CASE REPORTS
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Incidental finding of an ovarian epithelial tumor, adequate approach and fertility preservation – A case report

Slučajni nalaz epitelnog tumora ovarijuma, odgovarajući pristup i očuvanje plodnosti

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Abstract

Introduction. Ovarian carcinoma is the fifth leading cause of death in women. In 3–14% of cases, it occurs in women under the age of 40 who intend to have children. Studies have shown a high survival rate if the tumor is diagnosed and treated at an early stage, with a 5-year survival rate of 91.2%, which makes a conservative treatment a valid option. Preserving fertility is safe for grade 1 and 2 of the International Federation of Gynecology and Obstetrics (FIGO) stage I epithelial ovarian carcinomas. A sparing operation involves salpingoophorectomy on the tumor side, multiple biopsies of suspected sites, blind biopsies and infracolic omentectomy, as well as cytological analysis of the wash. **Case report.** A 25-year-old patient, G0, P0, went to the gynecologist due to severe pain in the lesser pelvis. An ultrasound examination revealed a cystic hypoechoic alteration in the right ovary of about 5 × 6 cm, suspected for torsion, and the patient was urgently operated. A right cystectomy was performed. The histopathological finding of the surgically removed cyst was: endometrioid adenocarcinoma of the ovary, histological grade 2 (HG2) and nuclear grade 2 (NG2), without lymphovascular invasion and no penetration of the capsule, submitted in parts. As the surgery performed did not reveal the degree of ovarian malignant tumor spreading, the FIGO stage could not be determined, and a second operation was necessary to stage the disease according to the FIGO protocol for ovarian cancer. **Conclusion.** Fertility preservation in patients with malignant ovarian epithelial tumors is a major challenge. The intense desire of the patient to have children has to be satisfied without reducing the success of treatment for this type of disease. The staging of the disease spreading is of paramount importance in order to make an adequate decision regarding the treatment.

Key words:
diagnosis; fertility preservation; gynecologic surgical procedures; histological techniques; incidental findings; neoplasm staging; ovarian neoplasms; ultrasonography.

Apstrakt

Uvod. Karcinom jajnika je peti vodeći uzrok smrti kod žena. Od ukupnog broja obolelih žena, 3–14% su mlađe od 40 godina i imaju želju za rađanjem. Studije su pokazale visoku stopu preživljavanja ukoliko se tumor dijagnostikuje i leči u ranom stadijumu, a petogodišnje preživljavanje iznosi 91,2%, pa se konzervativni način lečenja može smatrati validnom opcijom. Očuvanje fertiliteta je bezbedno za gradus 1 i 2 FIGO (*International Federation of Gynecology and Obstetrics*) stadijuma I epitelnih ovarijalnih karcinoma. Poštedna operacija podrazumeva salpingooforektomiju na strani tumora, multiple biopsije sumnjivih mesta, biopsije na slepo i infrakoličnu omentektomiju, kao i citološku analizu lavata. **Prikaz bolesnika.** Bolesnica stara 25 godina, G0, P0, javila se ginekologu zbog jakih bolova u maloj karlici. Ultrazvučnim pregledom dijagnostikovana je cistična hipoehogena promena na desnom jajniku promera 5 × 6 cm, suspektna na torziju zbog čega je bolesnica hitno operisana. Učinjena je desna cistektomija. Histopatološki nalaz operativno odstranjene ciste bio je: endometrijalni adenokarcinom ovarijuma, histološkog gradusa 2 (HG2) i nuklearnog gradusa 2 (NG2), bez limfovaskularne invazije i bez proboja kapsule, dostavljen u delovima. Kako urađenom operacijom nije utvrđen stepen rasprostranjenosti malignog tumora jajnika FIGO stadijum nije određen zbog čega je bilo neophodno uraditi reoperaciju u cilju određivanja stadijuma oboljenja prema FIGO protokolu za karcinom ovarijuma. **Zaključak.** Očuvanje fertiliteta kod pacijntkinja sa malignim tumorima jajnika predstavlja veliki izazov. Potrebno je zadovoljiti snažnu želju za ostvarivanjem materinstva, a da se ne smanji uspešnost u lečenju tog tipa oboljenja. Određivanje stadijuma raširenosti bolesti je od izuzetne važnosti za donošenje adekvatne odluke o načinu lečenja.

Ključne reči:
dijagnoza; plodnost, očuvanje; hirurgija, ginekološka, procedure; histološke tehnike; slučajni nalazi; neoplazme, određivanje stadijuma; jajnik, neoplazme; ultrasonografija.

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Introduction

Ovarian carcinoma is the fifth leading cause of death in women. In the US, 22,140 new cases were registered in 2017, among which 14,080 patients died of this disease. It is most often discovered in an advanced stage, and it is more common among older women aged between 55 and 64 [1]. In 3–14% of cases, it occurs in women under the age of 40 who intend to have children. Fertility preservation can safely be achieved in germinative type ovarian tumors, in stromal cell tumors, and in the case of borderline tumors. In the case of ovarian tumors of epithelial origin, enabling women to give birth represents a major challenge. About 30% of patients with epithelial ovarian carcinoma (EOC) are diagnosed with the International Federation of Gynecology and Obstetrics (FIGO) stage I, and 13% want to have a child, making the radical approach unacceptable for such patients [2]. Studies have shown a high survival rate if the tumor is diagnosed and treated at an early stage, with a 5-year survival rate of 91.2%, which makes a conservative treatment a valid option [3]. Preserving fertility is safe for grade 1 and 2 of the FIGO stage I EOC. In cases of grade 3 tumors, aggressive clear cell type tumors, anaplastic, and small cell tumors, a conservative approach is not advised [4]. A sparing operation involves salpingoophorectomy on the tumor side, multiple biopsies of suspected sites, blind biopsies and infracolic omentectomy, as well as cytological analysis of the wash.

We presented a case of a young woman who had not given birth and had been surgically treated due to lesser pelvis pains when an early stage EOC was discovered.

Case report

A 25-year-old patient, G0, P0, went to the gynecologist due to severe pain in the lesser pelvis. An ultrasound examination revealed a cystic hypoechoic alteration in the right ovary of about 5 × 6 cm, suspected for torsion. The left ovary and the uterus presented usual ultrasound characteristics for the age; there was no free fluid in the pouch of Douglas. Laboratory and biochemical analyses were regular, with cancer antigen 125 (Ca 125) tumor marker being 18.56 U/mL (reference value 0–35 U/mL). Due to severe pain, the patient was urgently operated on after being admitted to the hospital. Intraoperatively, on the right ovary, a torsioned cyst was found presenting a smooth capsule with clear content, whilst there was no free fluid in the abdomen. A right cystectomy was performed. The histopathological finding of the surgically removed cyst was: endometrioid adenocarcinoma of the ovary, histological grade 2 (HG2) and nuclear grade 2 (NG2), without lymphovascular invasion and no penetration of the capsule, submitted in parts.

As the surgery performed did not reveal the degree of ovarian malignant tumor spreading, the FIGO stage could not be determined, and a second operation was necessary to stage the disease according to the FIGO protocol for ovarian cancer. An additional computerized tomography (CT) of the abdomen and lesser pelvis, as well as the X-ray of the lungs, performed preoperatively, did not reveal pathological changes.

One month after the first surgery, the patient underwent a second operation. On this occasion, the lesser pelvis and abdomen were explored. No abnormality of the uterus and the adnexa was found, as well as no pathological changes or the serous intestine injury, parietal peritoneum was smooth, the liver was smooth with sharp margins, and nothing abnormal detected, lymph glands in the lesser pelvis and paraaortally were not palpable. A lavage fluid sample was sent for cytological analysis, and right salpingoophorectomy and lymphadenectomy of the right iliac and obturator region were performed as well as the infracolic omentectomy. The material was sent for histopathological analysis.

The histopathological results after the second operation showed that there were no significant pathological changes on the tissue samples taken, and the cytological test detected no abnormalities so that based on this and the previous operation, a FIGO stage IC1 of the disease was determined. Considering the fact that the patient had a strong desire to have children, having discussed this with her, the multidisciplinary team decided to have her undergo regular controls every 3 months and that after her pregnancy she has to undergo a radicalization of the previous surgery. A repeated verification of the Ca 125 tumor marker, as well as the CT scan of the abdomen and lesser pelvis at the check-ups, were satisfactory.

Discussion

EOC is the most common type of ovarian tumor and occurs in 90% of the patients. It exhibits various genetic mutations, and a subdivision in two types has been introduced based on genetic and pathohistological characteristics: type 1, which comprises serous low grade, endometrioid, mucinous and clear cell epithelial tumors of the ovary, and type 2, which comprises high grade serous, high grade endometrioid, malignant combined mesodermic and undifferentiated ovarian tumor. The serous pathohistological type is characterized by a mutation on the TP53 gene, in clear cell mutation it occurs on ARID1, PK3Ca, which is also characteristic of the endometrioid carcinoma, although they also present a mutation of the CTTNB1 gene. On the other hand, in mucinous ovarian carcinoma, the KRAS gene mutation is dominant. It is believed that tumors belonging to type 1 originate from the same forms of benign or borderline lesions or appear in the field of endometriosis, such as the endometrioid and clear cell histological type of the tumor. Those belonging to type 2 are more aggressive, and it is believed that they most likely originate from the oviduct fimbriae and that their manifestation on the ovaries is primary tumor metastases. If diagnosed at an early stage, they usually belong to type 1 as opposed to type 2, which is detected at a late advanced stage [5].

The incidence of endometrioid ovarian carcinoma is 10% concerning all epithelial carcinoma. It occurs in the

field of endometriosis or borderline form of adenofibromas, it's mainly diagnosed at an early stage as a unilateral cyst and is highly sensitive to platinum. All this gives encouraging indications that, in case of early detection, fertility preservation can be taken into consideration in patients who have yet to bear children [6, 7]. The European Society of Gynaecological Oncology (ESGO) recommendations indicate that fertility can be preserved in all epithelial low-grade tumors, G1-G2 endometrioid carcinoma, or expansive mucinous tumors.

The first reports on the preservation of fertility for EOC appeared in the 1960s and 1970s. Studies have shown that in case of stage IA, grade 1 and 2, the percentage of patients without relapse is 93.4% and 87.5%, respectively, and the survival rate is 98% and 95%, respectively. At this stage, no additional chemotherapy is needed because the prognosis is very good. In stage IC cases, chemotherapy is recommended for a better treatment outcome [8, 9].

Fertility preservation is not recommended in case of any stage of high-grade tumors, IC tumors, clear cell histological subtype of tumor irrespective of grade because the prognosis is very poor [10].

The decision regarding the type of surgery and the degree of radicality is affected by the histological type of the tumor, the degree of differentiation as well as the FIGO stage in which the tumor has been diagnosed. Adequate disease staging is extremely important because malignant tumors in young patients are mainly detected incidentally – like in the case of our patient. If all the procedures needed to stage the disease are not carried out during the first operation, a second surgical intervention is required. One study has shown that in a patient initially diagnosed as the FIGO stage IA, after a pelvic and paraaortic lymphadenectomy, the disease was staged as the FIGO IIIA [11]. In one study, Cass et al. [12] have found that 14 out of 96 (15%) women in the early stage of ovarian cancer had occult metastases in the lymph nodes at the moment of surgery. It is believed that patients with a relapse of the disease, which was discovered at an early stage, have not been adequately staged and that they already had occult metastases in retroperitoneal lymph nodes [13]. Pelvic and paraaortal metastases are found in 10–15% of such patients [14]. It is, therefore, essential that a complete procedure of disease diagnosis is carried out when making a decision to preserve the uterus and the remaining ovary. Studies comparing outcomes in patients with conservative treatment and those that underwent radical surgery for the FIGO I stages of epithelial ovarian tumors have shown that there was no significant difference in the outcome for these two types of treatment nor that the patients who had undergone radical surgery had a better prognosis [15, 16].

The main factors important for making a decision to preserve fertility are the FIGO stage of the disease, the histopathological type, and the tumor grade.

Many studies have confirmed that the histological grade of the tumor is the most significant prognostic factor. Namely, high-grade tumors are more aggressive and more often lead to a relapse. Vergote et al. [17] covered 1,545 patients with the FIGO stage IA in a retrospective study and came to the conclusion that a high grade correlates with the worst possible prognosis. The grade 3 is a significant predictor of tumor aggressiveness and survival level. The recommendation is that conservative treatment is not advisable for this histological grade nor for the aggressive forms of tumors such as clear cell, anaplastic, and small cell tumors [8, 9].

No significant difference in the disease outcome has been found by comparing FIGO stages IA and IC. Many researchers disagree with the view that the stage IC implies a worse prognosis. By comparing and analyzing the stage I EOC of the patients that have undergone sparing surgery, it has been shown that there was no difference in the survival and disease relapse between IA and IC stages [16, 18]. Additional application of chemotherapy in the stage IC cases significantly improves survival and delays disease recurrence [19].

Adjuvant chemotherapy is used in patients who have an increased risk of disease relapse, the FIGO stage IC1 and higher, and grade 2–3 tumors. In the first stage patients with the FIGO IA-IB, grades I and II there is no need to be applied [20]. The number of cycles ranges from three to nine, and they are administered after surgical treatment.

Many authors point out the good oncological and reproductive response in patients that met the conditions for sparing surgery in order to preserve fertility. The survival rate in these patients is not affected by the type of surgery but rather by the aggressiveness of the tumor, and the lethal outcome occurs more frequently due to other reasons than the relapse of the disease itself [10].

Conclusion

Fertility preservation in patients with malignant ovarian epithelial tumors is an important issue because the treatment has to meet multiple requirements. The intense desire of the patient to have children has to be satisfied without reducing the success of treatment for this type of disease. The staging of the disease spreading is of paramount importance in order to make an adequate decision regarding the treatment. Staging implies salpingoophorectomy on the tumor affected side, a biopsy of suspected sites and adhesions, blind biopsy, infracolic omentectomy, pelvic lymphadenectomy, and cytological analysis of abdominal cavity wash. If, regardless of the expected benign pathology, the histopathological examination confirms a malignant process, a reoperation is necessary to adequately stage the disease, as in the case of our patient. Subsequently, a decision is made on the extent of the surgical therapy. The preservation of fertility is safe with stage IA and IC, grade I and II, but adjuvant chemotherapy is recommended in the stage IC patients.

The patient declined the suggested chemotherapy. Regular Ca 125 tests, abdomen and lesser pelvis ultrasound and CT were normal, and the patient was feeling well.

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