that the pelvic mass had a low enhancement intensity, with the solid part uniformly enhancing and slowly fading, suggesting a benign mass, which is different from the "rapid wash-in and wash-out" and "centripetal enhancement" characteristics of ovarian cancer.

Contrast-enhanced computed tomography (CT) showed multiple pelvic masses with mild post-injection enhancement and unclear boundaries (Figure 1E), leading to a diagnosis of multiple pelvic masses and nodules. A contrast-enhanced magnetic resonance imaging (MRI) scan revealed significant uneven enhancement of the solid part of the anterior uterine lesion (Figure 1F), suggesting the potential malignant transformation of a cystadenoma. Serum tumor markers were elevated, with CA19-9 at 43 U/mL (reference <30.9 U/mL) and CA125 at 121.4 U/mL (reference <35 U/mL), while CA125 levels were generally higher in ovarian malignancy (>200 U/mL). The imaging results of enhanced CT and enhanced MRI combined with elevated serum tumor markers suggested that the mass may be malignant, requiring a slight adjustment of the surgical protocol and more preparation before surgery such as planning for pelvic lymph node dissection. Then the patient underwent laparoscopic resection of the abdominal mass. During surgery, a 15×12 cm mass was discovered at the bottom of the pelvis (Figure 1G), consisting of a soft, pinkish-white tissue with multiple purple-blue nodules on its surface and dense adhesions to the omentum. The dense adhesion between the mass and the omentum might be related to the inflammation, which also increased the difficulty of the operation. After the separation of the omentum, the mass had no adhesion to the uterus and the bilateral adnexa. The mass was resected, and the section was sieve-shaped, accompanied by a solid cystic area and fibrous peripheral tissue, which was consistent with the vesicular anechoic area described by ultrasound and consistent with the hemorrhagic, fibrotic, and cystic characteristics of endometriosis cysts.

Discussion

Endometriosis is a complex syndrome in clinical practice, characterized by an estrogen-dependent chronic inflammatory process. Current research indicates that its pathogenesis involves a complex interplay of genetic, hormonal, immune and environmental factors. PEM is a rare and distinctive variant of endometriosis, and it was first described and named by Mostoufizadeh and Scully in 1980.[7] The most commonly affected sites include the vagina,[8] cervix,[9] and rectum,[10] while involvement of the peritoneum is less frequent.

The pathogenesis of PEM remains unclear. The classic theories of endometriosis, such as the "retrograde menstruation theory"[11] and the "coelomic metaplasia theory",[12] are insufficient to fully explain the unique biological behavior of polypoid transformation. Recent studies have found that inflammatory factors (such as IL-6 and TNF-α) drive local microenvironment remodeling, activate the NF-κB pathway, and promote the transformation of fibroblasts into myofibroblasts (α-SMA+), ultimately forming polypoid structures.[13] At the molecular level, approximately 25% of cases carry KRAS or PIK3CA mutations, which are associated with abnormal activation of the MAPK/PI3K signaling pathway, suggesting that they may be in an intermediate stage of the "benign-malignant transformation spectrum".[13,14] Studies have reported that somatic genetic alterations of HMGA1 (6p21) and HMGA2 (12q15) exist in patients with PEM.[15] These rearrangements are only found in the stromal components and not detected in the glandular components. Therefore, it can be speculated that these genetic alterations may be involved in the occurrence and development of PEM by driving abnormal proliferation of stromal cells. This discovery not only deepens the understanding of the heterogeneity of endometriosis but also provides a potential entry point for exploring targeted therapy.

A search of PubMed using the keyword "polypoid endometriosis" yielded only around 50 relevant case reports from 1956 to 2023, with Parker et al reporting the largest sample size of 24 cases in 2004. After reviewing the literature, it was found that patients with PEM often presented with atypical clinical symptoms, with elevated CA125 levels in laboratory tests.[6] Hence, they were frequently misdiagnosed as having malignant tumors, with an initial diagnosis misdiagnosis rate as high as 42%.[6] However, the overall prognosis of PEM is favorable, with postoperative recurrence reported at 5.9%.[6]

The clinical management of PEM faces numerous challenges. Firstly, its imaging features lack specificity. Ultrasound or MRI often shows a solid or cystic-solid mass with indistinct borders, which can be easily misdiagnosed as ovarian cancer, adenosarcoma or metastatic cancer. Secondly, diagnosis relies on histopathological examination, which requires high-resolution microscopic features and immunohistochemical markers (such as ER/PR, CD10, Ki-67). However, due to insufficient experience, there may be a risk of missed diagnosis in primary medical institutions. More seriously, about 5%

to 10% of cases may be combined with borderline tumors or undergo malignant transformation (such as endometrioid adenocarcinoma.[5] If not identified in time, it may lead to treatment delay or excessive surgery.

Based on the morphological and histopathological findings, the tumor reported in this case had a polypoid appearance with multiple purple-blue nodules on its surface, consistent with the diagnosis of PEM. Its clinical manifestations, morphological characteristics, and imaging features differ from those of classical endometriosis. The primary differential diagnoses include adenosarcoma, deep infiltrating endometriosis, and ovarian tumor. According to World Health Organization (WHO) criteria, a diagnosis of adenosarcoma requires a mitotic rate of one to two mitotic numbers per 10 high-power fields (HPF)[16] and is characterized by bidirectional differentiation, periglandular stromal hyperplasia, stromal atypia, and a periglandular cuff of the cellular stroma. While PEM microscopy reveals a diverse arrangement of endometrioid glands, stromal cell hyperplasia is evident between the glands, distinguishing it from adenosarcoma. Deep infiltrating endometriosis often presents as purple-blue nodules or red lesions,[1] but lacks the polypoid histological features of PEM. PEM is often misdiagnosed as clear cell carcinoma. Both appear as hypervascular solid masses on imaging, but clear cell carcinoma has "nail-like" cells and clear cytoplasm, whereas PEM lacks atypical cells.[17]

Similar cases and literature reports, both domestically and internationally, have noted that imaging examinations often lead to the misdiagnosis of malignant tumors.[17] A case report from Japan showed that a 37-year-old woman was misdiagnosed with ovarian cancer due to an ovarian mass over 20 centimeters in diameter and elevated serum CA125 levels, and underwent a hysterectomy and oophorectomy. However, the permanent pathological section of the postoperative surgical specimen revealed that the lesion was actually PEM.[18] This article reports a case whose mass was located in the peritoneum, adhering to the greater omentum, with multiple cystic dark areas inside. The conventional ultrasound image was complex and difficult to make a clear diagnosis. After enhanced CT and MRI scans, it was also misdiagnosed as ovarian cancer. Conventional ultrasound and enhanced CT/MRI mainly rely on morphological features (such as heterogeneous echoes, enhanced necrotic areas), with relatively low specificity. In contrast, CEUS, as an emerging examination method, although it cannot clearly display deep pelvic lesions (such as retroperitoneal lymph nodes) and cannot independently assess distant metastasis (it needs to be combined with CT or MRI), it has the advantages of being safe, free of ionizing radiation, allowing multiple re-examinations in a short period of time, and not being limited by metal implants. CEUS can not only detect lesions on two-dimensional images but also make differential diagnoses by dynamically observing the microvascular perfusion pattern. Its sensitivity for differentiating benign and malignant lesions is 92%, and its specificity is 89%. In this case, the imaging of CEUS showed a heterogeneous cystic-solid mass with multiple internal non-perfusion areas that are oval, well-defined, and regular in shape. The solid part of the mass typically shows uniform enhancement, with coarse, regular internal vessels. Angiography showed centrifugal, vesicle-like enhancement radiating from the center. There is a clear distinction between the peripheral low-perfusion areas and the highly enhanced regions, with the enhancement reaching a peak before regressing slowly. Notably, the usual manifestations of malignant tumors, such as "rapid wash-in and wash-out", "centripetal enhancement", and "unclear borders", are absent.[19] Instead, the fibrotic margins around the mass appear as "black margins",[20] further supporting a benign diagnosis. Compared with traditional imaging methods, CEUS can dynamically observe the lesion enhancement pattern in real-time and provide key diagnostic information by capturing the microcirculation characteristics of the lesion, which highlights the unique value of CEUS as a non-invasive technique in the differential diagnosis of complex pelvic mass, especially for adhesion lesions that are difficult to be clearly diagnosed by CT/MRI.

This study had several limitations. The single-case design inherently introduces selection bias, as this rare presentation may not fully represent the spectrum of PEM manifestations. While CEUS demonstrated diagnostic value here, operator-dependent technical variability in image acquisition and interpretation requires acknowledgment. Retrospective image analysis after pathological confirmation could introduce confirmation bias; thus, prospective validation across multiple centers with standardized protocols is needed.

In conclusion, this case report, along with the review of relevant literature, highlights the importance of incorporating new ultrasound technologies, specifically venous CEUS, to better distinguish PEM from malignant tumors. In the future, advancing multimodal imaging criteria and noninvasive biomarkers will reduce misdiagnosis-driven surgeries, optimize preoperative planning, and improve outcomes for PEM patients.

Data Sharing Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of People's Hospital Affiliated to Ningbo University (Ethical approval number: 2024-N-013). All patients who were familiar with the contents and processes of the study and able to complete all the scheduled study processes signed the informed consent. Our study complies with the Declaration of Helsinki. Institutional approval is not required to release case details.

Patient Consent

Consent was obtained from the patient for the purpose of publication.

Funding

This work was supported by the following grants: Yinzhou District Health Science and Technology Program (No. 2024Y05); Zhejiang Provincial Medical and Health Science and Technology Project (No.2019RC274).

Disclosure

The authors report no conflicts of interest in this work.

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