USE OF MODERN LABORATORY TESTS IN DIFFERENTIAL DIAGNOSTICS OF EDUCATIONAL OVARIES

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ИСПОЛЬЗОВАНИЕ СОВРЕМЕННЫХ ЛАБОРАТОРНЫХ ИССЛЕДОВАНИЙ В ДИФФЕРЕНЦИАЛЬНОЙ ДИАГНОСТИКЕ ОБРАЗОВАНИЙ ЯИЧНИКОВ

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Annotation. Malignant ovarian tumors are the least accessible for early diagnosis among all malignant neoplasms of the reproductive system due to the asymptomatic course of the disease in the early stages. Determining the nature of an ovarian tumor (benign or malignant) at the stage of preoperative diagnosis is undoubtedly important, since there are fundamental differences in the tactics of management and treatment of patients. There are currently no unambiguous criteria for referring patients to a gynecological or oncological hospital.

Key words: benign and malignant ovarian tumors, tumor markers, malignancy index.

Аннотация. Злокачественные опухоли яичников являются наименее доступными для ранней диагностики среди всех злокачественных новообразований репродуктивной системы в связи с бессимптомным течением заболевания на ранних стадиях. Определение характера опухоли яичника (доброкачественная или злокачественная) на этапе предоперационной диагностики является, несомненно, важным, так как имеются принципиальные различия в тактике ведения и лечения больных. Однозначных критериев для направления больных в гинекологический или онкологический стационар до настоящего времени не существует.

Ключевые слова: доброкачественные и злокачественные опухоли яичников, опухолевые маркеры, индекс малигнизации.

Introduction. To most reliably assess the likelihood of a malignant process in the presence of space-occupying ovarian formations at the preoperative stage is a difficult task that a gynecologist must solve in order to correctly select further tactics for managing the patient. Ovarian masses, which are the most frequently detected pathology when examining women of reproductive and postmenopausal age, can be either benign or malignant.

To identify malignant ovarian tumors, the determination of the tumor marker CA-125 is traditionally used, but its sensitivity in diagnosing ovarian cancer (OC) is low, especially in the early stages [2, 4]. Despite the fact that CA-125 is often elevated in advanced stages of ovarian cancer, the tumor marker increases in less than 50% of cases in stage I disease and often remains normal in mucinous (32%), endometrioid (30-60%) and clear cell (40). %) adenocarcinomas [1, 8]. In addition, a number of benign and malignant diseases of other localization, the first trimester of pregnancy, menstruation, ethnicity, age, hysterectomy, smoking and obesity can lead to increased CA-125 values [2, 9]. CA-125 levels are often elevated in patients with endometriosis, which reduces the specificity of the test in identifying patients with ovarian malignancies [2, 11].

To improve the differential diagnosis of ovarian masses, other methods have been proposed: the HE4 tumor marker, the ROMA algorithm, calculated by the content of CA-125 and HE4, taking into account the menopausal status, and the RMI malignancy risk index, taking into account the menopausal status, the concentration of the CA-125 tumor marker and certain ultrasound criteria. However, data on the value of the additional use of the above methods at the stage of preoperative examination of women with neoplasms in the area of the uterine appendages is contradictory [1, 6].

Purpose of the study: to conduct a comparative analysis of the sensitivity and specificity of the CA-125, HE4, RMI and ROMA methods in the differential diagnosis of benign and malignant ovarian tumors at the stage of preoperative examination.

Materials and methods. Materials and methods. The prospective study involved 100 patients of the gynecological department admitted for surgical treatment of ovarian masses: 64 patients of the reproductive period and 36 of the postmenopausal period. The age of the patients ranged from 18 to 79 years, with an average of 41.5 years.

All patients participating in the study were examined according to the standard for ovarian mass formations, and the level of the HE4 tumor marker was determined using chemiluminescent immunoassay. Based on menopausal status, pelvic ultrasound results and the concentration of the CA-125 tumor marker in the blood serum, the RMI risk index for malignancy was calculated. An index value of more than 200 indicates the malignant nature of the ovarian mass formation [1, 15]. The ROMA algorithm was calculated using a calculator based on menopausal status and the content of tumor markers CA-125 and HE4 in the blood serum. For women of reproductive age, ROMA values equal to or more than 13.1% indicate a high risk of malignant ovarian tumor, while ROMA values less than 13.1% indicate a low risk of ovarian cancer. In postmenopausal women, ROMA values equal to or greater than 27.7% indicate high risk, and ROMA values less than 27.7% indicate low risk of ovarian cancer.

After the stage of surgical treatment and obtaining the results of histological examination of the surgical material, statistical processing of the obtained data was carried out using a computer program.

Results and discussion. The time interval from the moment of detection of space-occupying formations in the area of the uterine appendages to surgical treatment ranged from 1 month to 20 years, on average - 6 months. The reason for visiting a doctor in 62 patients was subjective complaints; in 3 women of reproductive age, neoplasms in the area of the uterine appendages were identified during an examination for infertility, in 3 - due to abnormal uterine bleeding. Patients of reproductive age made significantly more complaints than those in postmenopause (76.6% and 52.8%, respectively; $p = 0.014$). The main complaint (in 50 patients) was pain of varying nature and intensity in the hypogastric and iliac regions. In addition to pain, 12 patients were bothered by an enlarged abdomen and the sensation of a foreign body in the abdominal cavity and pelvis (the average size of the tumors was 133 ± 79 mm). Later, after surgery and the results of histological examination, it was noted that only 2 of them had malignant tumors, their size exceeding 200 mm. 32 patients had no complaints: ovarian masses were discovered "accidentally" during routine gynecological examinations and ultrasound of the pelvic organs.

The sizes of ovarian space-occupying lesions according to pelvic ultrasound data varied from 6 to 300 mm, with an average of 45 mm. Based on the results of histological examination of the surgical material, benign ovarian tumors were

identified in 91 patients, malignant in 7, borderline tumor in 1, and malignant peritoneal mesothelioma was diagnosed in 1 patient.

The sizes of benign ovarian space-occupying lesions varied from 6 to 200 mm (on average - 42 [25; 63] mm), malignant - from 50 to 300 mm (on average - 137.5 [96.5; 253.0] mm). The sizes of malignant ovarian tumors significantly exceeded the sizes of benign ones ($p < 0.001$).

Among benign ovarian neoplasms, the most common were epithelial tumors (n = 53): serous cystadenomas (n = 24), serous adenofibromas (n = 2), mucinous cystadenomas (n = 6) and endometrioid ovarian cysts (n = 21). Sex cord stromal tumors were represented by fibroma in 4 cases and thecoma in 1. Mature teratomas were identified in 9 women. Follicular cysts were found in 7 women, a corpus luteum cyst in 1. Three cases of fibromatosis, three cases of stromal hyperthecosis, and one case of stromal ovarian hyperplasia were identified. In 9 patients, histological examination revealed small cysts of the inclusion type, large white bodies, cysts with atrophy of the lining and atrophic changes in the ovaries. The borderline tumor was a serous papillary cystic tumor.

Malignant tumors in 100% of cases were epithelial and were represented by the following histological variants: serous carcinoma (n = 3), mucinous carcinoma (n = 3), clear cell carcinoma (n = 1). Four out of 7 (57.1%) patients with ovarian malignancies were postmenopausal.

During the preoperative examination, the values of the HE4 tumor marker went beyond the reference values in 5 women, RMI in 9 and ROMA in 7, which suggested the presence of thyroid cancer in these patients due to the high sensitivity and specificity of the above methods according to the literature [1, 16]. The level of CA-125 exceeded the discriminatory level in 21 women - they were suspected of having malignant or endometrioid neoplasms of the ovaries [1, 11].

In case of pre-occlusion tumor, the values of the tumor marker CA-125 varied from 0.6 to 260 U/ml, in case of ovarian cancer - from 31 to 547 U/ml (the discriminatory level of CA-125 is 35 U/ml). In cases of positive results with OC, the content of CA-125 was increased by at least 4 times.

The content of the HE4 tumor marker in the blood serum at pre-term dormancy in women in the reproductive period and postmenopause ranged from 8.8 to 92.1 pmol/l (with a normal value of up to 70 pmol/l) and from 30.9 to 100.4 pmol /l (at a norm of up to 140 pmol/l), respectively; with PVD - from 42.9 to 922.7 pmol/l and from 37.3 to 235.9 pmol/l, respectively.

The RMI risk index for malignancy was characterized by values ranging from 0.6 to 451.6 for primary cancer and from 124 to 2188 for ovarian cancer (the discriminatory level for this method is 200).

In the study, ROMA values at BCOP in women in the reproductive and postmenopausal periods ranged from 0.1% to 27.3% and from 2.5% to 22.8%, respectively; with ovarian cancer - from 6.5% to 99% and from 14% to 80.2%, respectively. Reference ROMA values: less than 13.1% before menopause and less than 27.7% in postmenopause.

In addition to patients with histologically confirmed OC, the values of all four studied indicators exceeded the discriminatory levels (CA-125 - 260 U/ml, HE4 - 92.1 pmol/l, RMI - 260, ROMA - 27.3%) in the patient 36 years old with mucinous cystadenoma in combination with widespread external genital endometriosis (endometrioid ovarian cyst and endometriosis of the pelvic peritoneum). In addition, the CA-125 tumor marker showed a false-positive result in another 14 patients of reproductive age, in 9 of whom, based on the results of histological examination, endometrioid ovarian cysts were identified (CA-125 level varied from 40 to 260 U/ml), in 1 - an epithelial tumor in the variant of serous cystadenoma (CA-125 - 36.7 U/ml), in 2 women - tumors of the sex cord stroma (fibroma and mature teratoma, CA-125 values - 74 and 81.5 U/ml, respectively). According to Bast et al., in benign ovarian tumors, an increase in CA-125 levels was noted in 8% of patients [2, 13]. An increase in CA-125 has been described in gynecological diseases such as endometriosis, uterine fibroids, menstruation and pregnancy. In these cases, the concentration of CA-125 ranges from 35-150 U/ml or within the so-called "border zone" - from 35 to 65 U/ml [1, 8].

The sensitivity (SE) of the CA-125 tumor marker in the study was 85.7% with a specificity (SP) of 83.6%, the area under the ROC curve (AUC) was 0.968 (Table 2). According to a meta-analysis of 53 studies from 1999-2009 by Dodge et al., the overall effectiveness of CA-125 in the diagnosis of ovarian cancer has a sensitivity of 78% and a specificity of 78% [2, 14].

The HE4 tumor marker in the study showed a false positive result in a 36-year-old patient with a follicular ovarian cyst in combination with a corpus luteum cyst and in a 36-year-old patient with mucinous cystadenoma in combination with widespread external genital endometriosis (endometrioid ovarian cyst and endometriosis of the pelvic peritoneum). The number of publications devoted to the analysis of HE4 in benign tumor tissues is relatively small. One US study examined its expression in benign ovarian tumors, including benign serous (n = 12) and mucinous cystadenomas (n = 12), endometriosis (n = 12), and benign ovarian cysts (n = 12). Moderate to intense HE4 staining was found in 11 of 12 mucinous cystadenomas and 11 of 12 ovarian cysts, whereas 5 of 11 serous cystadenomas showed only slight staining. Expression of this protein was also observed in all samples from endometriosis lesions. Plasma concentrations of CA-125 were increased both in women with ovarian cancer and in patients with severe endometriosis and endometrioid ovarian cysts. Average HE4

values, when compared with controls, were significantly higher in women with ovarian cancer and endometrial cancer, but not in women with endometriosis or endometrioid ovarian cysts [10]. The significance of additional determination of HE4 in patients with elevated CA-125 levels and suspected endometriosis is confirmed by data from a number of other foreign studies [3, 17].

Like the HE4 tumor marker, ROMA turned out to be false-positive in a 36-year-old patient with a follicular ovarian cyst in combination with a corpus luteum cyst and in a 36-year-old patient with mucinous cystadenoma in combination with widespread external genital endometriosis (endometrioid ovarian cyst and endometriosis of the pelvic peritoneum). due to false-positive CA-125 and HE4 in these patients. The ROMA algorithm in the study was characterized by sensitivity (SE) of 71.4% and specificity (SP) of 97.8%, the area under the ROC curve (AUC) was 0.929 (Table 2), which differs from the data presented by the authors of the algorithm: total sensitivity of ROMA - 93.8%, specificity - 74%. Various groups have concluded both that the combination of markers has superior diagnostic performance and that the addition of HE4 to CA-125 or the use of ROMA does not improve CA-125-based screening [1]. Such diametrically opposed findings can be explained by differences in the groups examined (the proportion of mucinous, borderline, metastatic tumors, etc.), which once again emphasizes the need for further research in this area [3, 9].

There was no relationship between the values of the diagnostic tests CA-125, HE4, RMI and ROMA and the histological types of ovarian tumors (P > 0.05).

Conclusions. The low specificity of the CA-125 tumor marker determines the need to use additional diagnostic markers and methods in order to more accurately differentiate between benign and malignant ovarian tumors. The sensitivity of the CA-125, HE4, RMI and ROMA methods in the study was 85.7%, 42.9%, 85.7% and 71.4%, respectively; specificity - 83.6%, 97.8%, 96.7%, 97.8%, respectively. The most valuable method for the differential diagnosis of benign and malignant ovarian tumors at the preoperative stage in the study was the risk index of malignancy RMI (the method was characterized by the largest value of the area under the ROC curve - 0.990), the least valuable was the tumor marker HE4 (AiC - 0.839). Determining the value of the HE4 tumor marker is highly informative for the differential diagnosis of ovarian malignancies with endometrioid cysts in patients with elevated CA-125 levels.

Literature

1. Van Gorp T., Cadron I., Despierre E. et al. HE4 and CA125 as a diagnostic test in ovarian cancer: prospective validation of the Risk of Ovarian Malignancy Algorithm. Br J Cancer. 2011; 104 (5): 863-70.

2. Мартынов С.А. Современные онкомаркеры в дифференциальной диагностике опухолей яичников вне и во время беременности (обзор литературы). Гинекология. 2014; 16 (4): 63-7.

3. Johnson C.C., Kessel B., Riley T.L. et al. The epidemiology of CA-125 in women without evidence of ovarian cancer in the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial. Gynecol Oncol. 2008; 110 (3): 383-9.

4. Кудратова З.Э., Турсунов Ф.У., Мусаева Ф.Р., Абдулхаев Иброхим АТИПИК МИКРОФЛОРА ЭТИОЛОГИЯЛИ ЎТКИР ОБСТРУКТИВ БРОНХИТЛАРИНИНГ ЎЗИГА ХОС КЛИНИК КЕЧИШИ // ReFocus. 2022. №4.

5. Daminov F. A., Mansurov T. T. FEATURES OF DIAGNOSIS AND TACTICS OF SURGICAL TREATMENTOFACUTE INTESTINAL OBSTRUCTION //International Journal of Early Childhood Special Education. – 2022. – Т. 14. – №. 3.

6. Даминов Ф., Карабаев Х., Рузибоев С. ЭНДОСКОПИЧЕСКИЙ МОНИТОРИНГ И ЭНТЕРАЛЬНОЕ ПИТАНИЕ У ОБОЖЖЁННЫХ С НАРУ-ШЕНИЯМИ ФУНКЦИЙ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА //Журнал вестник врача. – 2020. – Т. 1. – №. 2. – С. 29-32.

7. Даминов Ф. А., Набиева Ф. С., Очилов О. Ш. БИОЛОГИЧЕСКАЯ РОЛЬ КАЛЬЦИЯ В ОРГАНИЗМЕ ЧЕЛОВЕКА //Research Focus International Scientific Journal. – 2023. – Т. 2. – №. 7. – С. 56-58.

8. Бердиярова Ш.Ш., Юсупова Н.А. Особенности иммунометаболических нарушений иммунологической реактивности при гематогенных остеомиелитах, Вестник науки и образования, 29-32

9. Dushanova G. A., Nabiyeva F. S., Rahimova G. O. FEATURES OF THE DISTRIBUTION OF HLA-ANTIGENS AMONG PEOPLE OF THE UZBEK NATIONALITY IN THE SAMARKAND REGION //Open Access Repository. – 2023. – Т. 10. – №. 10. – С. 14-25.

10. Berdiyarova Sh.Sh., Ahadova M.M., Ochilov S.A. COMPLICATIONS OF TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS, LITERATURE REVIEW, Galaxy International Interdisciplinary Research Journal 293-298

11. Бердиярова Ш.Ш., Юсупова Н.А., Ширинов Х.И. Клинико-лабораторная диагностика внебольничных пневмоний у детей, Вестник науки и образования, 80-83

12. Kudratova Zebo Erkinovna, Karimova Linara Alixanovna Age-related features of the respiratory system // ReFocus. 2023. №1. URL: https://cyberleninka.ru/article/n/age-related-features-of-the-respiratory-system.

13. Ибрагимова Н. и др. ДИАГНОСТИКА, ЛЕЧЕНИЕ И ПРОФИЛАКТИКА САХАРНОГО ДИАБЕТА 2-го ТИПА //Центральноазиатский журнал академических исследований. – 2024. – Т. 2. – №. 1. – С. 9-13.

14. Nabiyeva F. S. et al. CREATION OF OPTIMUM CONDITIONS FOR PROPAGATION OF SACCHAROMYCES CEREVISIAE YEAST //Journal of new century innovations. – 2023. – Т. 23. – №. 1. – С. 85-91.

15. Isomadinova L.K, Qudratova Z.E., Babaxanova F.Sh.clinico-laboratory features of the course of covid-19 with hepatitis b journal of new century innovations №-3. 2023 P. 60-65.

16. Ибрагимова Н. и др. РАССТРОЙСТВА ИММУННОЙ СИСТЕМЫ. ПАТОГЕНЕТИЧЕСКИЕ ОСНОВЫ //Центральноазиатский журнал академических исследований. – 2024. – Т. 2. – №. 1. – С. 4-8.

17. Ибрагимова Н. С., Юлаева И. А. ПАТОГЕНЕТИЧЕСКИЕ, КЛИНИКО-ЛАБОРАТОРНЫЕ И ИНСТРУМЕНТАЛЬНЫЕ АСПЕКТЫ ДИАГНОСТИКИ СИНДРОМА ПОЛИКИСТОЗНЫХ ЯИЧНИКОВ У ЖЕНЩИН РЕПРОДУКТИВНОГО ВОЗРАСТА //Journal of new century innovations. – 2023. – Т. 26. – №. 3. – С. 180-184.