Successful pregnancy after conservative management of early stage endometrial carcinoma in a young nulliparous woman

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The incidence of endometrial cancer (EC) in the population of young women has been increasing. Total hysterectomy with bilateral salpingo-oophorectomy remains the standard therapy for early endometrial cancer [1]. However, doctor and patient attitudes towards radical cancer treatment methods, especially in young women of reproductive age, have been noticeably changing [1–4]. Women expect doctors to apply fertility-sparing therapy, if possible. Early endometrial cancer cases treated with preservation of reproductive function methods have been reported [5].

We present a case of a patient who conceived spontaneously and delivered a healthy newborn after hormonal treatment of early endometrial cancer.

A 29-year-old female patient, nullipara, obese (body mass index (BMI) 32.1 kg/m^2), presented to her gynecologist with a complaint of irregular, heavy bleeding. For the last year the menstrual pattern was irregular, every 30–60 days, hypermenorrhea lasting up to 14 days. An ultrasound examination revealed endometrial hypertrophy and polyp suspicion. The patient underwent diagnostic dilation and curettage. Histopathology revealed endometrial hyperplasia with atypia with adenocarcinoma foci (Figure 1). Magnetic resonance imaging and chest X-ray excluded more advanced cancer. Treatment options and the risk of cancer progression in case of saving childbearing potential were discussed with the patient, who eventually chose fertility-sparing therapy. She was strongly advised to lose weight with the help of a professional dietician. The patient was treated with high-dose oral progesterone, megestrol acetate 160 mg/day for 6 months after inserting the levonorgestrel intrauterine system (LNG-IUD). Endometrial curettage was performed after removing the levonorgestrel intrauterine system after 6 months. The histopathological examination revealed endometrium with decidual transformation. Mostly the endometrial glands were inactive. Single glands showed signs of hyperplasia without direct atypia. The assessment of atypia was difficult because of the gestagen influence (Figure 2). By that time she had reduced her weight by 30 kg (BMI 22 kg/m^2). Then she was given estro-

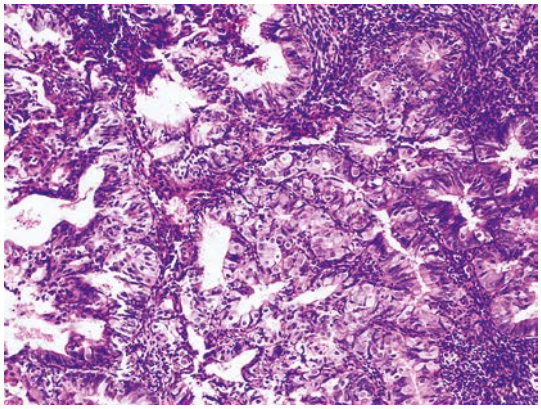

Figure 1. Pre-therapy. Endometrial glands with neoplastic transformation (H + E, 100×)

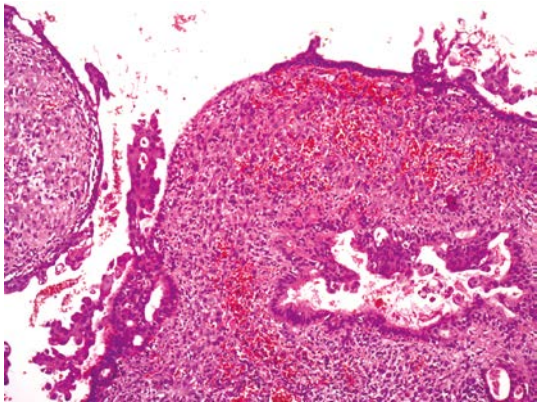

Figure 2. Post-therapy with high-dose systemic progesterone and local LNG-IUD for 6 months. Stroma with decidual transformation (drug-induced). Hyperplasia within the glandular tubes and on the endometrium surface – foci of residual hyperplasia (H + E, 50×)

gen-progesterone therapy to determine whether the pathological changes of the endometrium depended on the hormonal cycle. Although giving estrogen after a partial response does not seem to be the correct mode of treatment, we applied this treatment on purpose after the suggestion of the histopathologist. After half a year with the LNG system the endometrium showed a few residual foci of hyperplasia along with marked decidual transformation (Figure 2). We wanted to see if these changes would remain during the normal cycle or be shed during menstruation. Because the patient had an irregular menstruation pattern we gave her estradiol (day 5–25 of cycle) and norethisterone 5 mg (day 15–25 of cycle) for three months as part of the diagnostics. Repeat curettage after this treatment showed similar histopathological status and the residual foci did not progress to adenocarcinoma.

The patient was advised to conceive without delay. She was administered dydrogesterone 10 mg/day from day 14 until 28 of each cycle. Spontaneous pregnancy was obtained after 6 months and the patient delivered vaginally a full-term healthy female child. The placenta was not examined histopathologically as the patient delivered in another hospital. After the puerperium the levonorgestrel-releasing intrauterine device was inserted again. The patient is under careful surveillance for possible recurrence of disease.

A review of the literature shows that hormonal treatment in grade 1 FIGO I adenocarcinoma without myometrial invasion is safe and can be discussed with patients willing to spare their fertility. Proper selection for fertility-preserving therapy requires diagnostic accuracy. Fertility-sparing therapy can be recommended to patients with early-stage, well-differentiated endometrial carcinoma (FIGO stage IA, Grade 1), presenting no ovarian tumors or metastases, no suspected lymph nodes, and no contraindications for endocrine therapy. Aggressive tumors such as papillary serous, clear cell adenocarcinoma, adenosquamous carcinoma and carcinosarcomas are contraindications for conservative management, and patients with these tumor types should be discouraged from attempting conservative treatment with hormones [6].

The current FIGO classification (2009) for endometrial cancer divides stage I into IA and IB, depending on the depth of myometrial invasion (MI). It is not always possible to evaluate it in the material from dilation and curettage (D&C). The best method of assessing the myometrial invasion and extrauterine spread before surgery is contrast-enhanced magnetic resonance imaging (MRI) [7]. The D&C is preferred to endometrial biopsy and seems to comply with the need for thorough evaluation of grade and occult malignancy [6]. Evaluation of the endometrial tissue should determine the lymphovascular space invasion (LVSI), which is considered a risk factor for lymph node metastasis. A literature search revealed that in case of LVSI the incidence of pelvic lymph node involvement grows from 7% to 27% and the 5-year survival rate decreases from 86% to only 61% of patients [8].

The first-line hormonal treatment for early endometrial cancer is medroxyprogesterone acetate (MPA) (dosage 200–800 mg/day) or megestrol acetate (MA) (10–400 mg/day), which inhibit the estrogen receptor and endometrial cell mitosis, promote apoptosis and induce secretory endometrium [9]. Mostly, 6 months of continuous therapy is enough to obtain remission, although there are cases with a 9-month hormonal treatment [10]. Our patient also did not respond completely after 6 months, despite the fact that she received combined therapy: megestrol acetate and the LNG-IUD.

We obtained the resolution of adenocarcinoma foci, but the residual foci of atypical hyperplasia were still present. Although it seemed risky, with patient consent and wish and after thorough information, the chosen strategy was to conceive as soon as possible. Only one similar situation has been published. There is a report from a prospective study in which women were encouraged to conceive before the complete response to hormonal treatment. Remission was obtained by means of a low-dose cyclic natural progestin therapy (200 mg/day from day 14–25). The response rate was 57% and 43% of women conceived, of which 8 were in persistent disease or partial response. Another 3 complete responses were obtained after the delivery [11].

In conclusion, the case illustrates the favorable outcome of pregnancy after high-dose systemic and local progesterone therapy in early stage focal adenomatous endometrial carcinoma with atypical hyperplasia. Six months of continuous therapy and 6 months of cyclical progesterone therapy may achieve a good endometrial response for resolution of focal endometrial carcinoma, and this may favor implantation after the risk factors such as obesity have been controlled.

Conflict of interest

The authors declare no conflict of interest.

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