**E.K. KUKUBASSOV¹, R.O. BOLATBEKOVA¹, A.R. SATANOVA¹,
O.O. BERTLEUOV¹, D.B. KALDYBEKOV¹, I.O. KOVCHEGOV¹**

¹Kazakh Institute of Oncology and Radiology, Almaty, Kazakhstan

Successful live birth after fertility-sparing treatment in grade II endometrial cancer: A case report

Relevance: *The growing incidence of endometrial cancer among young women urges the use of fertility-sparing therapy.*

The purpose of this study was to demonstrate the results of using fertility-sparing therapy in a woman with endometrial cancer, FIGO stage IA GII.

Results: *After the combination hormone therapy with gonadotropin-releasing hormone (diphereline 3.75 mg every 28 days) using a hormone-releasing intrauterine device, the patient with endometrial cancer stage 1, GII demonstrated a complete response to treatment and delivered a live newborn.*

Conclusion: *Surgery remains the primary treatment for the early stages of endometrial cancer. However, hormone therapy can preserve fertility in young women with highly differentiated early-stage endometrial cancer. The described schemes of hormone therapy can be used in young patients.*

Keywords: endometrial cancer (EC), fertility-sparing therapy, hormone therapy (HT).

Introduction: Endometrial cancer (EC) is one of the leading gynecological malignancies [1]. EC incidence increases with age and reaches 40-50 cases per 100 000 population among women over 60 years. According to the Kazakh Cancer Registry, nearly 10,000 women were diagnosed with EC from 2008 to 2017; of them, 6% were in reproductive age. During the decade, the EC detection rate in Kazakhstan has increased from 10 to 12.6 per 100 000 female population. Age-adjusted incidence shows a significant increase in the risk of the disease at a younger age [2-4]. Young women with early-stage, highly differentiated EC show a good response to conservative progestin-based treatment [1]. In most studies, patients with preserved fertility had EC Stage 1, G1 [5]. However, the efficacy and safety of fertility-sparing treatment have not been confirmed for patients with EC GII. This actualizes the search for fertility-sparing therapy for young women with endometrial cancer.

Progesterone therapy is a possible method of treatment for young women with highly differentiated forms and early stages of EC who are interested in preserving fertility [6, 7]. In selected cases of atypical hyperplasia and early endometrial cancer, HT can give a good result in young women. In a systematic review of studies involving women with atypical hyperplasia and stage 1 EC (45 studies, 391 patients aged 19-80 years), who were prescribed various conservative treatment (e.g., medroxyprogesterone acetate (MPA), megestrol acetate, levonorgestrel intrauterine system, intramuscular 17-hydroxyprogesterone, oral contraceptive pills, norethisterone, dihydrogesterone, and natural progesterone) alone or in combination with other methods, 53.2% of patients on average showed a complete response without recurrence [8]. No prospective studies were done, and only 7 cases of conservative treatment with progestins or IUD were reported involving patients with stage IA, GII EC without invasion of the myometrium [8-10]. Fertility-spar-

ing treatment is recommended for patients with a histotype of endometrioid adenocarcinoma, stage 1A, G1 due to low response of low-grade tumors to progestins [11]. The patients with G1, G2, and G3 stages show the response rates of 37%, 23%, and 9%, respectively [12, 13].

The purpose of this study was to demonstrate the results of using fertility-sparing therapy in a woman with EC, FIGO stage IA GII.

Information about the patient: Patient N., 28 years, diagnosed with EC, FIGO stage 1A (cT1aNx cMo GII), with a history of primary infertility.

Obstetrical status: pregnancy – 0. **Gynecological anamnesis:** endocervicitis in 2013. Irregular menstruations from 12 years for 6-7 days.

Clinical data: Body mass index – 19. ECOG – 0.

Gynecological status: The cervix is not enlarged, elastic consistency. Uterus – not enlarged, mobile, painless. Attachments on both sides – not determined. Parametrium not involved.

Pelvic MRI of 31.08.2016: An area of extragenital endometriosis behind the cervix. The free liquid in the cavity of the true pelvis.

Chest X-ray of 19.09.2016: No focal or infiltrative changes in the lungs revealed.

Treatment: The patient had infertility since 2015. IVF was planned for 2016. In September 2016, the patient underwent hysteroscopy with biopsy. Histology on 07.22.2016 showed endometrial adenocarcinoma G2.

On 22.09.2016, the patient was admitted to the Center of Oncogynecology of the Kazakh Institute of Oncology and Radiology (KazIOR), where she underwent hysteroscopy and biopsy.

Postoperative histology on 27.09.2016 showed an early stage of the proliferation of the endometrium, with no signs of endometrial cancer (figure 1).

Figure 1 – Patient N., 28 years. Postoperative histology of 27.09.2016:
(a) an early stage of the proliferation of the endometrium, (b) no signs of endometrial cancer

Figure 2 – Patient N., 28 years. Postoperative histology of 09.06.2017:
(a) endometrium with indifferent glands, (b) decidualization of endometrial stroma cell, foci of necrosis, purulent-productive inflammation

Figure 3 – Patient N., 28 years. Postoperative histology
of 22.12.2017
Hyperplastic endometrium with focal non-atypical glandular
hyperplasia of the endometrium

The case was discussed by the Multidisciplinary group of the Oncogynecology department of KazIOR, the Tumor Board. The patient was administered Diphereline 3.75 mg №6 (every 28 days) followed by monitoring of treatment results using hysteroscopy.

From December 2016 to June 2017, the patient received hormone therapy (HT) with Diphereline 3.75 mg.

In June 2017, the patient underwent hysteroscopy at the Center of Oncogynecology of KazIOR.

Postoperative histology of 09.06.2017 showed endometrium with indifferent glands, decidualization of endometrial stromal cells, foci of necrosis, purulent-productive inflammation (figure 2).

On 14.12.2017, a hormone-releasing intrauterine device (IUD) was installed after the curettage of the uterine cavity.

Postoperative histology of 22.12.2017 showed: in scraping from the cervical canal – multilayered slipped epithelium, mucus, elements of inflammation; in scraping from the uterine cavity – hyperplastic endometrium with focal non-atypical glandular hyperplasia of the endometrium (figure 3). Based on the histology results, the Tumor Board prescribed HT using IUD (“Mirena” by Bayer, Finland).

The patient was diagnosed with pregnancy in January 2018. The pregnancy was uneventful. The patient remained under gynecological and obstetrical supervision and gave premature birth to a baby at the 31st week of pregnancy. The newborn male weighed 2,300 kg, height – 44 cm; the Apgar score was 5-6.

Results: For two years, the patient received hormone gonadotropin-releasing therapy using IUD. After six months of HT, endometrial curettage was repeated. Histopathological examination showed the response of endometrial tissues to HT. After six months of treatment, hysteroscopy with endometrial biopsy and endometrial curettage were performed. HT resulted in regression of the disease. About two years after the successful treatment, the patient had a spontaneous pregnancy. The child was born by normal delivery.

Discussion: Fertility-sparing treatment is not considered a standard in EC. Fertility preservation is indicated with EC G1 IA and up to G2 in women with strong gestational desire, who accept the risks of postponing definitive surgical treatment and are willing to comply with intensive follow-up.

Most cases of endometrial cancer remit before 6 months. However, if remission is not observed within 12 months, then remission becomes very unlikely. Therefore, hysterectomy is recommended in the absence of response to treatment after 6 months, in the case of resistance to treatment within 12 months, once the reproductive period is completed or menopause is established [14].

Surgery remains the primary treatment for the early stages of EC. The golden standard of EC staging requires a total hysterectomy with salpingo-oophorectomy, peritoneal washings, with lymph dissection in case of enlarged lymph nodes, or the removal of the large omentum in high-risk cases (the degree of differentiation of GII-GIII, a tumor with an invasion of more than half the thickness of the myometrium, a tumor occupying the entire uterine cavity) [15, 16].

One of the advantages of this case is that despite the numerous publications related to fertility preservation in cancer patients, particularly in women with gynecological cancer, to the best of our knowledge, this is the first case of successful conservative treatment. However, our results cannot be extrapolated to other hospitals that may adhere to other treatment protocols or possess a different level of professional training.

Informed Consent: The patient gave written informed consent to the publication of this case report and accompanying images. A copy of the written consent is available at the attending physician.

Conclusions: The use of combination gonadotropin-releasing hormone therapy plus IUD may be an option for endometrial cancer stage IA GII without invasion of myometrium in young patients who want to preserve their fertility.

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