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Case Series

Varied presentation of endometrial carcinoma: a case series

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ABSTRACT

Endometrial carcinoma (EC) is the second most common genital tract malignancy. While postmenopausal bleeding remains the hallmark symptom of endometrial cancer, atypical and varied presentations can occur. They prevent early diagnosis, particularly in younger and perimenopausal women. We present here a case series of four patients aged 30 to 54 years, where the initial diagnosis was not EC. Evaluation of all these patients was done with clinical examination, Transvaginal sonography (TVS) and Diagnostic Hysteroscopy. After diagnosis of EC, further treatment was instituted as per standard guidelines. Histopathology in all four cases was Endometrioid Adenocarcinoma. Staging varied from FIGO Stage IA to IV-B. Thus, this case series highlights the importance of good history taking, clinical examination and investigations for early diagnosis of EC.

Keywords: Abnormal uterine bleeding, TVS, Hysteroscopy, Histopathology

INTRODUCTION

Endometrial carcinoma (EC) represents an important cause of morbidity and mortality among women worldwide. Global Cancer Statistics 2020 estimated more than 417,000 new cases and approximately 97,000 deaths from endometrial cancer worldwide.[1] Most ECs are detected early due to the presenting symptom being postmenopausal bleeding which often prompts early evaluation.[2]

Important risk factors for EC include excess body weight, diabetes mellitus, hypertension, nulliparity and prolonged exposure to unopposed oestrogen.[3,4] Excess body weight is an important modifiable risk factor and has been estimated to account for approximately 34% of corpus uteri cancers in women worldwide.[5] Hereditary predisposition, particularly Lynch syndrome, accounts for a smaller but clinically important proportion of EC.[6] Individual case reports of atypical presentations of endometrial carcinoma have been described in literature.[7,8] We hereby present a case series of 4 cases with atypical presentations. We highlight atypical presentations, our systemic approach, diagnostic pitfalls and final diagnosis and treatment. Presentation varied from per rectal bleeding, young nulliparous woman with amenorrhea and a large adnexal mass, persistent vaginal discharge in a postmenopausal woman with early onset menopause and long-standing uterine prolapse. These presentations initially suggested common benign gynaecological or non-gynaecological conditions, highlighting the importance of maintaining high clinical suspicion for endometrial malignancy.

CASE SERIES

Case 1

A 54-year-old (P3L3), obese (BMI 41Kg/m^2) presented with mild bleeding per rectum for 5 days. Per rectal

bleeding as presenting complaint in endometrial cancer is very rare.[9] She was a known hypertensive and diabetic on treatment. She had an episode of Cerebrovascular accident with right sided hemiparesis for 1year. Patient had history of fracture of left distal fibula 10 days back. Examination revealed a bulky uterus and healthy-looking cervix with mild bleeding through os. TVS and MRI showed an enlarged uterus (9.4x5x3.8cm) with thickened endometrium (14 mm). Diagnostic hysteroscopy showed thickened polypoidal endometrium with increased vascularity.

Histopathology came out to be Endometrioid Endometrial Carcinoma (Grade 2). Patient underwent Total Abdominal Hysterectomy with Bilateral Salpingo-oophorectomy and pelvic and para-aortic lymphadenectomy (as 2 enlarged nodes were palpated in this area). Histopathological examination confirmed Endometrioid Carcinoma with <50% myometrial involvement and all lymph nodes free of tumor (FIGO stage IA2 Grade 2).[10] Patient is currently on follow up.

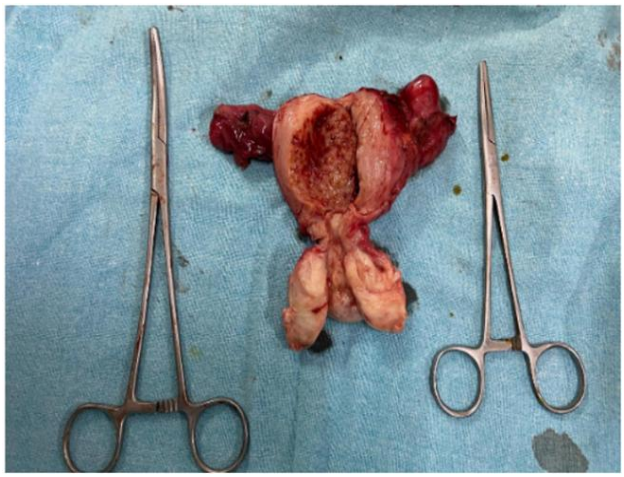


Figure 1: Gross specimen of post-operative uterus.

Case 2

A 30-year-old (BMI 22 kg/m^2), married for 4 years, nulliparous, trying to conceive, presented with 2 months of amenorrhea followed by heavy bleeding per vaginum and pain abdomen with nausea and vomiting for 15 days. She was extremely pale. A 14 week-sized uterus was palpated abdominally along with a 9x10 cm firm to hard mass in right iliac fossa. She was admitted with a provisional diagnosis of incomplete abortion but urine pregnancy test came out to be negative. Her history revealed that she had a past history of open adenomyomectomy and left endometriotic cyst removal 6 years back. She had also received 3 doses of Leuprolide 2 months prior to coming to our hospital for pain abdomen.

TVS revealed a 9.7x10.4 cm multiloculated cystic right adnexal mass with vascular mural papillary projections and calcifications along with a bulky uterus filled with heterogenous hyperechoic material. CECT showed enlarged lymph nodes upto para-aortic. After correction of hemoglobin, she underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (right ovary enlarged 6x5 cm and was adherent to uterus and bowel), Infracolic omentectomy, pelvic and para-aortic lymphadenectomy.

Histopathological report showed Grade 2 endometrioid carcinoma with >50% myometrial invasion. Cervical stroma, right ovary and fallopian tube, omentum and pelvic nodes were involved with tumor but para-aortic nodes were free of tumor (FIGO stage IV B).[10] She was initiated on adjuvant Chemoradiation and is currently on follow up.

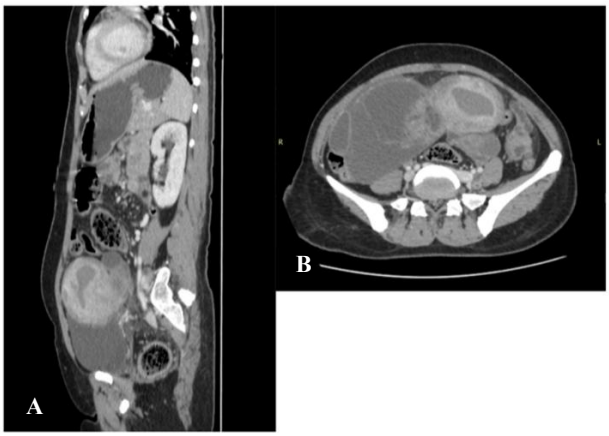


Figure 2: CECT images (A) 1st image showing few enlarged Para-aortic lymph nodes, Retroperitoneal lymph nodes, Bilateral Common Iliac and Obturator nodes and (B) 2nd image shows a solid cystic multiseptate mass in right ovary with enhancing solid mural nodule.

Case 3

A 52-year-old (P1), postmenopausal for 9 years (BMI 27 Kg/m^2), came with complaints of vaginal discharge for 6 months for which she had been taking treatment but without relief. Later on, repeated history taking, it was found that the discharge was occasionally blood stained for 3 months. Local examination showed a hypertrophied cervix with minimal clear discharge and normal sized uterus. TVS revealed normal sized uterus with thickened endometrium (19.5 mm) having internal cystic spaces. Hysteroscopy showed endometrial cavity filled with multiple polypoidal growth. Biopsy came out to be Grade 1 endometrioid endometrial carcinoma. MRI showed distortion of endomyometrial junction and invasion limited to <50% of myometrium.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy done. Histopathological examination confirmed the diagnosis (FIGO stage IA2-Grade 1) with <50% myometrial involvement.[10] Adnexa, cervix and lymph nodes were free of tumor. She is currently on follow up.

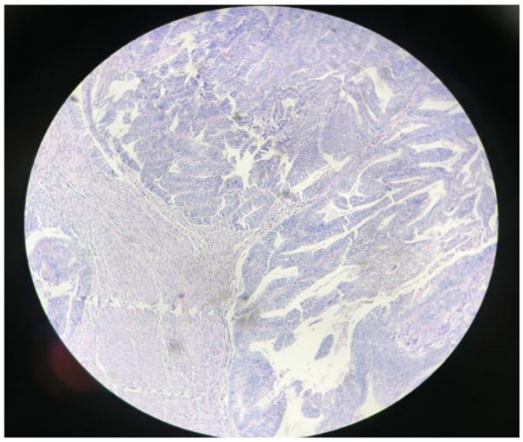
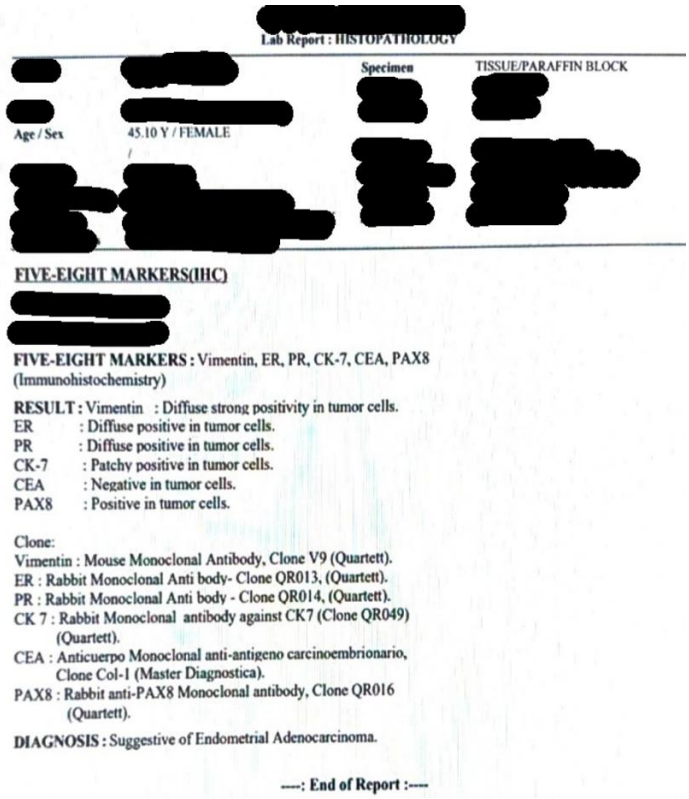


Figure 3: Endometrioid endometrial carcinoma-histologic Grade 1.

Case 4

A 45-year-old obese (BMI 36 Kg/m^2) presented with a 10 years history of something coming out per vaginum and heavy menstrual bleeding with dysmenorrhea for 1 year. She also had inter menstrual spotting for 2 months. On local examination there was 2nd degree descent of cervix

with cystocele and a bulky uterus. She had been planned for vaginal hysterectomy with cystocele repair at a peripheral hospital but was referred to our center as she was not fit for surgery. TVS revealed Uterus size 9.8x5.2x6.6 cm with ET 11 mm. Hysteroscopy showed a polypoidal growth at fundus and cavity otherwise normal. Biopsy showed endometrial adenocarcinoma. MRI revealed a 6.5x3.5x5.1 cm endometrial mass with >50% myometrial invasion but no serosal breach. A 10x7 mm left internal iliac node and left hydrosalpinx seen. Total abdominal hysterectomy, bilateral salpingo–oophorectomy and bilateral pelvic lymphadenectomy was done. Para aortic lymphadenectomy and omentectomy could not be done due to intraoperative desaturation necessitating completion of procedure and transfer ICU (Intensive Care Unit) where she was kept for 2 days. HP confirmed endometrioid carcinoma Grade 3 with >50% myometrial invasion, one left internal iliac node positive (FIGO stage IIIC1, Grade 3).[10] Ovaries and cervix were free of tumor. Patient was discharged on 10th post-operative day and is on chemotherapy now.



[redacted]
Lab Report : HISTOPATHOLOGY

Specimen TISSUE/PARAFFIN BLOCK

Age / Sex 45.10 Y / FEMALE

[redacted]

FIVE-EIGHT MARKERS(IHC)

[redacted]

FIVE-EIGHT MARKERS : Vimentin, ER, PR, CK-7, CEA, PAX8 (Immunohistochemistry)

RESULT : Vimentin : Diffuse strong positivity in tumor cells.
ER : Diffuse positive in tumor cells.
PR : Diffuse positive in tumor cells.
CK-7 : Patchy positive in tumor cells.
CEA : Negative in tumor cells.
PAX8 : Positive in tumor cells.

Clone:
Vimentin : Mouse Monoclonal Antibody, Clone V9 (Quartett).
ER : Rabbit Monoclonal Anti body- Clone QR013, (Quartett).
PR : Rabbit Monoclonal Anti body - Clone QR014, (Quartett).
CK 7 : Rabbit Monoclonal antibody against CK7 (Clone QR049) (Quartett).
CEA : Anticuerpo Monoclonal anti-antigeno carcinoembrionario, Clone Col-1 (Master Diagnostica).
PAX8 : Rabbit anti-PAX8 Monoclonal antibody, Clone QR016 (Quartett).

DIAGNOSIS : Suggestive of Endometrial Adenocarcinoma.

----: End of Report :----

Figure 4: Shows the IHC markers of the patient.

DISCUSSION

Endometrial carcinoma (EC) commonly presents with abnormal uterine bleeding, particularly postmenopausal bleeding, which often facilitates early clinical evaluation and diagnosis.[2,11] However, the present case series demonstrates that EC may present in many atypical clinical scenarios in which the initial diagnosis may point towards a non-malignant and sometimes non-endometrial condition. The principal novelty of this series is the highlighting of four distinct diagnostic pitfalls in history and examination within a single case series: complaint of

per rectal bleeding, endometrial carcinoma in a young nulliparous woman with amenorrhea and a large adnexal mass, persistent vaginal discharge in a postmenopausal woman with early onset menopause, and endometrial carcinoma coexisting with longstanding uterovaginal prolapse. Although individual atypical presentations of EC have been reported, our atypical presentation series is a unique combination of clinical scenarios.[7,8]

The first case where endometrial carcinoma presented with per rectal bleeding which is a rare presentation.[9] Although initially complaint of per rectal bleeding led to anal and rectal examination along with pelvis, but pelvic examination demonstrated bleeding through the cervical os and subsequent evaluation revealed endometrial carcinoma. This highlights the importance of correlating the patient's description of bleeding with clinical examination, particularly in women with risk factors for EC. In contrast to the classical presentation of postmenopausal bleeding described in the literature, this case demonstrates how an apparently non-gynecological symptom may mask the true diagnosis unless the thorough clinical examination is done.[2,11] The obesity, hypertension and diabetes in this patient are recognized risk factors for EC.[3,4]

The second case represents a particularly unusual presentation because of the patient's young age, nulliparous status and normal BMI. Incidence of endometrial cancer is only 2-3 per 100,000 at the age of 30 yrs.[12] The combination of amenorrhea, subsequent heavy bleeding, abdominal pain and a large adnexal mass initially suggested pregnancy-related or adnexal pathology rather than endometrial malignancy. The eventual diagnosis of Grade 2 endometrioid carcinoma with ovarian, cervical, tubal, omental and pelvic nodal involvement and FIGO stage IVB disease demonstrates that young age and the absence of obesity do not completely exclude EC. This case is particularly important in the context of the present series because it contrasts with the typical epidemiological profile of EC and illustrates how an associated adnexal mass may dominate the initial diagnostic impression.

The third case shows endometrial cancer in early onset menopause, which represents a lower risk for endometrial cancer and fourth case shows endometrial cancer in prolapse at 45 years age with overall risk of less than 0.2% for UV prolapse at 45 years age.[13-15] These cases demonstrate how apparently benign or unrelated gynecological conditions though unusual may coexist with endometrial malignancy. Previous reports of atypical EC presentations demonstrate that malignancy may occasionally present without the classical symptom of postmenopausal bleeding.[7,8] In the fourth case, longstanding uterovaginal prolapse provided an alternative explanation for the patient's symptoms; however, the associated heavy menstrual bleeding and intermenstrual spotting prompted further evaluation and led to the diagnosis of Grade 3 endometrioid carcinoma with pelvic nodal involvement. Thus, the present series of cases suggest all these scenarios which had reduced chances of suspecting endometrial cancer, were finally diagnosed due to diligent clinical examination, and investigations. Coexisting non-gynecological and benign-appearing gynecological conditions did not prevent our optimal evaluation of abnormal symptoms and clinical findings.

An important common finding across all four cases was the role of systematic clinical assessment followed by appropriate imaging and endometrial tissue diagnosis. Transvaginal ultrasonography identified endometrial abnormalities or associated pelvic pathology in all patients, while hysteroscopy permitted direct visualization of the endometrial cavity and identification of polypoidal or abnormal endometrial lesions in selected cases. Hysteroscopic guided evaluation and endometrial sampling for histopathological confirmation is a must for complete evaluation and diagnosis of EC.[2] In our series, definitive diagnosis was established by histopathology in all four patients, with disease ranging from FIGO stage IA to stage IVB. Atypical presentation may have delayed diagnosis in 3 cases leading to advanced stage. Taken together, these cases demonstrate that the diagnostically complex scenarios in EC. The series therefore adds to existing spectrum of atypical EC presentations by demonstrating four different clinical scenarios with optimal diagnostic pathway. A high index of suspicion, careful characterization of bleeding or vaginal discharge, thorough pelvic examination and optimal use of imaging and endometrial sampling modalities remain essential. EC must be kept in mind when persistent, unexplained or discordant symptoms occur with clinically benign diagnosis initially.

CONCLUSION

This case series highlights the importance of maintaining a high index of suspicion, performing systematic clinical examination, and using appropriate diagnostic modalities such as TVS and hysteroscopy. Women with benign or inconclusive histology, but persistent symptoms or suspicious ultrasound findings, should be offered a hysteroscopy with a directed biopsy to directly visualize the uterine cavity. The pitfall of "premature closure" attributing a symptom like abnormal uterine bleeding (AUB) or discharge entirely to a visible benign issue is a primary driver of delayed diagnosis and higher-stage progression in endometrial carcinoma.

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