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Nonstandard treatment of endometrial cancer in patient in a procreative age wishing to keep fertility-case report

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Introduction: Endometrial cancer is the most common malignant neoplasm of female reproductive organs that develops from the lining of the womb. The peak incidence falls on the 5th decade of life. Diagnosis of endometrial cancer in young women under 30 years of age is very rare. Detection of cancer at such a young age is an extremely difficult case, because the treatment must consider the reproductive plans of patients so that they can maintain important fertility for them.
Case report: In 2018, a 25-year-old patient was admitted to the Clinic of Oncological Gynaecology and Gynaecology to treat endometrial cancer in FIGO IB. The operation involving the removal of the uterus with fallopian tubes was rejected due to the young age of the patient and her reproductive plans. Prior to hospitalization, the patient was offered the possibility of hormonal treatment that saves fertility. After presenting a 6-month regimen of hormone therapy with medroxyprogesterone acetate (MPA), using a levonorgestrel-releasing intrauterine device, the patient refused consent for its implementation for personal reasons. The patient was proposed to perform electroresection of the endometrial polyp, fractionated erosion of the cavity and cervical canal during hysteroscopy. However, it was marked that it's possible to not completely remove the cancer during the procedure. The patient agreed to this therapeutic procedure. The procedure was performed without any complications. Quarterly cytological control tests and bi-annual endometrial biopsies are correct and for over a year, there is no recurrence of endometrial cancer and the patient is feeling well.

Conculsion: Electroresection of endometrial changes during hysteroscopy in endometrial cancer can be a promising therapeutic option in the early stages of endometrial cancer (FIGO I) in women who want to maintain fertility. However, this requires further validation. It should be remembered that the occurrence of endometrial cancer at such a young age may be a component of genetic syndromes such as Lynch syndrome. Patient awareness of possible relapses and emphasis on quick response in case of disturbing symptoms is extremely important in order to detect a recurrence as quickly as its possible, and thus extend the patient's life, maintaining its good quality.

Key words: *Endometrial cancer, Fertility, Conservative treatment*

Introduction

Endometrial carcinoma is the most common gynaecological neoplasm in developed countries and one in fourth causes of cancer in woman with increasing incidence [1]. Usually this cancer occurs in postmenopausal women with a peak incidence in the age range 60-69 [2-4]. The cancer occurs only in 2-14% of cases before the age of 40 [5-8].
The most reported risk factors of endometrial cancer are anovular cycles associated with polycystic ovarian syndrome (PCD), hypertension, diabetes, obesity, the sole use of estrogens and the use of tamoxifen[9].
There are two types of endometrial cancer: type I - endometrioid and type II – non-endometrioid [10].

Type I (endometrioid) occurs in about 80% of cases and is associated with hyperestrogenism. It is usually formed based on mucosal hyperplasia, although there are reports of the development of this type of cancer on the basis of endometrial atrophy[10,11]. This cancer has the most favourable course and prognosis, it usually occurs in obese women in perimenopausal age who have other risk factors: late menopause, childlessness, diabetes, hypertension [12].

Type II endometrial cancer (non-endometrioid) occurs in approximately 10-20% of cases and is estrogen-independent. It develops based on atrophic changes of the endometrium or coexists with endometrial polyp [11,13]. Type II endometrial cancer usually occurs in older and slim women, is usually more advanced at the time of diagnosis, its course is aggressive, and the prognosis is poor [13,14].

Endometrial polyps may appear in women of childbearing potential, but most often they occur in patients from 40 to 60 years old who are obese, suffer from hypertension or take tamoxifen [15]. Endometrial hyperplasia correlates with the polyp in about 3% of polyp cases [16]. In contrast, the development of endometrial cancer based on polyps was found in almost 2% of all diagnosed polyps.
Diagnosis is based on histopathological assessment of specimens obtained during endometrial biopsy. Histopathological result should provide an information on the histological type and differentiation grade [17].
The necessary preoperative management need to involve clinical assessment, including inguinal evaluation, speculum examination, bimanual examination, rectal examination, abdominal ultrasound, transvaginal ultrasound and, if indicated, transrectalultrasound. Diagnostic process should evaluate the risk assessment for Lynch syndrome, including immunohistochemical staining in females under 45 years with probable FIGO stage I and if ovariectomy is not included in the treatment plan [17].

The first choice treatment of endometrial cancer is surgical treatment (hysterectomy with bilateral removal of the appendages), which makes it possible to determine the stage of the cancer and thus make a decision on the use of adjuvant therapy. Other methods of treating endometrial cancer are radio and chemotherapy as well as hormone therapy. In the case of radiation therapy, doses and sequences of teletherapy and brachytherapy are adjusted individually for each patient and used as a supplement after surgery in cases at increased risk of recurrence [18,19,20]. Young patients before 40 mostly wish to preserve their fertility. Therefore, there is a therapeutic alternative for women wishing to become pregnant in the future.

Case report:

We present a case report of 25-year old woman who has been diagnosed and treated in the Clinic of Oncological Gynaecology and Gynaecology at the end of 2017 and early 2018. Her menarche occurred at the age of 13 and her menstrual cycle was regular. Her family had no known history of EC or other cancers. There is no medical history of surgical procedures. She didn't take any medicine permanently. First visit to a gynaecologist was at the age of 20, after regularly once a year. Cytological and ultrasound examinations in accordance with PTG guidelines - correct results. She was sexually active but did not use hormonal contraception. The patient did not have children yet. At the end of 2017, intermenstrual bleeding appeared with additional pain in the lower abdomen. Because of it, she visited her gynaecologist who in ultrasound showed endometrial polyp and significantly thickened endometrium - about 2.2 cm. He referred the patient to the Clinic of Oncological Gynaecology and Gynaecology for review and treatment. Laboratory test results were normal. Patient was qualified for endometrial biopsy via hysteroscopy. The procedure was performed without complications. Histopathological and imaging examinations revealed - G1 endometrial adenocarcinoma in stage FIGO IA limited to a polyp. The therapeutic process considered the young age of the patient and her reproductive plans. Surgical treatment was excluded (uterine excision with fallopian tubes). Conservative treatment was offered to the patient: a 6-month medroxyprogesterone acetate (MPA) hormone therapy regimen using a levonorgestrel-releasing intrauterine device. After 3 weeks of its implementation, the patient gave up due to intense adverse effects, among: insomnia, severe headaches and dizziness, acne, severe gastrointestinal disorders. The patient was offered electroresection of endometrial changes by hysteroscopy, however, it was noted that during the procedure it is possible incomplete removal of the cancer and that this procedure was not in line with current recommendations. The patient agreed to this therapeutic option and its possible consequences. The procedure was performed. The magnetic resonance check-up test after the procedurę revealed unexplored uterus, in anterior flexion and anterior tilt. Endometrium up to 5mm thick, a small amount of fluid in the uterine cavity. No evident infiltration of neoplasm in the uterus, especially in endometrial projection was seen. Ovarian enlarged ovaries, both follicular, dominant follicle visible in the left up to 17mm in size, without tangible pathological changes. Other organs and structures of the small pelvis without obvious abnormalities. Enlarged suspected lymph nodes in the scope of the examination were not found. Physiologically small amount of free fluid in the small pelvis. Bone structures without signs of destruction. Quarterly cytological control tests and bi-annual endometrial biopsies are normal and for over a year and a half, there is no recurrence of endometrial cancer and the patient is feeling well.

Discussion:

Most endometrial adenocarcinomas occur after menopause. However, 20%–25% of them are diagnosed before the menopause and 2%–14% occur among younger women (less than 40) [5-8].

Surgery is the classic treatment option for endometrial cancer. It consists of total hysterectomy and bilateral salpingo-oophorectomy, with a pelvic and aortic lymphadenectomy if required. In case of the high risk of recurrence chemotherapy and radiotherapy are indicated. Hormonal therapy may be incorporated in the treatment of low-stage endometrioid cancers showing high histopathological differentiation. The recommended treatment includes medroxyprogesterone or megestrol acetate [17].

Fortunately, most cases of endometrial adenocarcinoma in young women were of endometrioid type, well differentiated (Grade 1) and at early stages with a superficial invasion (Stage I). Therefore, these carcinomas had a good prognosis (survival rate at five years: 93%). That fact may offer other therapeutic possibilities instead of the standard radical treatment [21].

Endometrial ablation is widely performed as an alternative to hysterectomy in the treatment of uterine bleeding associated with benign endometrial or myometrial pathology [22-33].

In Gaia et al study, four of 3769 reviewed patients developed endometrial cancer after complete endometrial ablation (1.06 out of 1000) [34]. They shows that endometrial cancer after endometrial ablation is a rare but possible occurrence, whether the technique is performed by “roller-ball” coagulation or by resecting loop. The patients with endometrial polyps after resection may present a higher risk for developing endometrial cancer. The occurrence of endometrial cancer may come a long time after endometrial ablation, and the recurrent bleeding may become evident when the cancer stage is already advanced [34]. Due to that high risk of the conservative treatment, careful observation of patient after procedure is essential.

The most important factor for conservative treatment as presented is a well-differentiated endometrial carcinoma that does not deeply invade the myometrium. There cannot be any suspicious pelvic or pre-aortic nodes. The patient's condition must allow to implement the conservative treatment. It is extremally important to inform the patient about non-standard treatment and the risk of cancer recurrence. The patient should express her readiness to complete the follow-up protocol [35]. A follow-up includes medical history and physical examination, full gynaecological examination and cytology. It should be performed every 3 months during the first 2 years of patient monitoring, every 6 months for up to 5 years, and then once a year. A follow-up in the health care center where the patient received treatment is recommended[17].

Conclusion :

According to the presented case, endometrial cancer might be detected seen in women under 30. Conservative treatment for endometrial cancer with a low histological grade is possible if a complete pre-therapeutic assessment is achieved and if a right follow-up during and after the treatment is pursued.

Electroresection of endometrial changes during hysteroscopy in endometrial cancer can be a promising therapeutic option in the early stages of endometrial cancer (FIGO I) in women who want to maintain fertility.

These kinds of therapy is not standard management and should not be recommended routinely. Patients must be informed of the oncological risks (failure, progression of the disease, ovarian metastasis, etc.) and be subjected to periodic check-ups to quickly detect cancer recurrence and early treatment initiation, thus prolonging the patient's life.

Abbreviations:
EC – Endometrial Cancer
PTGiN – Polskie Towarzystwo Ginekologów i Położników (The Polish Society of Gynaecologist and Obstetricians
FIGO – Federation of Gynecology and Obstetrics

References:

1. Cancer Facts and Figures. 2018 (20.08.2019) http://www.cancer.org/acs/groups/content/@epidemiologysurveilance/documents/document/acspc-029771.pdf.
2. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet. 2005 6-12;366(9484):491-505.
3. Krajowa Baza Danych Nowotworowych. Zakład Epidemiologii i Prewencji Nowotworów Centrum Onkologii – Instytut w Warszawie, www.onkologia.org.pl
4. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55(2):74-108.
5. Jadoul P, Donnez J. The conservative treatment may be bene cial for young women with atypical endometrial hyperplasia or endometrial adenocarcinoma. Fertil Steril. 2003;80:1315–24.
6. Digabel JF, Gariel C, Catala L, Dhainaut C, Madelenat P, Descamps P. Hyperplasies atypiques et carcinomes de l'endomètre de stade I chez la femme jeune désirant une grossesse: le traitement conservateur est-il envisageable?. Gynecol Obstet Fertil. 2006;34:27–33.
7. Benshushan A. Endometrial adenocarcinoma in young patients: evaluation and fertility-preserving treatment. Eur J Obstet Gynecol Reprod Biol. 2004; 117:132–37.
8. Ota T, Yoshida M, Kimura M, Kinoshita K. Clinicopathologic study of uterine endometrial carcinoma in young women aged 40years and younger. Int J Gynecol Cancer. 2005;15:657–62.
9. BélièreM,RadikofG,GalantC,PietteP,MarbaixE,DonnezJ.Identi cation of women at high risk of developing endometrial cancer on tamoxifen. Eur J Cancer. 2000;36:35–6.
10. Bokhman JV. Two pathogenetic types of endometrial carcinoma. Gynecol Oncol. 1983;15(1):10-17.
11. Sajdak S, Moszyński R. Rozrosty endometrium – rozpoznawanie i leczenie. W: Sajdak S, Skrzypczak J. (red.) Endometrium. Modulacja, rozwój, zanik. Blackhorse, Warszawa 2004; 8: 65 – 74.
12. . Bakkum-Gamez JN, Gonzalez-Bosquet J, Laack NN, Mariani A, Dowdy SC. Current issues in the management of endometrial cancer. Mayo Clin Proc. 2008;83(1):97-112.
13. Martin – Ondarza C, Gil – Moreno A, Torres-Cuesta L, García A, Eyzaguirre F, Díaz-Feijoo B, Xercavins J. Endometrial cancer in polyps: a clinical study of 27 cases. Eur J Gynaecol Oncol. 2005;26(1):55-8.
14. Kelly P , Dobbs SP , McCluggage WG. Endometrial hyperplasia involving endometrial polyps: report of a series and discussion of the significance in an endometrial biopsy specimen. BJOG. 2007 Aug;114(8):944-50. Epub 2007 Jun 12.
15. Uterine polyps. MayoClinic.com. (21.08.2019). http://www.mayoclinic.com/health/uterine-polyps/DS00699/DSECTION=1.
16. Ohkawara S, Jobo T, Sato R, Kuramoto H. Comparison of endometrial carcinoma coexisting with and without endometrial hyperplasia. Eur J Gynaecol Oncol. 2000;21(6):573-7.

17. Sznurkowski JJ, Knapp P, Bodnar L, et al. Zalecenia Polskiego Towarzystwa Ginekologii Onkologicznej dotyczące diagnostyki i leczenia raka endometrium. Curr Gynecol Oncol. 2017;15:34–44.
18. Kornafel J, Szelachowska J, Bojarowska K. Rola radioterapii w leczeniu raka błony śluzowej trzonu macicy. W: Markowska J. red. Ginekologia onkologiczna. Elsevier Urban & Partner, Wrocław, 2006. T. 2: 752-758.
19. Creutzberg CL, van Putten WL, Wárlám-Rodenhuis CC, van den Bergh AC, de Winter KA, Koper PC et al. Outcome of high-risk stage IC, grade 3, compared with stage I endometrial carcinoma patients: the Postoperative Radiation Therapy in Endometrial Carcinoma Trial. J Clin Oncol. 2004 Apr 1;22(7):1234-41.
20. Keys HM, Roberts JA, Brunetto VL, Zaino RJ, Spirtos NM, Bloss JD A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. Gynecol Oncol. 2004 Mar;92(3):744-51.
21. Vaccarello L, Apte SM, Copeland LJ, Boutselis JG, Rubin SC. Endometrial carcinoma associated with pregnancy: a report of three cases and a literature review. Gynecol Oncol. 1999;74:118–22.
22. De Cherney AH, Desmond MC, Lavy G, Polan ML (1987) Endometrial ablation for intractable uterine bleeding: Hystero- scopic resection. Obstet Gynaecol 78:668–670
23. Vancaillie TG (1989) Electrocoagulation of the endometrium with the ball-end resectoscope. Obstet Gynaecol 74:425–427
24. Rutherford AJ, Glass MR (1990) Management of menorrhagia. Br Med J 301:290–291
25. Serden SP, Brooks PG (1991) Treatment of abnormal uterine bleeding with the gynaecologic resectoscope. J Reprod Med 36:697–699
26. Ke RW, Taylor PJ (1991) Endometrial ablation to control excessive uterine bleeding. Hum Reprod 6:574–580
27. Magos AL, Baumann R, Lockwood GM, Turnbull AC (1991) Experience with the first 250 endometrial resection for menorrha- gia. Lancet 334:1074–1078
28. Dwyer N, Hutton J, Stirrat GM (1993) Randomised trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. Br J Obstet Gynaecol 100:237–243
29. Sculpher MJ, Bryan S, Dwyer N, Hutton J, Stirrat GM (1993) An economic evaluation of transcervical endometrial resection versus abdominal hysterectomy for the treatment of menorrhagia. Br J Obstet Gynaecol 100:244–252
30. Broadbent JA, Magos AL (1993) Transcervical resection of the endometrium (TRCE). In: Sutton C, Diamond MP (ed) Endoscopic Surgery for Gynaecologists. WB Sauders, London, pp 294–300
31. Pinion SB, Parkin DE, Abramovich DR (1994) Randomised trial of hysterectomy, endometrial laser-ablation and transcervical endometrial resection for dysfunctional uterine bleeding. Br Med J 309:979–983
32. Garry R (1995) Good practice with endometrial ablation. Obstet Gynaecol 86:144–151
33. Raiga J, Mage G, Glowaczower E (1995) Factors affecting risk of failure after endometrial resection. J Gynecol Surg 11:1–6
34. Gaia G., Botchorishvili R., Canis M., et al: Endometrial cancer following endometrial resection. Gynecol Surg 2007; 4: pp. 179-185
35. Chiva L, Lapuente F, Gonzalez-Cortijo L, et al. Sparing fertility in young patients with endometrial cancer. Gynecol Oncol. 2008;111:101–4.