

ENDOMETRIOID TUMOR OF THE OVARY AND UTERUS, METASTASIS OR NOT – CASE REPORT

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The simultaneous occurrence of two genital tumors is a relatively unknown fact. They are rare and make 0,63% of all genital malignancies. If endometrial carcinoma is present only in the endometrium then this is called stage IA; if endometrial carcinoma is present only in one half of the myometrium this is IB stage, while IIIA stage tumor spreads to the serosa or adnexa. Carcinoma localized at the ovary without the rupture of the capsule is of stage IA, while ovary carcinoma that spreads to the oviduct or uterus is of IIA stage.

A female, 55 years old, was hospitalized in the Clinic of Gynecology and Obstetrics Clinical Center Kragujevac because of the tumor that filled the whole of the small pelvis and a necessary surgical intervention. Immunohistochemically, expressions of ER, PR and HER 2 receptors were determined.

Women with independent primary endometrial uterus and ovary tumors have a similar prognosis to that of women suffering from this disease in a separate form.

Risk factors and clinical indicators of results of women with synchronized tumors are different than those based on histological division. Women with synchronized tumors are in most cases younger, obese, premenopausal and barren. Patients with serious endometrial carcinomas are similar to patients with ovary carcinomas. In future, it will be necessary to provide better evaluation of etiology of these diseases. Also, molecular diagnoses of tumor in the endometrium and ovary will provide us with real confirmation. *Acta Medica Medianae 2007;47(4):15-19.*

Key words: *synchronized tumors, independent tumors, metastatic tumors, joined tumors*

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Introduction

The presence of two genital tumors at the same time is a relatively unknown fact. These are rare and make 0,63% of all genital malignancies. Among them, the association of endometrial ovarium carcinoma with uterus carcinoma is the most frequent. While both etiology and pathogenesis are unknown, because of embryonal tissue similarity there is an assumption that those might, as particular objects, develop into independent neoplasmas at the same time under the influence of some hormones (1,2,3).

If endometrium carcinoma has affected only endometrium, it is staged as IA, if it is present in one half of the myometrium, it is IB, and IIIA tumor has spread to the serosa or adnexum. Carcinoma localized at the ovary,

without the rupture of the capsule, is in stage IA, and ovary carcinoma which has spread to the oviduct or uterus is IIA.

It is needed to classify disease correctly as further treatment and prognosis depend on it. Some authors prefer histology criteria to make a difference between metastatic disease and independent occurrence. Sometimes, this distinction is difficult or even impossible. The major criterion for endometrial carcinoma and ovarian metastasis is a multiple nodular ovarian tumor. Minor criteria are ovaries smaller than 5 cm, bilateral affection, deep myometrial invasion, vascular invasion and oviduct affection. Major criterion, or 2 or more minor criteria, as well as the absence of ovarian endometriosis are enough to make the diagnosis of metastatic disease (1,4,5,6,7).

Case report

A female, 55 years of age, was hospitalized in the Clinic of Gynecology and Obstetrics, Clinical Centre Kragujevac, medical history file number 21439, on October 8, 2002, because of tumor that filled up the whole of the small pelvis and a necessary surgical intervention. As she had pains in the abdomen, she went to a gynecologist

when gynecological and ultrasound examinations were done, when the disease was diagnosed. According to gynecological anamnesis, menarche appeared at the age of 13, with 5 days of menstrual duration. The last menstruation was five months ago. She denied any previous gynecological disorders. There were two pregnancies in pregnancy anamnesis that ended with vaginal births and four deliberate miscarriages. She was fat, never suffered from any significant disease, never had had any operation. No malignancy in family anamnesis. Basic laboratory analyses - both blood and urine analyses were carried out and they were within normal limits. Laparotomy with classical hysterectomy and mutual adnexectomy and partial resection of omentum were carried out in OETA. Intervention and postoperative course were regular.

Preoperative diagnosis:

Tu pelvis per magna.

PH findings N. number 4888 on November 15, 2002.

1. Uterus with right adnexa 80 gr weight, brown coloured with smooth glowing surface. Irregular round-shaped uterus with 65 mm in diameter, wall thickness 8-12 mm on section, lumen completely filled up with the fragile cauliflower-like mass greyish-pink coloured. Cervix with diameter of 20x15 mm, lengthways 30 mm, greyish-yellow coloured and of smooth glowing surface, with oval positioned external aperture. Oviducts are twisted and passable with the length of 40 mm, the ovary of 30x20x15 mm in diameter and brown coloured.
2. The tissue with 2220 gr weight, greyish-yellowish-brown coloured, of uneven surface, irregular round shaped, with diameter of 270 mm. Mostly compact areas grey-white coloured on section, mainly necrotic and hemorrhagic altered, in a lesser part of it there are cavities filled up with liquid or solid gelatinous contents.
3. Greasy tissue of omentum with the weight of 100 g, without a visible pathomorphological disorder.
4. About a 12 ml of clear, brown, stirred up contents.
5. Adenocarcinoma endometrii, endometrial, with areas of benign squamous metaplasia, (Adenocarcinoma endometrioides cum differentiatio squamosa), a well-differentiated type (histological grade I), nuclear grade II. Tumor has mainly exophytic growth, without penetration into the miometrium. There is a low intensity desmoplasia, almost without a stromal mononuclear reaction. There are no signs of lymph and blood vessels invasion on serial sections analyzed. Other changes: Corpus albicans ovarii. Hyperkeratosis et papillomatosis epithelii squamosi cervicis uteri. The light degree of cervicitis chronica.
6. Adenocarcinoma endometrioides ovarii, with areas of benign squamous metaplasia. Adenocarcinoma endometrioides cum differentiatio

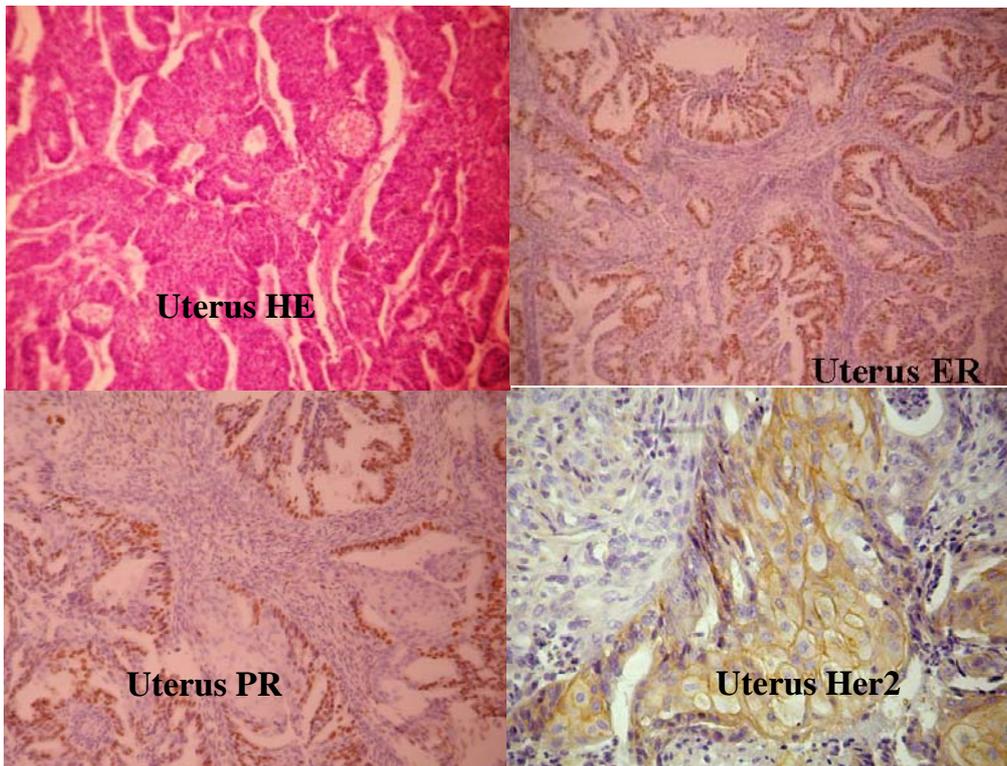
- squamosa, medium differentiated type (histological grade II), nuclear grade II, with massive areas of necrosis and bleeding, with the presence of lymph and blood vessels invasion, however without a capsule penetration.
7. Greasy tissue of omentum is permeated by richly vascularized, granulated tissue and inflammatory infiltrate of light to medium degree, with rare multinuclear giant cells. There were no elements of secondary deposit in the material analyzed.
8. On the smear there were nonstructured eosinophilic contents and very rare mesothelial ordinary morphologic cells.
9. After immunohistochemical endometrium and ovarium tumor analysis, the following results were obtained: in endometrial tumor, more than 80% of all cells show an intensive expression of estrogenic and progesterone receptors, except in the squamous metaplasia zones, which are Er and Pr negative. Also, diffuse progesterone positivity was present in the ovarian tumor, and only 10% of cells were estrogen positive.

Moderate expression of HER2 receptors (2+) was determined both in endometrial and ovarian tumor in squamous metaplasia zones; more than 10% of cells showed thin and moderate continual and discontinual membrane positivity. Both tumors had negative expression on HER 2 receptors in areas of clear endometrial differentiation.

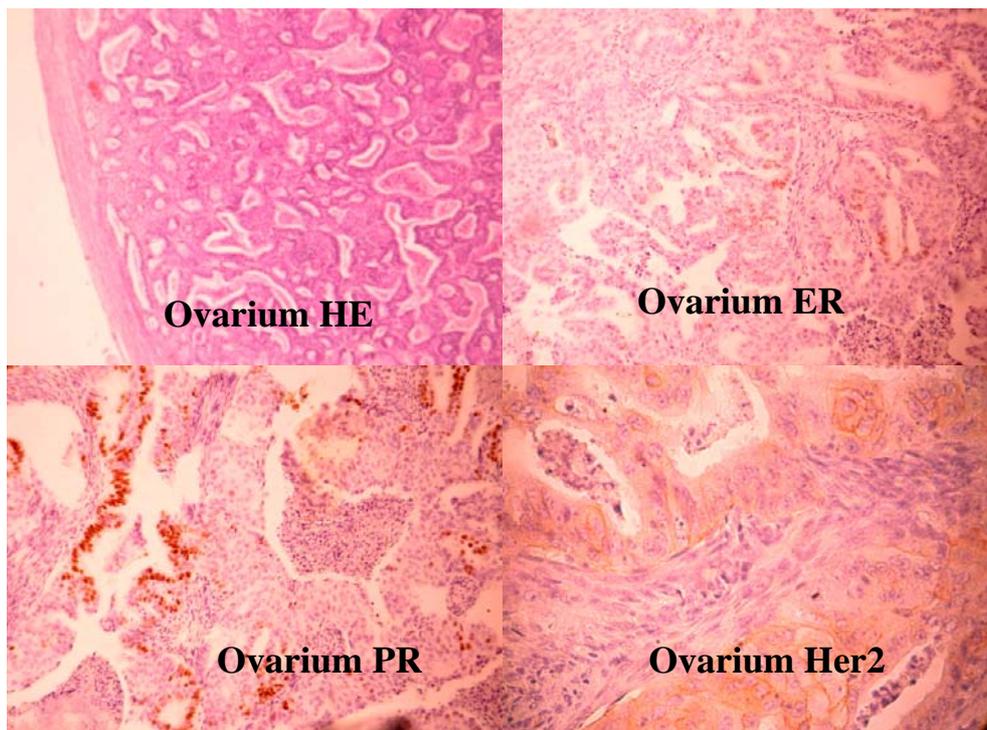
Discussion

Initial challenge for gynecologic oncologist is to classify diseases of women with associated genital malignancies, especially of the endometrial carcinoma of the uterus and ovary. Women with independent primary uterus and ovary endometrial carcinoma have similar prognosis to that of women with isolated occurrence of the disease (8,9).

Pathologists include the histology criteria. The tumor in our case (Figures 1 and 2) is superficial and does not penetrate into miometrium; therefore, it can be classified as IA stage. Tumor that penetrates deeply into the miometrium might indicate ovarium metastases, because it is well known there is no invasion or the invasion is superficial in cases of independent tumors. In cases of metastases from ovarium into uterus, we have large ovarian but small endometrial tumor. Its growth is rather exophytic. There are no signs of lymph and blood vessels' invasion, with areas of benign squamous metaplasia. There is no penetration into oviducts, which speaks in favor of independent growth. The size of ovarium is 270 mm, therefore over 50 mm, also unilateral, medium differentiated type (histological grade II), nuclear grade II, with massive areas of necrosis and bleeding, with present lymph and blood vessels invasion, but without the capsule penetration and also without malignant cells from ascites, which classify it as IA stage (10,11).



Picture 1. Uterus- receptors



Picture 2. Ovarium – receptors

Our patient was 55 years of age, and it is well known that independent tumors occur in younger women more frequently, in contrast to independent tumors of endometrial or ovarian carcinoma which most frequently occur in the seventh decade of life (12,13).

Our patient was fat with BMI of 28,5. In cases of fat women, those with BMI over 25, the risk to develop endometrial carcinoma of the uterine body is rising. The explanation is that it comes to

peripheral conversion of androstenedione into estrone in the fatty tissue. Such hyperestronemia may cause proliferation of endometrium, endometrial hyperplasia and, in some cases endometrial carcinoma. Correlation between corpulence and ovarium carcinoma is not so clear. Certain studies suggest that corpulence in the adolescence increases the risk of ovarian carcinoma (12,14).

Our patient has boreed two children. It is known the female patients with synchronic uterus

and ovarium tumors are barren women in one third to one half of all cases. There are several reasons for that. Hormonal influence is very important (8,15).

Some studies claim that the uterine body, oviducts and ovarian epithelium are one morphologic entity, which explains an independent development of the tumor in different compartments of mullerian tubes. The estrogen impact is crucial (12,16).

Families with hereditary nonpolyposis colorectal carcinoma (HNPCC), and Lynch's syndrome have more probability for endometrial carcinoma genesis in younger age (17,18).

Immunohistochemical analysis of some receptors might be a good indicator of the process development and treatment success. Classical hysterectomy with mutual adnexotomy and partial omentectomy were performed in the case of our female patient. Because of the lack of sufficient evidence clarifying whether it was the case of synchronic (based on clinical and PH findings), or

metastatic endometrial carcinoma of endometrium and ovarium, female patient was classified as a higher stage, so she underwent complete radiation and chemotherapy. On March 1, 2008 there were no relapses of the disease. The five- and ten-year survival in synchronous tumors is excellent, 86 and 80%, in contrast to metastatic disease, which is of a higher stage (1,19,20,21).

Conclusion

Risk factors and clinical outcome indicators in women with synchronous tumors are different than those based on histology division. Women with synchronous tumors are mainly younger, fat, premenopausal and barren. Female patients with serious endometrial carcinoma are more like female patients with ovarian carcinoma. In the future, a better evaluation of the etiology of these diseases is needed. Also, molecular diagnostics of tumors in endometrium and ovarium would give us a real confirmation.

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ENDOMETRIOIDNI TUMOR OVARIJUMA I UTERUSA, METASTAZA ILI NE – PRIKAZ BOLESNIKA

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Prisustvo dva genitalna tumora u isto vreme je relativno nepoznata činjenica. Oni su retki i čine 0,63% svih genitalnih malignoma. Ako je karcinom endometrijuma zahvatio samo endometrijum, onda je stadijum IA, ako je došao samo do polovine miometrijuma onda je IB, dok se kod IIIA tumor proširio na serozu ili adneksa. Kod karcinoma koji je lokalizovan na ovarijumu, bez probijanja kapsule, stadijum je IA, dok dok je kod karcinoma ovarijuma koji se proširio na jajovod ili uterus IIA.

Ženska osoba stara 55 godina primljena je u GAK Kliničkog centra u Kragujevcu zbog operativnog zahvata, zbog tumora koji ispunjava celu malu karlicu. Imunohistohemijski su određena ekspresija ER, PR i HER 2 receptora.

Žene sa nezavisnim primarnim endometrijalnim tumorima uterusa i ovarijuma su slične po prognozi kao i kod žena kod kojih se bolest javi pojedinačno.

Faktori rizika i klinički pokazatelji ishoda kod žena sa sinhronim tumorima različiti su od onih koji se baziraju na histološkoj podeli. Žene sa sinhronim tumorima su najčešće mlađe, gojazne, premenopauzalne i nerotkinje. Bolesnice sa ozbiljnim endometrijalnim karcinomima više liče na bolesnice sa ovarijalnim karcinomima. U budućnosti će biti potrebno pružiti bolju evaluaciju etiologije ovih bolesti. Takođe, molekularno dijagnostikovanje tumora u endometrijumu i ovarijumu pružiće nam pravu potvrdu. *Acta Medica Medianae 2008;47(4):15-19.*

Ključne reči: *sinhroni tumori, nezavisni tumori, metastatski tumori, udruženi tumori*