Case Reports

Endometrial adenocarcinoma in a young woman

D. Caserta, G. Bordi, S. Scarani, M. Moscarini

Department of Woman's Health and Territory's Medicine, University of Rome Sapienza, S. Andrea Hospital, Rome (Italy)

Summary

Background: Endometrial carcinoma usually occurs in post-menopausal women, but in three to five percent of cases, it affects patients under 40 years of age, who wish to preserve their fertility. Patients with polycystic ovarian syndrome (PCOS) and the features of this syndrome (including obesity, hyperinsulinemia, and hyperandrogenism) are at great risk of developing endometrial carcinoma. *Case report:* The authors report a case of endometrial adenocarcinoma at Stage I in a 37-year-old obese woman with PCOS who underwent surgical staging. *Discussion:* In young women with obesity and PCOS, a periodic evaluation of the endometrium and implementation of risk-reducing measures for the development of endometrial cancer are needed.

Key words: Endometrial adenocarcinoma; Atypical endometrial hyperplasia; Obesity; Polycystic ovarian syndrome; Surgery; Conservative treatment.

Introduction

Endometrial carcinoma is the most common cancer among women and the most common gynecological malignancy in Western countries, with an incidence of 15-20 per 100,000 women per year [1, 2]. Although it is primarily a disease of postmenopausal women, 25% of patients are in premenopausal age, with three to five percent 40 years of age or younger [3].

According to the international literature, the majority of cases of endometrial adenocarcinoma in young women were well-differentiated (Grade 1) and at early Stages with a superficial invasion (Stage I) [4].

Young patients with endometrial carcinoma tend to have a history of estrogen use or hormone-related disorders such ovarian dysfunction, chronic anovulation, infertility, obesity, and polycystic ovarian syndrome (PCOS) [5]. These condition are associated with unopposed estrogen status, which induces endometrial proliferation resulting in increased risks of endometrial hyperplasia and carcinoma.

The standard treatment of endometrial carcinoma is surgical staging, which would destroy the reproductive function. The classic treatment consists of total hysterectomy and bilateral salpingo-oophorectomy, with a pelvic and aortic lymphadenectomy, if required. However, in young women with low histological grade and early stage of the disease, conservative hormonal therapy has also been attempted with close follow-up.

In this report, the authors present the case of a 37-year-old patient with endometrial cancer diagnosed at Stage IA, grade 1 according to the American Joint Committee on Cancer (AJCC) 2010 classification of endometrial cancer.

Case Report

A 37-year-old woman was referred to this present hospital for menorrhagia. The patient's past medical and surgical histories were uneventful. Her gynaecological history revealed that she was nulliparous and had used an oral contraceptive for the last two years for treating oligomenorrhea. Her menarche had occurred at the age of 16 years, her menstrual cycles were irregular, and her last menstrual period occurred 45 days prior to the first visit to this hospital. Her recent pap smear was negative.

On physical examination, she was hirsute (Ferriman Gallwey classification Grade III) and obese, with a body mass index (BMI) of 35.2 kg/m² and a waist circumference of 110 cm. A speculum examination showed an apparently healthy-looking cervix. Pelvic examination was normal.

Blood tests for thyroid function and prolactin concentrations were normal. Her oral glucose tolerance test values were within normal range. She was normotensive (blood pressure of 110/70 mmHg). Her fasting lipid profile was normal (total cholesterol 198 mg/dl, triglycerides 99 mg/dl, HDL 50 mg/dl, and LDL 128 mg/dl). The urine analysis, renal function test, coagulation tests, liver function test, and electrocardiography were all normal.

A transvaginal ultrasound demonstrated a normal-sized uterus and an endometrial thickness of 20 mm in secretory phase of cycle. The ovaries were micropolycystic. Right ovarian volume was 7.7 ml, left ovarian volume was 7.2 ml. Sonohysterography showed a hyperplastic endometrium and the presence of an endometrial polyp.

A hysteroscopy was performed to investigate the suspected intrauterine lesion, and it revealed the presence of a polypoid mass of ten mm in diameter protruding from the fundus of the uterus and two polyps of five and three mm in diameter, respectively, in proximity to the left tubal ostium. The polyps were removed using an electrical loop. The histological examination diagnosed the presence of a well-differentiated adenocarcinoma in the context of atypical complex endometrial hyperplasia.

The patient was informed about diagnosis and prognosis. Conservative medical treatment including high-dose progestin, follow-up endometrial biopsy, and the benefits and demerits of surgery were explained in detail to the patient. The patient chose to procede with surgical treatment and an informed consent was obtained. During laparotomy the uterus appeared normal and the

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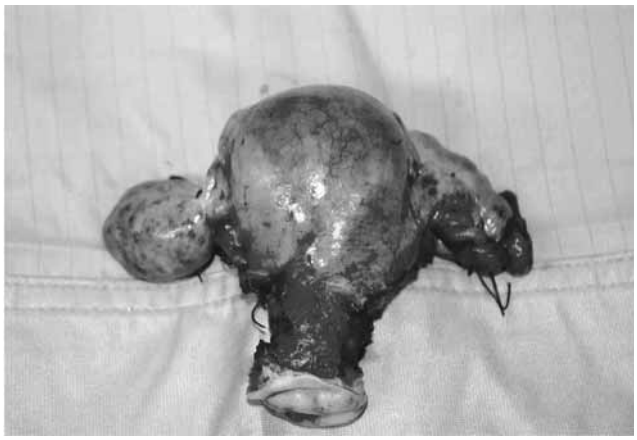
Fig. 1



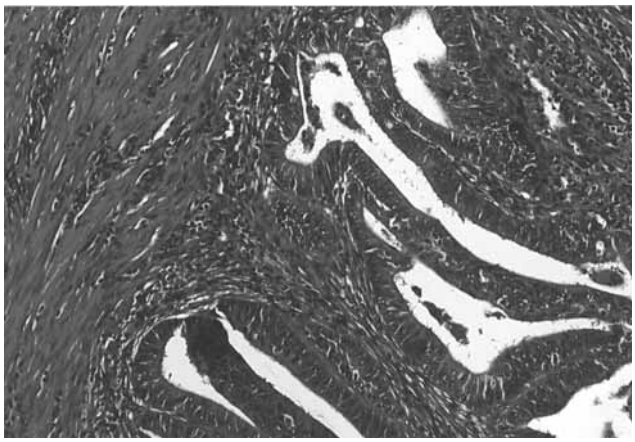


Fig. 2

Figure 1. — Surgical specimen: uterus with unremarkable fallopian tubes and polycystic ovaries.
Figure 2. — Histopathologic image of endometrial adenocarcinoma at x100 magnification (Hematoxylin-eosin stain).

ovaries were micropolycystic. There was no free liquid in the pelvis. The pelvic lymph nodes were not enlarged. She underwent a total hysterectomy and bilateral salpingo-oophorectomy with iliac lymphadenectomy. Peritoneal washing was performed by rinsing the cavity with 100 cm^3 of physiological saline.

At histological examination the uterus measured 8.5 × 7 × 4.5 cm and it was attached with unremarkable fallopian tubes and with ovaries of brown colour and irregular profile (Figure 1). The adenocarcinoma originated in the context of complex atypical hyperplasia (Figure 2). On sectioning, the tumor was limited to the endometrium. The superficial myometrium was unremarkable. In both ovaries, multiple subserosal cystic follicles were observed. Histopathology diagnosis was consistent with endometrioid adenocarcinoma at Stage IA, grade 1 according to the AJCC 2010.

The patient was discharged on the fifth postoperative day. At the two-week postoperative follow-up visit, the patient no longer had vaginal bleeding and her abdominal wound was well-healed. She was advised to continue her follow-up care at the present hospital; hence she did not required any further treatment.

Discussion

The risk factors associated with endometrial adenocarcinoma include obesity, nulliparity, unopposed estrogen, chronic anovulation, early menarche, late menopause, diabetes mellitus, and hypertension.

Endometrial carcinoma was the first cancer to be recognized as being related to obesity. The percentage of endometrial cancer cases attributed to excess body weight is increasing, and recent estimates suggest that up to 90% of type 1 endometrial cancer patients are obese [6]. Alterations in endogenous hormone metabolism may provide the main links between endometrial cancer risk and obesity. Obese women have high levels of endogenous estrogen due to the conversion of androstenedione to estrone and the aromatization of androgens to estradiol in peripheral adipose tissue. High serum estrogen and androgen levels have been correlated with risk for endometrial cancer [6]. In obese postmenopausal women, the increased risk of this malignancy is mainly due to elevated circulating estrone levels and to decreased sex hormone binding globulin levels. Conversely, in premenopausal women, obesity may affect endometrial cancer risk through its tendency to cause anovulation and luteal phase deficiency [7].

Obesity is strongly associated with PCOS, in which prolonged anovulation and consequent exposure of the endometrium to estrogen, unopposed by progesterone, could increase the risk of endometrial cancer by inducing endometrium proliferation [8].

PCOS is considered to be a common endocrine disorder in women of reproductive age, with population prevalence estimates of six to ten percent of women of reproductive age [9]. An international consensus group proposed that at least two of three criteria have to be met in order to diagnose PCOS. These criteria are oligo-anovulation (usually manifested as oligomenorrhea or amenorrhea), elevated levels of circulating androgens (hyperandrogenemia) or clinical manifestation of androgen excess, and polycystic ovaries as defined by ultrasonography [10]. In addition to reproductive and hyperandrogenic concerns, women with PCOS are more likely to be insulin resistant, overweight, and obese, and several studies have demonstrated that PCOS is associated with an increased risk of glucose intolerance and type 2 diabetes mellitus, independent of BMI [11]. PCOS has also been associated with an increased prevalence of lipid-related abnormalities, hypertension, subclinical atherosclerosis, and vascular dysfunction [12].

A recent systematic review showed that women with PCOS were almost three times more likely to develop endometrial cancer [13]. Women with PCOS have several risk factors for endometrial cancer, including unopposed estrogen stimulation of the endometrium in anovulatory women, obesity, diabetes, insulin resistance, insuline-like growth factors, nulliparity, cyclin D1, glutathione-S-transferase, and progesterone resistance [14]. Several studies demonstrated that the incidence of PCOS was significantly higher in young patients with endometrial cancer than in older patients [15, 16].

In the present case report, the patient was severely obese, hirsute, and nulliparous, and she complained of oligomenorrhea. Chronic anovulation due to unopposed

estrogens represents a factor which increases the risk of endometrial adenocarcinoma by inducing endometrium proliferation.

At the histological examination, the adenocarcinoma had developed in an area of endometrial atypical hyperplasia. Endometrial hyperplasia with cellular atypia is considered a precancerous lesion. Endometrial cancer has been reported a concurrent condition in 42.6% of women who have been diagnosed with atypical endometrial hyperplasia by endometrial biopsy [17]. Endometrial hyperplasia occurs in 35% of women with PCOS who are not receiving either contraceptive steroids or periodic progestin withdrawal. Those at higher risk of endometrial hyperplasia are women who have intermestrual interval of more than three months or an endometrial thickness of more than seven mm [18]. Several studies have appeared to support this association, and it is common practice among gynaecologists and physicians to prescribe hormonal treatments to reduce this perceived risk, although there is no consensus on the subgroup of patients with PCOS in whom this treatment is required [19].

The most important prognostic factors of endometrial cancer are histological grade, cancer stage, and myometrial invasion. Fortunately, most cases of endometrial adenocarcinoma in young women are at early stages with a superficial invasion (Stage I) and 90% of all cases are well-differentiated (grade 1) [4].

Surgery is the classic treatment for endometrial cancer. It consists of total abdominal hysterectomy and bilateral salpingo-oophorectomy, with a pelvic and aortic lymphadenectomy, if required. For clinical Stage I tumors, cell type, histologic grade, depth of myometrial invasion, peritoneal cytology, vascular invasion, and age are all significant independent risk factors. Since only cell type and grade can be determined without performing hysterectomy, the International Federation of Gynaecology and Obstetrics (FIGO) has defined endometrial cancer as a surgically-staged disease.

There is a therapeutic alternative for young women wishing to become pregnant in the future, but this is not standard management and should not be routinely recommended. Only strictly selected patients with early-stage disease should be indicated for long-term medical treatment and careful evaluation before and after treatment should be performed. Patients must be carefully informed of the oncological risks.

The authors did not consider the conservative management in the present patient because she did not desire to preserve fertility, had poor compliance, and chose surgical treatment.

Conclusion

The association between obesity, PCOS, atypical endometrial hyperplasia, and endometrial cancer has relevant implications for clinical practice as it calls for the implementation of risk-reducing measures, including the potential of introducing a screening programme for early cancer detection.

Based on the data presented in this report, the authors would carefully suggest the greater monitoring of premenopausal women with PCOS and/or the associated symptoms of obesity and irregular periods, by performing accurate physical examination and diagnostic studies.

Regarding treatment, although there are several examples of successful medical therapies in the literature, surgery remains the gold standard, whereas medical treatment should not be routinely recommended, but it must be reserved for selected patients who understand and accept that it is not a standard treatment.

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Address reprint requests to:
D. CASERTA, M.D.
Department of Woman Health and Territory's Medicine
S. Andrea Hospital
Via Di Grottarossa, 1035-1039
00189 Roma (Italy)
e-mail: donatella.caserta@uniroma1.it