

Endometrial Adenocarcinoma in a 33-Years-Old Virgin Female

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Endometrial cancer is the third most common gynecologic cancer, and mainly occurs in menopausal women and rare in women of reproductive age. Endometrial cancer in young women can be difficult to diagnose, where the dysfunctional uterine bleeding is the most common cause. Most of these patients present with clinical evidence of polycystic ovarian disease but in some reports the patients lacked these features. The causes of endometrial cancer in this age group may be familial, associated with Lynch syndrome, or sporadic^{1,2}.

In postmenopausal women, endometrial thickness is positively correlated with the presence of endometrial malignancy and endometrial biopsy can be decided according to the endometrial thickness, however in women of reproductive age, there is no clinical guideline to determine when the endometrial biopsy should be performed³.

With this background we present a case of endometrial carcinoma in a young woman who had presented with prolonged vaginal bleeding. A 33-year-old virgin visited gynecology department complaining from abnormal uterine bleeding. An endometrial biopsy revealed FIGO (International Federation of Gynecology and Obstetrics) grade II endometrial adenocarcinoma. In the treatment of endometrial cancer, conservative management should be considered if the patient is nulliparous or wants the fertility preservation. However, this patient offered radical hysterectomy.

Key words: Virgin, Young Adult, Endometrial Neoplasm, Fertility Preservation

INTRODUCTION

The incidence of endometrial cancer has been steadily increasing in younger and older females with almost 2% to 14% percentage of the cases occur in women 40 years of age and younger. Various factors have been suggested for this change, including late marriage accompanying women's social advancement and increased obesity and diabetes due to Westernization of diet⁴. Endometrial cancer can be classified in to two different types according to their estrogen dependency, Types I is estrogen-dependent, and occurs in younger women, begin as endometrial hyperplasia and progress to carcinoma, inherited factors have also been considered as important risk factors, especially in young women. The other one, type II endometrial cancer is estrogen-independent, and not associated with endometrial hyperplasia, and tend to occur in older, postmenopausal women⁵.

Standard treatment of low-risk EC (such as grade 1–2 endometrial adenocarcinoma and cancer limited to endometrium) is surgical staging with total hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymph node evaluation. The 5-year survival rate of low risk EC is 90% or more, which is a very good prognosis. These options can be applied to a menopausal or a premenopausal woman who do not care for the conception. Medical treatment with progestogens can be used in young patients who want to preserve their fertility with grade I, stage IA endometrial cancer under the complete evaluation and careful selection, all the risks should be informed to the patients because this is not a standard therapy^{6,7}.

CASE REPORT

A 33-year-old virgin single Indonesian patient admitted to the gynecology department of Bahrain defense force hospital; with a complaint of irregular menstruation and heavy menstrual bleeding on and off for 4 months, with excessive continuous bleeding in the last

two weeks not stopped with any medication. Before these 4 months her cycle was regular but prolonged from 10-12 days per month. She had history of fibroid uterus, with no past history of hormonal treatment and no other remarkable medical history. Her family history was negative for ovarian, uterine and colonic cancer. she got menarche at 15 years old, her height 155.7cm and her weight was 50.5kg. Her BMI was 20.80 kg/m² calculated as body weight divided by the square of height (kg/m²), with no history of any sexually activity.

At the time of consultation, a trans-abdominal ultrasonography showed thickened endometrium of 18 mm with protruding mass around the cervical area, both ovaries were normal. She admitted to the hospital for examination and treatment, her hemoglobin level was 6.7 g/dL, which was corrected to 9.70 g/dL after transfusion of three units of packed red blood cells. She received medical treatment in form of hemostatic medication and MRI advised.

Two weeks later, the patient presented to the emergency department complaining from dizziness, palpitation with marked pallor with no jaundice, her pulse was 120 bpm with sinus tachycardia, BP 90/60, her hemoglobin again dropped to 6 gm, and during abdominal examination there was; tender lower abdomen. She had severe vaginal bleeding, and she refused per vaginal examination. Transabdominal scan revealed bulky uterus with blood collected and clotted within uterine cavity, endometrial stripe 6 mm, large fibroid 7.7 x6,6x9.6 cm in lower part of the uterus and cervix and no ovarian cyst or adnexal mass seen. Patient admitted again and received 2 units of packed red blood cells. Her hemoglobin level improved to 9.5 gm and MRI scan was done. Her blood investigation revealed border line tumors markers, CA125 was 63.3 IU, CA19-9 was 41.2IU, and CA15-3 was within normal. Therefore, the Patient was booked for laparotomy and myomectomy.

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MRI REPORT

Relatively bulky anteverted uterus measuring approximate 96.8x75.8x72.7mm with lobulated swelling of non-homogenous signal intensity measuring approx. 61.3x59.1x55.8mm with few areas of tiny cystic degeneration within, is seen involving the uterine cervix and to less extent the lower uterine segment. The mass shows thick ring enhancement after I.V contrast injection. The uterine cavity is markedly widened and measures 52.0x31.9mm and shows heterogeneous signal intensity and heterogeneous enhancement after I.V contrast injection (Figure 1).

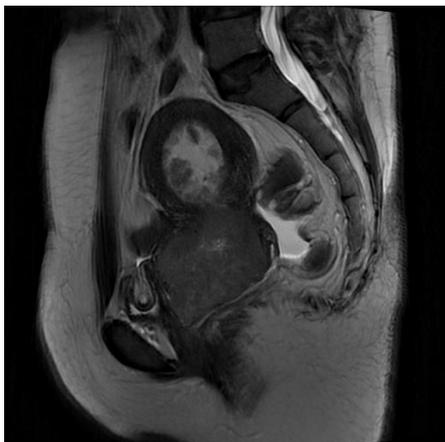


Figure 1: Magnetic resonance imaging showing lobulated swelling of non-homogenous signal intensity measuring approximately 61.3 mm × 59.1 mm × 55.8 mm, with few areas of tiny cystic degeneration involving the uterine cervix and the lower uterine segment to a lesser extent

Normal size of the left ovary (34.2x20.5mm) with mild enlarged right ovary (61.0x29.7mm). Both ovaries show few follicular cysts. The right ovary shows a simple appearing cyst 37.1x29.0mm. No sizeable pathologic masses. Normal appearance of the pelvic bones, Normal pelvic muscles and the muscles of the gluteal region with Normal appearance of the urinary bladder. Impression: Bulky uterus with large cervical mass (suspected Malignant). Pathologic correlation is highly recommended (Figure 2).



Figure 2: Magnetic resonance imaging showing, thick ring enhancement after I.V contrast injection. The uterine cavity is markedly widened and measures 52.0 mm × 31.9 mm and shows heterogeneous signal intensity and heterogeneous enhancement after I.V contrast injection

Laparotomy was performed under general anesthesia, omental biopsy and peritoneal washing were taken, liver, spleen and kidney were

normal, no palpable lymph node, no ascites, there was peritoneal adhesion looking like active endometriosis, and the ovaries were stuck in the ovarian fossa with marked adhesion. Her uterus was bulky 12 weeks with palpable mass within lower anterior uterine wall, firm in consistence extending to the whole of the cervical canal which failed to be approached abdominally. Therefore, the decision of pelvic examination under anesthesia was taken.

During pelvic examination, the hymen was intact, the cervix was hypertrophic free Mobile with friable growth originating from the endocervix about 7x7 cm with excessive bleeding. there was, no thickness in the parametrium or nodules during rectal examination. The specimen sent for frozen section and verbal report was!! Well differentiated adenocarcinoma in the cervical biopsy and uterine curettage taken with good hemostasis, vaginal pack and Foley's catheter kept in.

During Post-operative hospital staying, the patient remained vitally stable, a febrile, vaginal packed and Foley's catheter remained in situ for one day then removed with minimal bleeding. She kept on antibiotic and low molecular weight heparin injection for 7 days and again she received 2 units of packed RBCS. staging CT scan done and final histopathological result for the specimen showed grade 2 endometrioid endometrial adenocarcinoma, NOS; evidence of invasion FIGO 2A at least, omental biopsy showed patchy of chronic inflammation. ADDENIUM: the tumor cells are strongly positive for vimentin and negative for CEA; confirming the diagnosis of endometrioid adenocarcinoma. In our case, we could not find any hereditary relations from a detailed family history, so, did not perform a genetic study.

The case referred to a gynecologic oncologist for further care. After extensive discussion and all the risk explained to the patient including (failure, progression of the disease and ovarian metastasis) the decision was to proceed with definitive surgical management. the patient underwent total abdominal hysterectomy with bilateral salpingectomy and suspect malignancy pelvic lymphadenectomy.

DISCUSSION

No standard Screening test for endometrial cancer due to lack of appropriate cost effective and acceptable test. About 90% of women with endometrial carcinoma have abnormal uterine bleeding as their presenting symptom. Any women presenting with these complaints irrespective of the age and virginity should be thoroughly evaluated for malignancy risk factors and clinical findings⁸.

Here; we report a case of a 33 years old virgin with endometrial carcinoma. The known risk factors for developing endometrial cancer are obesity, null parity, infertility, hypertension and diabetes, and all these factors are also known to be associated with polycystic ovary syndrome⁹. It was surprising to see endometrial carcinoma without any these factors, in contrast our patient was thin with low BMI, High BMI correlates with good prognostic features including low tumor grade, and presentation at early stage. Our Patients with low BMI had higher-grade tumors and presented at advanced stages with worse clinical outcomes. Indeed, Duska et al demonstrated that patients with a BMI lower than 25 were more likely to have advanced disease and high-risk histology compared with those women with high BMI¹⁰.

Our patient was virgin 33 years old and there was difficulty in her gynecological examination due to her virginity, however, the physician should consider the endometrial biopsy to rule out endometrial cancer if there are clinical findings such as thickened endometrium, or clinical history suggesting long-term unopposed estrogen exposure. Office

Endometrial biopsy was not done keeping in mind the patient's age, virginity for which office genital biopsies are difficult and ultrasound diagnosis of fibroid uterus which causes miss diagnosis. With the changing trends of diseases, it is important to evaluate the young patients also for malignancy.

The case we described was a young patient with a grade II endometrioid adenocarcinoma with myometrial invasion, and unfortunately conservative management couldn't be considered because of their poor prognosis. Several studies are available in literature about fertility sparing approach. Progestin treatment combined with hysteroscopic ablation for endometrium seems to be the most validated conservative management. Anyhow this treatment is not free risk, because it is not always effective and disease progression during or after treatment is possible with restricted evaluation and selection of patients before starting treatment is mandatory.

The majority of controlled studies about the conservative treatment concerns patients with endometrioid adenocarcinoma grade I There are only few cases with grade II endometrial carcinoma reported and there are not available cases with grade III carcinoma treated with hormones¹¹. Study done by Laurelli et al, twenty patients with endometrial cancer, grade I, stage IA with positive estrogen and progesterone receptor underwent hysteroscopic ablation of the tumor and received hormone therapy, megestrol acetate (160 mg/day) or Levonorgestrel (52 mg) IUD for 6 months, all but one responded to that treatment¹².

Brown et al 2012 reported a case of an 18-year-old girl with grade II endometrioid adenocarcinoma, treated with Levonorgestrel IUD. Endometrial biopsy performed every 3 months revealed a complete regression of endometrial cancer and hyperplasia¹³.

Recommendations were expressed by Eskander et al, whereby only patients with grade I, stage IA endometrial cancer and expression of progesterone receptors could start conservative treatment. Moreover, it was necessary to exclude myometrial invasion, lymph vascular space invasion, metastatic disease and suspicious synchronous ovarian cancer¹⁴.

A retrospective study of Park et al, demonstrated the effectiveness of high dose progestin therapy in the conservative management of endometrial cancer in young patients when limited to the endometrium¹⁵. Although in the majority of the literature about fertility-sparing management reported treated patients with grade I stage IA endometrial cancer, Benshushan considered conservative treatment only for early endometrial cancer (stage I, grade I) with MRI or transvaginal ultrasound staging, before starting treatment. CA 125 should be also taken. Moreover, he considered a clear counseling mandatory, informing the patient about risks and benefits, including that hormonal therapy is not the standard treatment for endometrial cancer and disease progression during treatment is possible¹⁶.

On the other hand, a case reported by Mitamura et al, a 14 years old girl with a grade II endometrial cancer was treated with medroxyprogesterone acetate for a month. After one month of treatment, endometrial biopsy revealed no hormonal response and hysterectomy was performed. The uterine examination showed myometrial invasion which was not revealed by previous CT scan and MRI¹⁷.

CONCLUSION & RECOMMENDATION

Although endometrial cancer in virgin women during reproductive period is rare and there is difficulty in examination due to their virginity, the physician should consider the endometrial biopsy to

rule out endometrial cancer specially if there are clinical findings suspected malignancy. Prolonged and heavy menstrual periods, and intermenstrual spotting, may indicate hysteroscopic examination with biopsy, irrespective of the age, as hysteroscopy make it easy to visualize the cavity and to obtain the biopsy from the specific site. In a case young patient with fibroid uterus, an effort should be made to exclude associated neoplastic endometrial pathology.

Authorship Contribution: All authors share equal effort contribution towards (1) substantial contributions to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

Potential Conflict of Interest: None.

Competing Interest: None.

Sponsorship: None.

Acceptance Date: 11 January 2021

Ethical Approval: Approved by the Ethics Research Committee, Bahrain Defense Force Hospital - Royal Medical Services, Bahrain.

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