CASE REPORT

Lib Oncol. 2022;50(2-3):138–141
doi: 10.20471/LO.2022.50.02-03.21

SUCCESSFUL PREGNANCY IN WOMEN WITH ENDOMETRIAL CARCINOMA

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Summary

Endometrial cancer is the sixth most common cancer in women worldwide and fourth in Europe. Global estimates show rising incidence in both developed and developing countries. Standard surgical treatment leads to permanent loss of fertility. With current trends of reproductive-age women delaying childbearing, rising endometrial carcinoma incidence rates and a growing epidemic of obesity, research on conservative treatment remains a priority. Fertility-sparing treatment involves the use of oral progestins and levonorgestrel-releasing intrauterine devices, both shown to be beneficial and safe in early-stage endometrial carcinoma.

We present a case of a 40-year-old female with endometrial adenocarcinoma grade 1 diagnosed during infertility workup. After one year of levonorgestrel-releasing intrauterine devices and almost three years after initial diagnosis was made, pregnancy was achieved. Term elective C-section delivery was done and a healthy infant was born. Today, a 46-year-old female, with six years of disease-free survival, still opts for conservative treatment.

Aim of this paper is to show how conservative management with steady follow up in highly motivated individuals could be a reliable option for females of reproductive age with endometrial malignancies. Concept of fertility-sparing treatment should give hope to patients with malignant disease and unfulfilled reproductive goals.

KEYWORDS: *endometrial carcinoma, fertility-sparing treatment, assisted reproductive technology*

INTRODUCTION

Endometrial cancer is the sixth most common cancer in women worldwide(1) and fourth in Europe(2). Global estimates show rising incidence in both developed and developing countries. Most women are diagnosed postmenopausal, but with 14–25% of premenopausal patients and 5% under 40 years of age(3). Endometrial adenocarcinoma accounts for 80% of all uterine cancers and include endometrioid, serous and clear cell carcinoma. Risk factors include age and hyperestrogenism associated with nulliparity, obesity, and metabolic syndrome. Standard treatment involves total hysterectomy and bilateral salpingo-oophorectomy. Treatment has excellent survival outcomes, particularly for low-grade endometrioid tumors. Younger women of reproductive age have signifi-

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cantly better disease-specific survival than older women independent of other prognostic indicators(4). However, it leads to permanent loss of fertility among women who wish to preserve their reproductive potential. With current trends of reproductive-age women delaying childbearing, rising endometrial carcinoma incidence rates, and a growing epidemic of obesity, particularly in developed countries, research on conservative non-surgical treatment approaches remains a priority. Fertility-sparing treatment predominantly involves the use of oral progestins and levonorgestrel-releasing intrauterine devices, which have been shown to be beneficial and safe in women with early-stage endometrial carcinoma(5).

CASE

We present a case of a 40-year-old female with an uneventful medical history and no prior pregnancies. She had begun infertility workup and had undergone hysteroscopic endometrial polypectomy two years prior. Histopathology report showed atypical polypoid adenomyoma. The second hysteroscopic procedure showed recurrence of atypical polypoid adenomyoma but also with foci of endometrial adenocarcinoma grade 1. Regarding patients' desire for pregnancy, a decision was made to proceed with fertility sparing management of the malignant disease. After preconception workup, another hysteroscopic procedure was done, with no malignant cells in the sample. Magnetic resonance imaging of the abdomen and pelvic region wasn't part of workup. Furthermore, a levonorgestrel-releasing intrauterine device was inserted. After four months, hysteroscopic endometrial sampling was repeated, with an unremarkable histopathology report. Subsequently, after one year, the intrauterine device was extracted and assisted reproductive technology was initiated. Finally, almost three years after initial diagnosis was made and 14 months after intrauterine device extraction, pregnancy was achieved. Pregnancy was marked by symptoms of threatened abortions but otherwise without major obstetric complications. Elective caesarean section for oncologic indication was done at 39 weeks of gestation and a healthy female infant was born. Histopathological report of placenta and endometrial sample obtained during C-section was without abnormalities. Postpartum period was uneventful for the mother and for the child.

Today, a 46-year-old female, with 6 years of disease-free survival, still does not consent to recommended surgical procedure. She opts for conservative treatment with regular endometrial sampling procedures and magnetic resonance imaging. Continuously histopathological reports haven't shown recurrence of adenocarcinoma.

DISCUSSION

Recent studies show promising reproductive outcomes in endometrial carcinoma patients who undergo fertility-sparing treatment. A Chinese multi-center retrospective study including 107 women with atypical endometrial hyperplasia or endometrial carcinoma showed that for women who chose spontaneous pregnancy, the clinical pregnancy rate was 54.2% and the live birth rate was 41.7%. The median time from fertility-preserving therapy withdrawal to clinical pregnancy was 5.5 months. Women who chose assisted reproductive technology, the clinical pregnancy rate was 59.5% and the live birth rate was 35.7%, the median time from fertility-preserving therapy withdrawal to clinical pregnancy was 19.5 months(6). A multi-center study of 141 Korean women aged <40 years who were diagnosed with grade 1 endometrial carcinoma and treated with oral progestins showed that 73% of women who attempted conception, including a group undergoing assisted reproductive technology, were successful, and that 66% had at least 1 live birth. Although the incidence of infertility in this cohort was higher than in the general population, those who received fertility treatments had similar 5-year disease-free survival rates compared to those who did not. Women who had at least 1 pregnancy had better disease-free survival rates compared to those who did not(7). A recent analysis of 118 Korean women with stage 1A grade 1-2 endometrial carcinoma treated with oral progestins and the levonorgestrel-releasing intrauterine device reported a live birth rate of 67% among those who tried to become pregnant. The median disease-free survival was 26 months among those who became pregnant, compared to 12 months among those who did not, suggesting that successful pregnancy may improve disease-free survival(8). Other studies also reported that the pa-

tients with endometrial cancer and atypical endometrial hyperplasia, who achieved live birth had a significantly lower risk of recurrence than those without live birth and that there was not a significant difference between the patients with and without infertility treatment(9,10). In conclusion, a systematic review of reproductive outcomes following fertility-sparing treatment for gynecological cancers showed the best results for endometrial carcinoma in contrast to other gynecological malignancies (cervical carcinoma, ovarian carcinoma and gestational trophoblastic disease). Of women diagnosed with endometrial cancer 46% conceived (58% with fertility treatments) and the live birth rate was 77%(11). Our case supports aforementioned findings as fertility sparing treatment in early-stage endometrial carcinoma is not a novelty. However, a 6 yearlong disease-free survival period is a significant finding. It is well known that pregnancy is associated with reduced endometrial cancer risk. However, as presented studies and our case showed, a theoretical protective role of pregnancy, due to physiological state of high progesterone level, is noticed in patients with early-stage endometrial carcinoma(12). Also, discutable and unknown is potential risk of dissemination of malignant cells during caesarean section. Furthermore, no recommendations for type of delivery are available in patients with uterine cancer. Therefore, we opted for surgical procedure while it enabled simpler endometrial sampling and gross inspection of uterus.

CONCLUSION

The incidence of endometrial carcinoma is rising, particularly in developed countries with rapid economic growth. Worldwide increases in obesity and a global decline in reproductive rates will increase the need for fertility-sparing approaches to treatment. The aim of this paper is to show how conservative management with steady follow up in highly motivated individuals could be a reliable option for females of reproductive age with early-stage endometrial malignancies. Concept of fertility-sparing treatment should give hope to patients with malignant disease and unfulfilled reproductive goals.

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Sažetak

USPJEŠNA TRUDNOĆA U PACIJENTICE S KARCINOMOM ENDOMETRIJA

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Karcinom endometrija je šesti najčešće karcinom u žena u svijetu i četvrti najčešći u Europi. Bilježi se porast incidencije kako u razvijenim tako i u nerazvijenim državama svijeta. Klasično liječenje je kirurško i ono dovodi do trajnog gubitka reproduktivog potencijala. S obzirom na navedeno povećanje incidencije karcinoma, epidemiju pretilosti i kontinuirano povećanje dobi u kojoj se žene odlučuju na trudnoću, istraživanja konzervativnih metoda lječenja postaju prioritet. Liječenje sa svrhom očuvanja fertilnosti uključuje progestinske oralne preparate i levonorgestrelske intrauterine sustave, koji su se pokazali kao uspješni i sigurni u liječenju ranog stadija karcinoma endometrija.

U ovom radu predstavljamo slučaj četrdesetogodišnje pacijentice s endometralnim adenokarcinomom maternice gradusa 1 otkrivenim tijekom obrade neplodnosti. Nakon jedne godine terapije levonorgestrelskim intrauterinim sistemom i tri godine nakon postavljanja dijagnoze pacijentica ostaje trudna. Elektivnim carskim rezom se porodi zdravo donošeno žensko dijete. Danas četrdesetšestogodišnja pacijentica, šest godina od inicijalne dijagnoze i dalje se odlučuje na konzervativnu terapiju.

Cilj ovog rada je ukazati kako konzervativna terapija uz redovne kontrole kod visoko motiviranih pojedinaca može biti pouzdana opcija za karcinom endometrija kod žena reproduktivne dobi. Koncept liječenja uz očuvanje fertilnosti daje nadu pacijentima s malignom bolesti i neispunjenim reproduktivnim ciljevima.

KLJUČNE RIJEČI: *medicinski pomognuta oplodnja, karcinom endometrija, liječenje uz očuvanje fertilnosti*