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Case Report

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Endometriosis Presenting with Massive Ascites: A Case Report

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ABSTRACT

Endometriosis presenting as massive ascites is uncommon and often mimics malignancy. Cytologic detection of benign endometrial cells in ascitic fluid is uncommon but can expedite diagnosis and prevent unnecessary interventions. We present a case of abdominopelvic endometriosis in a 30-year-old female, which could be diagnosed directly by cytologic examination of the ascitic fluid and subsequently confirmed on biopsy. Tightly cohesive clusters of benign endometrial cells were highlighted on SurePathTM Liquid-based cytology (LBC) smears and the cell block prepared from the sample could be subjected to immunohistochemistry (IHC) to confirm the nature of these cells. LBC by concentrating ascitic fluid sample helped in detecting benign endometrial cells in the present case, thereby clinching the diagnosis of endometriosis on cytology. Incorporating cytologic evaluation into the diagnostic workup can aid clinicians in preventing misdiagnosis, minimizing overtreatment, and ensuring timely management.

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List of Abbreviations

ADA: Adenosine Deaminase
CECT: Contrast Enhanced Computed Tomography
H&E: Haematoxylin and Eosin
IHC: Immunohistochemistry
LBC: Liquid-Based Cytology
MGG: May-Grünwald Giemsa
MRI: Magnetic Resonance Imaging
PET: Positron Emission Tomography
SAAG: Serum- Ascites Albumin Gradient
TES: Thoracic Endometriosis Syndrome

Introduction

Endometriosis is a common benign disorder with a prevalence of approximately 10% in the general population [1]. Patient commonly presents with dysmenorrhea, chronic pelvic pain, dyspareunia, and infertility. Diagnosis is primarily clinical with support from trans-vaginal ultrasonography or magnetic resonance imaging (MRI). Management includes hormonal therapy, analgesics, and surgical excision based on symptoms and desire for fertility. Clinical presentation of ascites due to abdominal endometriosis is an uncommon phenomenon, and therefore, it is often misinterpreted clinically as tuberculosis or malignancy. The predominant population of haemosiderin-laden macrophages in the ascitic fluid is a non-specific finding, with a few case reports mentioning the endometrial cells and reactive mesothelial cells in ascitic and/or pleural fluid samples [2,3]. The endometrial cells in effusion samples are often scanty, leading to a low overall diagnostic accuracy of cytology of about 10% in the previous review articles [4]. We highlight the importance of liquid-based cytology (LBC) samples in the interpretation of these effusion samples as LBC leads to cellular concentration and better preservation of cellular morphology, highlighting these rare endometrial cells as 'top-hat appearance' in a sea of pigment-laden macrophages.

Case Report

A 30-year-old thin-built, married nulligravida woman presented with a six-moth history of insidious-onset, moderate, sharp right-sided lower chest pain accompanied by progressive abdominal distension. Physical examination revealed gross ascites, with no other significant findings. Her hemogram, and biochemistry investigations were within normal limits. She denied any history of weight loss, anorexia, cough, or any other relevant systemic symptoms, and had no relevant past medical, surgical, family, treatment, and personal history. With a clinical suspicion of tuberculosis, a chest X-ray and Mantoux test were performed, which were within normal limits. The serum concentration of CA-125 was mildly elevated. Contrast enhanced computed tomography (CECT) scan of the abdomen revealed gross ascites, scalloping the liver surface with bulky right adnexa having a solid-cystic lesion measuring 36 x 35 mm in size. F-18 FDG PET-CT (Positron emission tomography) also showed low-grade FDG-avid lesions in the right ovary, hypodensities in the left ovary, and a faintly FDG-avid hypodensity in the sub-diaphragmatic location. Non-FDG-avid gross abdominopelvic ascites was noted.

Ascitic tap was done through a paracentesis, and approximately 50 ml of haemorrhagic ascitic fluid was sent for cytologic examination. Both air-dried, May Grunwald-Giemsa stain (MGG) stained smears and the SurePathTM LBC smears were prepared. The

smears were cellular and showed scattered reactive mesothelial cells and sheets of pigment-laden macrophages. The pigment was bluish-brown, indicating the presence of haemosiderin, and this was confirmed by Perl's Prussian blue stain (Figure 1). LBC preparation, in addition to demonstrating the haemosiderin-laden macrophages, also showed a few tightly cohesive clusters of small-sized cells with variably shaped nuclei, degenerate chromatin, and inconspicuous nucleoli. A typical 'top-hat' appearance of endometrial cells as seen in cervical Pap sample was noted in an occasional cluster with a dark core of stromal cells surrounded by epithelial cells. A possibility of endometriosis was suggested on ascitic fluid cytology.

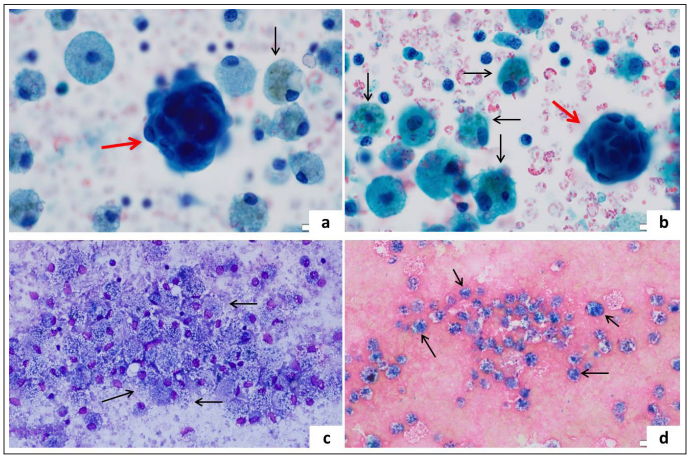

Figure 1: A panel of microphotographs of endometriosis in ascitic fluid; **A & B:** Sheets of hemosiderin-laden macrophages [black arrows] with tightly cohesive clusters with "top-hat" configuration of benign endometrial cells [red arrows] (SurePathTM preparation, Papanicolaou stain; **A & B:** 40x); **C:** Hemosiderin- laden macrophages [black arrows] (May-Grünwald Giemsa, 20x); **D:** Perl's Prussian blue stain highlighting hemosiderin laden macrophages [black arrows] (Perl's stain, 20X)

A diagnostic laparoscopy was done, which revealed nodules and cystic lesions with a powder-burnt appearance over the anterior abdominal wall and on the undersurface of the diaphragm, along with dense adhesions (Figure 2). Multiple biopsies from anterior abdominal wall lesions, right ovarian tissue, right broad ligament, and lesions from the under-surface of the diaphragm were obtained. In the meanwhile, immunochemistry was performed on the cell block prepared from ascitic fluid. The endometrial cells were positive for estrogen receptor and PAX8. Histopathological examination of anterior abdominal wall lesions, right broad ligament, and lesions from the under-surface of the diaphragm showed multiple foci of endometriosis (Figure 3). Biopsy from right ovarian tissue showed normal ovarian parenchyma only. There was no evidence of tuberculosis. Approximately 4-5 litres of thin, chocolate-colored ascitic fluid were drained during paracentesis. The ascitic fluid drained post-operatively also showed similar features of endometriosis, with LBC smears concentrating the sample and clinching the correct diagnosis. The patient was started on hormonal therapy, and she was well on her last follow-up visit, six months after the diagnosis.

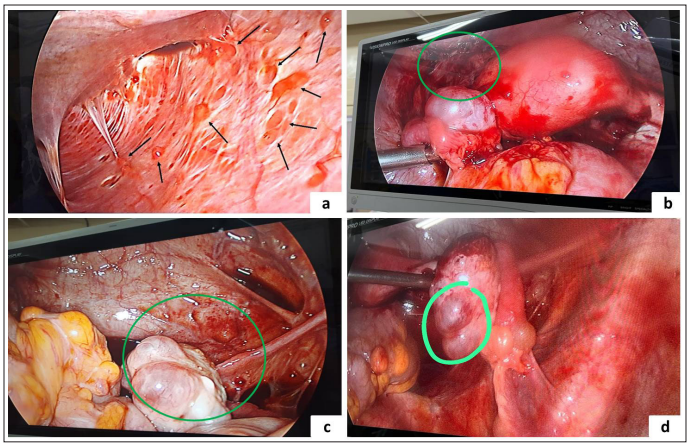

Figure 2: Images taken during laparoscopy; **A:** Multiple, variably-sized nodules/ endometriotic foci on the undersurface of the diaphragm [black arrows]; **B:** Burnt out endometriotic lesion on the anterior aspect of left ovary [green ring]; **C and D:** Endometriotic nodules on the anterior aspect of right ovary [green rings]

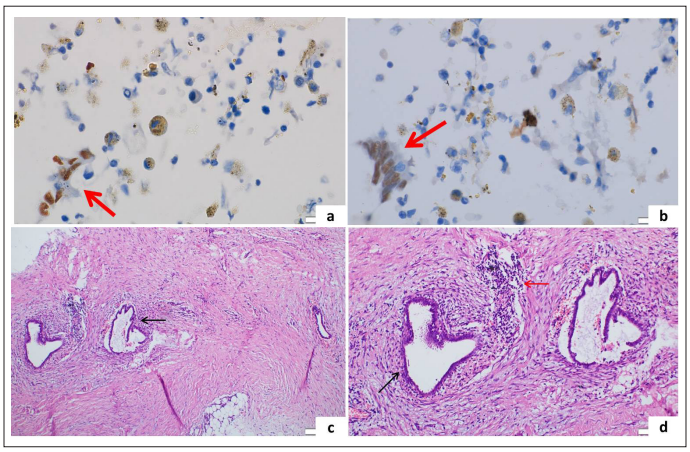

Figure 3: A: Immunochemistry performed on the cell block section showing nuclear positivity for estrogen receptor [red arrow] (IHC, 40X); B: Nuclear positivity for PAX8 [red arrow] (IHC, 40X); C: Endometriotic foci [black arrow] in the biopsy taken from the nodule in the anterior abdominal wall (H&E; 20x); D: Endometrial glands [black arrow] and stroma [red arrow] seen in the biopsy of the nodule present at the undersurface of the diagram (H&E; 20x)

Discussion

Endometriosis, i.e., ectopic presence of endometrial tissue outside the uterine cavity, is usually associated with chronic haemorrhages leading to the presence of haemosiderin-laden macrophages, occurs in approximately 6-10% of women in the reproductive age group [1]. Endometriosis usually occurs in the pelvic peritoneum. However, other sites include the recto-vaginal septum, abdominal cavity, diaphragm, and scar sites in the abdominal wall [5,6]. The prevalence of extra-pelvic endometriosis is about 12% [7]. Abdominopelvic endometriosis is usually accompanied by thoracic endometriosis. The term "thoracic endometriosis syndrome" (TES) is used to describe clinical condition associated with endometriosis within the thoracic cavity with clinical manifestations including lung nodules, catamenial pneumothorax, defined as spontaneous pneumothorax occurring within 72 hours before or after the onset of menstruation, hemothorax, and hemoptysis [1]. Approximately 50-84% of patients with TES also have concurrent pelvic

endometriosis [8]. The present case presented only with ascites without pleural effusion, and the thoracic cavity was spared. Brews et al. first described diaphragmatic endometriosis as a separate and distinct entity in 1954 [9]. Since then, less than 100 cases have been reported on diaphragmatic endometriosis. Diaphragmatic endometriosis usually presents with dyspnea, chest pain, upper abdominal pain, weight loss, and shoulder aches in most patients.

Sampson's theory of retrograde menstruation is the most prominent theory explaining the possible etiopathogenesis of endometriosis. Other theories proposed include coelomic metaplasia theory, lymphatic and/or hematogenous dissemination theory, and prostaglandin theory. Endometriosis primarily presenting as gross ascites is uncommon and can lead to a diagnostic dilemma. Ascites related to endometriosis commonly masquerades as ascites associated with ovarian malignancy, especially if a tumor marker such as serum CA125 is raised. Cytologic examination of endometriosis-related ascitic fluid usually reveals the presence of hemosiderin-laden macrophages, which can be a non-specific finding [10]. A few case reports on conventional smears have previously described the presence of endometrial cells and macrophages [8,9].

SurePathTM LBC is a state-of-the-art technique based on the density-gradient concentration principle. As the LBC preservative lyses the red blood cells and concentrates the sample, the chances of picking up diagnostic cells become higher. LBC, in the present case, highlighted the presence of the endometrial cells as a typical 'top-hat appearance" usually described in cervical samples. The endometrial cells are monomorphic, small-sized cells with a high nuclear-cytoplasmic ratio, scanty cytoplasm, small variably-shaped nuclei with kidney-bean-shaped nuclei, small distinct nucleoli, and dispersed, dark chromatin. These cells are usually seen as tightly cohesive clusters with typical 'top-hat appearance' indicating the central dark core of endometrial stromal cells wrapped by benign appearing endometrial glandular cells. In the conventional cytologic sediment smears, the endometrial epithelial cells are often seen occasionally as cohesive ball-like clusters, and the stromal cells may be seen as dispersed population of monomorphic cells with round to oval nuclei with granular chromatin, and scant cytoplasm. A biopsy helps confirm the diagnosis, revealing foci of endometriosis. The previous reviews show that the cytological diagnosis is achievable only in about 9% of the cases [10].

Other differential diagnostic entities malignant causes such as ovarian or peritoneal carcinoma, ovarian germ cell tumor or metastatic carcinomas from breast or colorectal origin. Infectious causes like tuberculous peritonitis and hepatic causes including cirrhosis and Budd–Chiari syndrome can also lead to gross ascites. Endometriosis usually leads to a low-SAAG (Serum–Ascites Albumin Gradient), high-protein, often serosanguinous or haemorrhagic fluid with negative cytology for malignancy and normal ADA (Adenosine Deaminase) levels, versus malignant effusion (positive cytology), tubreculosis (high ADA), and cirrhosis (high SAAG).

Conclusion

With the use of LBC techniques such as SurePathTM and ThinPrepTM LBC techniques, a suggestive cyto-diagnosis can be offered in such challenging cases with the recognition of these rare clusters as benign endometrial cells, in cases with compatible clinical and radiologic findings. This can be of utmost importance in starting the timely and precise treatment in young patients with endometriosis.

Declarations

Ethics Approval and Consent to Participate

This study protocol was reviewed in the departmental review committee, Department of Cytology and Gynecologic Pathology, PGIMER, Chandigarh and the need for approval was waived.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of Data and Materials

All data generated or analysed during the preparation of this manuscript are included in this article. Further enquiries can be directed to the corresponding author.

Competing Interests

The authors declare that they have no competing interests

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Authors' Information (optional)

Not applicable

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