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Spontaneous Pregnancy After Conservatively Treated Endometrial Adenocarcinoma

Konservatif Tedavi Edilen Endometriyum Karsinomu Sonrası Spontan Gebelik

Kadın Hastalıkları ve Doğum

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Özet

Yirmi altı yaşındaki hasta kliniğimize primer infertilite tanısı ile başvurdu. Infertilite tetkikleri sırasında kalın ve düzensiz endometriyum saptanması üzerine yapılan endometriyal örneklemede 'iyi diferansiye endometriyal adenokarsinom. Grade 1' saptandı. Manyetik rezonans incelemede (MR) endometriyal kavitede 36X19mm kitle izlendi. Pozitron Emisyon Tomografi (PET), uterin lezyon dışında normal olarak saptandı. Full küretaj uygulandı ve işlem sonrası MR ile rezidü endometriyal lezyon, myometriyal ve servikal invazyon izlenmedi. Hasta ile görüşüldükten sonra, hastanın gebelik isteği nedeni ile yüksek doz gestagen tedavisi planlandı. Megestrol asetatın 12 ay kullanımından sonra ultrasonda atrofik endometriyum izlendi ve histolojik olarak ta tanı doğrulandı. Megestrol asetat kesildi ve hasta adet görmeye başladı. Kontrole çağrılan hasta spontan gebe kalarak başvurdu. Rutin obstetrik izleme alınan hasta, 39. haftada sezaryen ile doğum yaptı. Fertilite isteği olan erken evre endometriyum adenokarsinomu saptanan genç kadınlarda konservatif tedavi bir seçenek olarak sunulmalıdır.

Anahtar kelimeler: *Endometriyum kanseri*, *Gebelik*, *Konservatif tedavi*

Abstract

A 26 year old women complaining of primary infertility has applied to our clinic. During infertility workup, her endometrium was irregular and thick so endometrial sampling was performed and 'well differentiated endometrial adenocarcinoma, Grade 1' was detected. Magnetic resonance imaging (MRI) showed 36x19mm mass in endometrial cavity. Positron Emission Tomography (PET) was normal except uterine lesion. Full curettage was performed and after curettage, we confirmed that there was no detectable endometrial mass or myometrial invasion or cervical involvement by MRI imaging. After counseling, the patient wished to retain her ability to conceive, so high dose progestin therapy was recommended. After megestrol acetate usage for 12 months, we found atrophic endometrium by ultrasound examination, and this was confirmed as atrophic endometrium by histological examination. Then, megestrol acetate treatment was stopped and the patient resumed her menses. She was scheduled for a control visit but she turned out to be pregnant. Then she received routine obstetrical care and delivered by Cesarean section at 39 weeks in gestational periods. We conclude that conservative treatment of early stage endometrial adenocarcinoma in young women wishing fertility is an option in carefully selected cases.

Keywords: *Endometrial cancer*, *Pregnancy*, *Conservative therapy*

Introduction

Endometrial adenocarcinoma in child bearing age is relatively uncommon, except polycystic ovary syndrome or estrogen producing tumor. The risk of endometrial carcinoma was increased 4.8-folds in infertile patients and 10.3-folds in infertile women with chronic anovulation [2]. Endometrial cancer in younger patients is generally associated with a better prognosis because the tumors are detected at an early stage and hormonally dependent. In

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such a setting, disease with grade 1 endometrioid adenocancer associated minimally myometrial invasion can be treated with high dose progestins followed by curettage in patients who wish to preserve fertility [1].

Here we report a case of spontaneous pregnancy after conservative treatment of endometrial cancer.

Case Report

A 26 year old women complaining of primary infertility for 2 years has applied to our clinic. She had abnormal vaginal bleeding and spotting between periods for nine months. She was not hirsute and her pelvic examination found to be normal. Full infertility work up was normal and her cervical smear test was negative. Hysterosalpingography demonstrated normal bilateral tubal patency. Transvaginal ultrasound showed polycystic ovary and irregular- diffuse endometrial thickening in day 2 of menstruation. It was type 3 endometrial sonographic images on ultrasonographic evaluation. Endometrial sampling was performed. The pathologic evaluation revealed well differentiated endometrial adenocarcinoma (Grade 1). *Magnetic resonance imaging* (MRI) showed 36 x 19 mm endometrial carcinoma. Positron Emission Tomography (PET) using 2-[F-18] fluoro-2-deoxy-D-glucose (FDG) examination was normal except hypermetabolic (SUV-standardized uptake value- max: 7.2) uterine 35x15x15 mm focal lesion. Full curettage was performed and after curettage, we confirmed that there was no detectable endometrial mass or myometrial invasion or cervical involvement by MRI imaging. After counseling, the patient wished to retain her ability to conceive, so high dose progestin therapy was recommended. Continue oral megestrol acetate was prescribed 160 mg daily for 8 weeks. After 8 weeks, there was no lesion on endometrium with hysteroscopic examination, and the pathologic evaluation revealed complex hyperplasia with cellular atypia. The control MRI was normal. She continued to receive megestrol acetate for three months. After 3 months, full curettage and MRI repeated and were normal. After megestrol medication during 12 months, atrophic endometrium was confirmed through the histological examination. She resumed menses after stopping megestrol. She was scheduled for a control, but she turned out to be pregnant. Then she received routine obstetrical care and delivered by Cesarean section at 39 weeks in gestational periods. The baby was3100 g, male, and Apgar score was 8 at 1 min, 9 at 5 min. Placenta was grossly and microscopically normal, there was no evidence of residual tumor in the uterus and adnexa or abdominal organ. Patient was recommended to evaluate for her condition six weeks after delivery.

Case Discussion

Preserving reproductive potential has become an important issue in endometrial cancer diagnosed in young women and the survival rates in these women are favorable [3]. Pregnancies have been reported, mostly after endometrial curettage and successful hormonal therapies for early stage, low grade endometrioid adenocarcinoma in young women [1-3]. In order to improve treatment and follow-up of endometrial carcinoma patients, the importance of various prognostic factors has been extensively studied. Over the past few decades, several studies have demonstrated the prognostic importance of different parameters including lymph node status, histological type of carcinoma, histological grade, stage of disease, depth of myometrial invasion, lymphovascular space involvement and cervical involvement [4,5]. We did not detect myometrial invasion and lymph node metastasis using MRI and abdominopelvic CT scan examinations respectively.

As for endometrial cancer, the National Comprehensive Cancer Network (NCCN) 2012 guidelines for uterine neoplasms affirm that although hysterectomy and appropriate staging is the recommended treatment for endometrial cancer, initial hormonal therapy can be considered for young women with either atypical endometrial hyperplasia or grade I endometrial carcinoma, and who desire fertility preservation. However, their ultimate recurrence rate remains high (44%) and the disease progression rate is 5 - 6% [6]. More over, the ACOG 2005 bulletin considers that progestational agents may be a treatment option for selected candidates, but that the disease

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will likely recur in most patients, which requires the need of continued histologic monitoring, approximately every 3 months. We took a conservative approach in treating this patient, with periodic evaluation of the endometrium by ultrasound, MRI and endometrial curettage.

The reported daily doses of progestins were variable, 40 - 400 mg of megestrol acetate or 200- 600 mg of medroxyprogesterone acetate, and the durations of medication were 3 -18 months [1]. The median length of treatment for complete response was 3 months (range, 1-12 months) [3]. These patients were followed up every 3-4 months by serial sonography, MRI and hysteroscopy. The patient assumed to be achieved after having two consecutive normal endometrial samples in periodic samplings every 3-6 months [3]. We prescribed initially megestrol acetate 160 mg daily and observed the regression of the endometrial carcinoma. The risk of disease progression occurring during or after progestin therapy would be approximately 5%, while Randall et al. did not experience the patients with progressive disease except patients with persistent lesions [7].

Conservative treatment is indicated only in the case of well differentiated, early stage disease without extrauterine lesions. For these purposes, MRI would be helpful for evaluation of invasion depth of tumor and detecting extrauterine tumor and the endometrial biopsy should be performed for grading of tumor [1].

The dilatation and curettage was more accurate than office endometrial biopsy in predicting tumor grade, the dilatation and curettage also incorrectly graded approximately 25% of the patients, with higher grade tumor being missed in about 10% [8]. For the reduction of misdiagnosis, as additional diagnostic tool, hysteroscopic examination would be helpful.

The biggest concern with conservative management of endometrial carcinoma is disease progression while on treatment or after initial response to medical treatment [9]. Women opting for conservative management should be aware that hormonal therapy is not the standard form of management. Many questions still remain unanswered, such as ideal progestin regimen, duration of treatment, predictive criteria for responsiveness, and need or timing for completion hysterectomy after childbearing, to cite only few. In a 2004 meta-analysis, Ramirez et al. reviewed the literature regarding hormonal treatment of grade I endometrial cancer. A variety of progestational agents were used, most often medroxyprogesterone acetate or megestrol acetate. It was observed an overall response rate of 77%, the median time to regression was 12 weeks and among responders the recurrence rate was 24% [10]. All recurrences occurred within 1 year of diagnosis and all patients who remained disease free (76% of the initial responders) required treatment with progesterone for only 1 month to achieve a response. Today, there is no clear consensus on the optimal follow-up interval. Elective hysterectomy following successful pregnancy should be considered to avoid a long stressful follow-up and possible morbidity or mortality due to a delay in detecting the recurrence.

The majority of young patients with endometrial carcinomas tend to have coincident polycystic ovary syndrome or ovulatory disorders further hindering their fertility. Patients should probably be counseled in order to attempt immediate pregnancy after conservative treatment [1]. We conclude that conservative approach with careful observation might be possible in an early stage endometrial adenocarcinoma in young women wishing to conceive. Long term follow up is required after delivery for the risk of endometrial cancer recurrence.

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Information Presantation

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