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BRCA-ASSOCIATED OVARIAN CANCER: EXPERIENCE PERSONALIZED TREATMENT. A CLINICAL CASE

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ABSTRACT

Relevance: *Ovarian cancer is one of the deadliest gynecological tumors, claiming the lives of thousands of women every year. Late diagnosis (more than 70% of cases at stage III-IV) is due to the absence of specific symptoms and low screening effectiveness. A personalized treatment approach, including the analysis of BRCA1/2 mutations and the use of PARP inhibitors, has become a significant achievement. Detection of BRCA1/2 mutations has important prognostic value, contributing to early risk prediction and mortality reduction. Genetic counseling for patients with hereditary predispositions allows for prevention through early diagnosis, targeted therapy, and preventive interventions.*

The study aimed to *analyze a clinical case of treatment of a patient with BRCA-associated ovarian cancer with a rare form of mutation for the possibility of personalizing the treatment.*

Methods: *This study presents a clinical case of a patient with advanced ovarian cancer associated with a rare BRCA1 mutation. Mutation detection was performed using sequencing, while treatment efficacy was assessed through computed tomography and measurement of CA-125 levels.*

Results: *The tumor process was stabilized for more than three years. Comprehensive treatment (diagnostic laparoscopy, chemotherapy, surgery, targeted and supportive therapy) stabilized the tumor process. Genetic testing has made it possible to adapt therapy, improving the prognosis. The next of kin were tested for prevention.*

Conclusion: *A personalized approach with BRCA1/2 mutation analysis and PARP inhibitors improves clinical outcomes. Advances in molecular oncology have increased patient survival. However, problems remain: resistance to therapy, limited efficacy in patients without BRCA mutations, and the need for further research into the mechanisms of interaction of PARP inhibitors with other drugs.*

Keywords: *ovarian cancer, BRCA1 and BRCA2 mutations, chemotherapy, PARP inhibitors, a clinical case.*

Introduction: Ovarian cancer is one of the most lethal forms of gynecological tumors, annually taking the lives of tens of thousands of women worldwide [1]. A characteristic disease feature is late diagnosis, which occurs at stage III-IV in more than 70% of cases [2]. This is due to the absence of specific symptoms in the early stages and the insufficient effectiveness of screening methods. A personalized approach to treatment based on the analysis of *BRCA1/2* mutations and the use of PARP inhibitors has become a significant step forward in the fight against this disease.

According to GLOBOCAN 2020, approximately 313,000 new cases of ovarian cancer and 207,000 deaths are reported worldwide annually [1]. In Kazakhstan, more than 1,200 new cases of ovarian cancer are registered annually, accounting for 2.9% of the overall structure of oncological diseases as of 2020. Over the past 15 years, there has been a 21% increase in the detection of ovarian cancer [2]. Projections suggest that by 2040, the incidence will increase by 5%, driven by population aging and growth [3]. *BRCA1* and *BRCA2* are tumor suppressor genes involved in DNA repair through homologous recombination. Their dysfunction leads to the accumulation of DNA damage and increased genomic instability [4]. *BRCA* mutations are associated with heightened sensitivity to platinum-based chemotherapy and PARP inhibitors [5]. Studies have demonstrated that patients with *BRCA* mutations have better progression-free survival (PFS) outcomes than patients without mutations. In the SOLO-1 study, 50% of patients receiving olaparib showed no disease progression over five years [6]. Platinum-based chemotherapy remains the cornerstone of ovarian cancer treatment. Drugs such as carboplatin and paclitaxel are effective in the initial treatment stages, but the high recurrence rate underscores the need for maintenance therapy [7]. PARP inhibitors (olaparib) have become central to maintenance therapy. These drugs block the DNA repair system, inducing apoptosis in tumor cells with *BRCA* mutations [8]. SOLO-1 Study: Olaparib extended median PFS to 56 months in patients with *BRCA* mutations [6]. PRIMA Study: Niraparib demonstrated efficacy in *BRCA*-mutated and non-mutated patients, increasing PFS by 13.8 months [9]. ARIEL-3 Study: Rucaparib significantly improved PFS in patients with recurrent disease [10]. The PAOLA-1 studies evaluated the combination of PARP inhibitors with bevacizumab, an antiangi-

ogenic drug. In patients with *BRCA* mutations, the combination of olaparib and bevacizumab extended PFS to 37.2 months compared to 17.7 months in the control group [11]. Modern technologies such as next-generation sequencing (NGS) support identifying *BRCA* mutations and determining the levels of genomic instability, which are critical factors in choosing therapy [12]. Prognostic markers include homologous recombination deficiency (HRD) status and PARP1 expression levels [13].

Objective: to analyze and describe a clinical case of treatment of a patient with *BRCA*-associated ovarian cancer with a rare form of mutation with the possibility of personalizing therapy.

Material and Methods: This study presents a clinical case of a patient with advanced ovarian cancer associated with a rare *BRCA1* mutation, receiving treatment at the Almaty Oncology Center in Kazakhstan. To identify mutations in the *BRCA1* and *BRCA2* genes, mass parallel sequencing (NGS) was performed on the MiniSeq platform (Illumina) using the AmpliSeq® *BRCA* Panel for Illumina reagent kit (Illumina, San Diego, CA, USA), which is a targeted panel covering all exon regions and flanking intron sequences of the *BRCA1* and *BRCA2* genes. Given the patient's age and sensitivity to platinum-based therapy, a rare *BRCA1* mutation was detected. The effectiveness of treatment was monitored using computed tomography (CT) and CA-125 tumor marker levels.

Clinical case:

Patient Information: Patient A, born in 1978 (age at diagnosis – 43 years), visited the Almaty Oncology Center (Almaty, Kazakhstan) complaining of increased weakness and abdominal volume. It is known from the anamnesis that the patient's mother had endometrial cancer, and two relatives had breast cancer. The patient noted a deterioration in her health since July 2021, when the above symptoms appeared, after which she sought medical help.

Clinical data: The functional status was assessed at 2 points on the ECOG scale during the initial examination. A significant amount of free fluid in the abdominal cavity was revealed among the critical symptoms.

Diagnostics: Clinical tests at the visit revealed anemia (hemoglobin 92 g/L, erythrocytes 3.2×10^9/L). No other clinically significant deviations were noted. The CA-125 tumor marker level as of 08/10/2021 was 289 U/mL. CT scanning of the chest on 08/12/2021 found no infiltrative changes. CT scan of the abdomen and pelvis on 07/20/2021 revealed a soft tissue formation in the pelvis originating from the left ovary and massive ascites.

Diagnostic laparoscopy revealed peritoneal carcinomatosis affecting up to 70% of the peritoneum, a tumor conglomerate in the pelvis with no clear organ differentiation, and ascites up to 6000 mL, which was evacuated. Morphological examination confirmed the diagnosis as metastatic adenocarcinoma (tumor biopsy). The final diagnosis was stage IIIc ovarian cancer (T3cNxM0) with carcinomatosis of the abdomen and pelvis and ascites.

Treatment: Given the extent of the disease, the patient's condition, and the lack of technical feasibility for optimal surgical intervention, it was decided to initiate platinum-based chemotherapy. From October 14, 2021, to February 22, 2022, the patient received six courses of neoadjuvant chemotherapy with the following regimen: carboplatin AUC5 and paclitaxel 175 mg/m^2. During antitumor therapy, the patient's condition improved significantly. Functional status improved to 1 point on the ECOG scale, moderate weakness persisted, and anemia resolved, with hemoglobin levels increasing to 124 g/L.

The patient underwent chemotherapy with asthenia and thrombocytosis. Control Computed tomography of the chest, abdomen and pelvis with intravenous contrast (03/09/2022) showed a decrease in the size of the retroperitoneal lymph nodes and no changes in the nodular formations along the anterior abdominal wall, an increase in the size of the uterine body and inguinal lymph nodes was recorded. Colonoscopy with biopsy showed a morphological picture characteristic of carcinoma. 01/20/2022, and positive dynamics in stabilizing the level of the CA-125 tumor marker to 18 U/mL were recorded.

On March 30, 2022, interval cytoreduction was performed, including laparotomy, total hysterectomy with bilateral salpingo-oophorectomy, resection of the sigmoid colon with a side-to-side anastomosis, and omentectomy. The postoperative period was uneventful.

According to the results of morphological examination of the postoperative material, serous cystadenocarcinoma of the ovary (G3) was revealed with signs of decay, minimal signs of therapeutic pathomorphosis, germination of all layers of the colon wall and adjacent adipose tissue. No tumor cells were found at the resection edges; there are also no signs of a tumor in the omentum tissue and lymph node.

On 19.04.2022, the CA-125 tumor marker level was 13.75 U/mL. From 13.04.2022 to 30.06.2022, the patient underwent four courses of adjuvant chemotherapy with targeted therapy in the following regimen: carboplatin (AUC5), paclitaxel 175 mg/m^2, and bevacizumab 700 mg (10 mg/kg). The therapy was well tolerated against the concomitant treatment.

On 29.07.2022, the CA-125 tumor marker level was 23.00 U/mL.

Control CT of the chest, abdomen and pelvis with intravenous contrast from 22.07.2022 revealed metastatic lesions of the iliac lymph nodes and lymphadenopathy of the inguinal lymph nodes (Figure 1).

From 10.08.2022 to 26.10.2022, four courses of chemotherapy with targeted therapy were administered in the following regimen: gemcitabine 1600 mg intravenously by drip on the 1st and 8th days of the cycle and bevacizumab 700 mg (10 mg/kg) intravenously by drip. The patient tolerated the treatment satisfactorily despite concomitant therapy.

On 10.10.2022, the CA-125 tumor marker level was 4.52 U/mL.

Control CT of the chest, abdomen and pelvis with intravenous contrast on 07.11.2022 confirmed the presence of metastatic lesions of the iliac lymph nodes and lymphadenopathy of the inguinal lymph nodes. The comparison with the CT of 22.07.2022 revealed no significant dynamics (Figure 2).

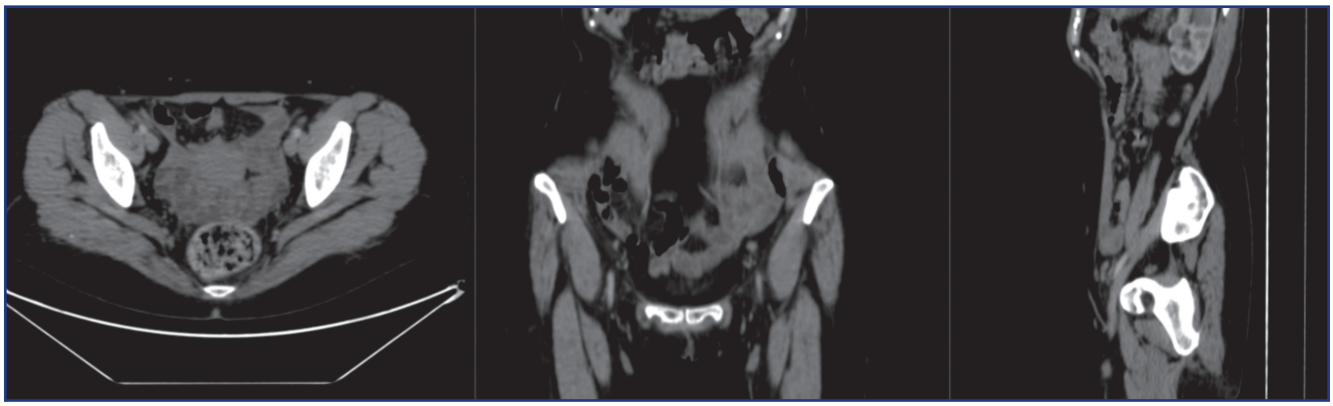

Figure 1 – CT of the chest, abdomen and pelvis with intravenous contrast on July 22, 2022

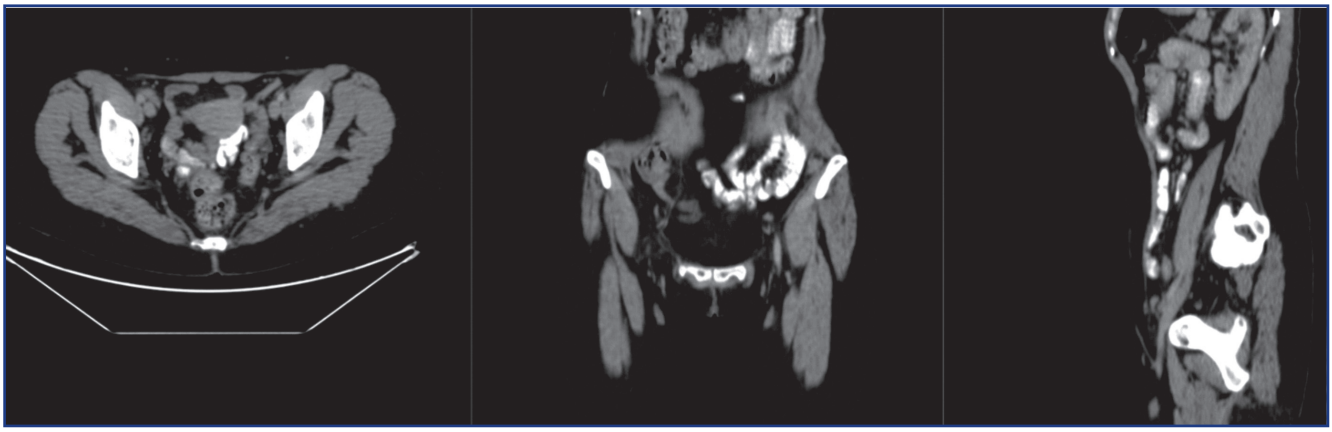

Figure 2 – CT of the chest, abdomen and pelvis with intravenous contrast on November 07, 2022

According to the council's decision, from November 25, 2022, to February 8, 2023, four more courses of chemotherapy with targeted therapy were administered in the following regimen: gemcitabine 1600 mg intravenously by drip on the 1st and 8th days of the cycle and Bevacizumab 800 mg (10 mg/kg) intravenously by drip. On February 21, 2023, the patient received targeted monotherapy with bevacizumab at a dose of 800 mg, which was administered intravenously by drip infusion. On 17.02.2023, the CA-125 tumor marker level was 7.25 U/mL. Control CT of the chest, abdomen and pelvis with intravenous contrast from 03.01.2023 showed an increase in the size of the iliac lymph nodes compared to the CT data from 11.07.2022, which indicates the progression of the process (Figure 3).

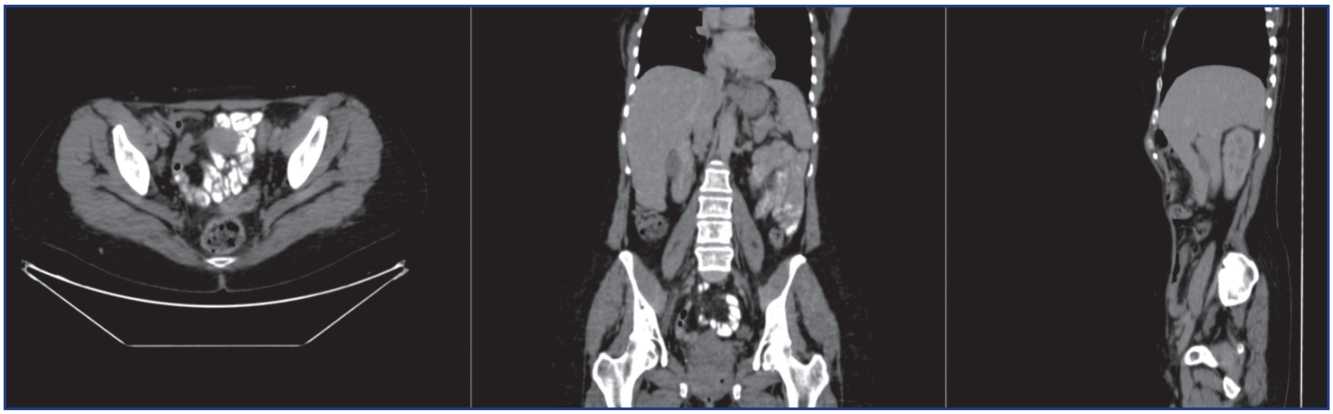

Figure 3 – CT of the chest, abdomen and pelvis with intravenous contrast on January 03, 2023

According to clinical recommendations, the patient underwent four courses of anti-relapse chemotherapy (PCT) from June 16 to August 21, 2023, in carboplatin AUC5 and paclitaxel 175 mg/m^2 regimen. Monitoring of the tumor marker CA-125 level showed a value of 24.8 U/mL on 18.08.2023, and 31.6 U/mL on 14.09.2023. Postoperative material was sent for testing for mutations in the *BRCA* gene. In a heterozygous state, a pathogenic variant was detected in the *BRCA1* gene NM_007294.4 (*BRCA1*); c181T>G (p.Cys61GLY). Given this genetic change and platinum-sensitive relapse of serous epithelial ovarian cancer, since November 2023, the patient has been receiving

maintenance therapy with the PARP inhibitor olaparib at a dosage of 600 mg per day (2 capsules 2 times a day). The drug was provided as part of charitable assistance by "Kazakhstan Khalkyn" Public Fund. During olaparib therapy, the patient experienced side effects such as nausea and episodes of diarrhea that occurred during the first month of treatment. These adverse events did not require dose adjustment or drug discontinuation.

A control CT scan with intravenous contrast performed on 06.12.2023 showed a picture of metastatic lesions of the iliac lymph nodes and lymphadenopathy of the inguinal lymph nodes. Compared with the CT results of 06.09.2023, an increase in the size of the iliac lymph nodes was observed. The CA-125 tumor marker level was 30.28 U/mL on 28.12.2023, 34.95 U/mL on 17.01.2024, and 37.15 U/mL on 12.02.2024. CT with intravenous contrast of 04.03.2024 showed a further increase in the size of the iliac lymph nodes, with stable sizes of the inguinal lymph nodes. Hyperplasia of the retroperitoneal lymph nodes (suspected metastasis) and an increase in the size of the para-aortic lymph nodes (suspected metastasis) were also detected compared to the CT of 06.12.2023 (Figure 4).

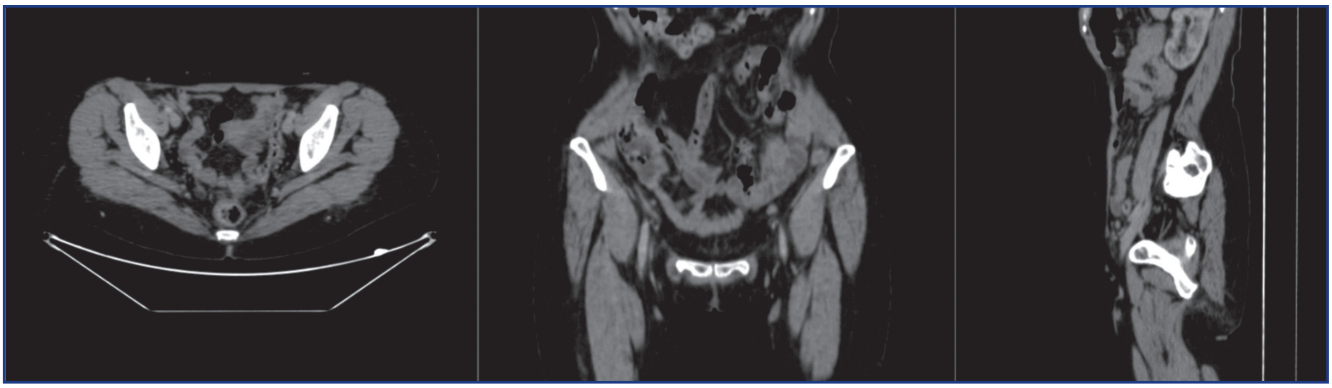

Figure 4 – CT of the chest, abdomen and pelvis with intravenous contrast on March 04, 2024

The CA-125 tumor marker level amounted to 41.0 U/mL on 11.03.2024 and 40.3 U/mL on 10.04.2024. Taking into account the progression of the disease, the patient received eight courses of targeted therapy from 13.05.2024 to 30.10.2024: bevacizumab 900 mg (10 mg/kg) and olaparib 600 mg (2 capsules 2 times a day) on an outpatient basis. The drugs were provided as part of charitable assistance by "Kazakhstan Khalkyna" Public Fund. The patient tolerated the therapy satisfactorily, with accompanying supportive treatment. The patient continues outpatient therapy, receiving Lynparza (olaparib) 600 mg, 2 drops, 2 times a day.

Control CT with intravenous contrast from September 23, 2024, showed mts-lesion of the iliac and para-aortic lymph nodes and lymphadenopathy of the inguinal lymph nodes; a stabilization of the process was noted in comparison with the CT of 04.06.2024 (Figure 5).

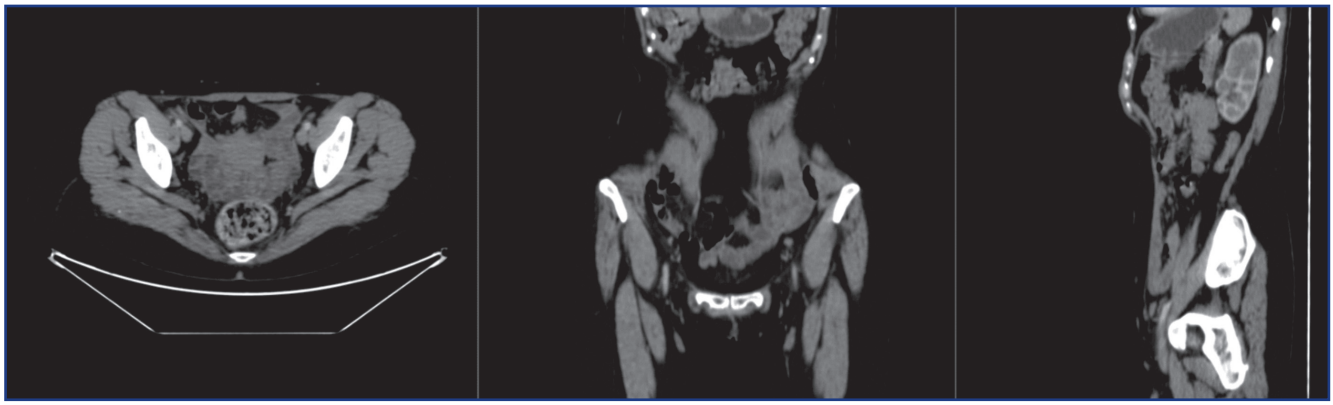

Figure 5 – CT of the chest, abdomen and pelvis with intravenous contrast on September 23, 2024

Results: The comprehensive treatment strategy, including diagnostic laparoscopy, neoadjuvant and adjuvant chemotherapy, surgery, and supportive therapy with PARP inhibitors, has allowed for the stabilization of the tumor process for more than three years.This strategy contributed to tumor stabilization and improved overall clinical outcomes. Genetic testing played a key role in treatment planning, enabling therapy to be tailored to the patient's molecular profile. The identification of a rare *BRCA1* mutation (NM_007294.4 (*BRCA1*); c.181T>G (p.Cys61Gly)) in a heterozygous state confirmed sensitivity to platinum-based chemotherapy and PARP inhibitors, which significantly prolonged disease control. CA-125 tumor marker levels were monitored throughout treatment and correlated with disease progression and therapeutic response. Initially, tumor regression and bio-

chemical remission were achieved; however, subsequent imaging detected metastatic involvement of the iliac and para-aortic lymph nodes, requiring therapy adjustments. The patient continues maintenance treatment with olaparib in combination with bevacizumab, demonstrating disease stabilization with no evidence of new metastatic lesions. Despite periods of disease progression, the personalized treatment strategy has extended progression-free survival and improved the patient's quality of life. This case underscores the importance of individualized therapy in *BRCA*-associated ovarian cancer and highlights the need for further research into resistance mechanisms and the optimization of combination treatment approaches (Table 1).

Table 1 – Timeline of the presented clinical case of ovarian cancer with *BRCA1* mutation

Year	Key Event
2021	Symptom onset (July 2021)
	CA-125: 289 U/mL (August 2021)
	Chest CT: no changes (August 2021)
	Abdominal and pelvic CT: tumor in the left ovary, massive ascites (July 2021)
	Diagnostic laparoscopy, biopsy: peritoneal carcinomatosis (70% of peritoneum), tumor conglomerate, ascites (6000 mL) (August 2021)
2021-2022	Neoadjuvant chemotherapy (Carboplatin AUC5 + Paclitaxel 175 mg/m²) (October 2021 – February 2022)
2022	CT: lymph node reduction (March 2022)
	Interval cytoreduction: laparotomy, total hysterectomy, bilateral salpingo-oophorectomy, sigmoid colon resection, omentectomy (March 2022)
	CA-125: 13.75 U/mL (April 2022)
	Adjuvant chemotherapy + Bevacizumab (April-June 2022)
	Lymph node metastases (CT, July 2022)
	Chemotherapy + Bevacizumab (Gemcitabine) (August-October 2022)
	CA-125: 4.52 U/mL (October 2022)
	Continuation of chemotherapy + Bevacizumab (November 2022 - February 2023)
2023	Bevacizumab monotherapy (February 2023)
	BRCA1 mutation detected (Sequencing, September 2023)
	Anti-relapse chemotherapy (Carboplatin + Paclitaxel) (June-August 2023)
	Olaparib maintenance therapy (November 2023)
	CT: progressive lymphadenopathy (December 2023)
2024	CT: disease progression (March 2024)
	Targeted therapy (Bevacizumab + olaparib) (May-October 2024)
	CT: disease stabilization (September 2024)
	The patient continues maintenance therapy with olaparib and bevacizumab

Discussion: Long-term disease control in a patient with advanced ovarian cancer over three years highlights the effectiveness of a personalized approach based on detecting a germline *BRCA1* mutation. The comprehensive treatment strategy, including diagnostic laparoscopy, neoadjuvant and adjuvant chemotherapy, surgery, and maintenance therapy with a PARP inhibitor, contributed to tumor stabilization.

Identifying a germline *BRCA1* mutation allowed for a tailored therapeutic approach, optimizing treatment outcomes. This case underscores the significance of molecular genetic testing in selecting individualized treatment regimens, thereby enhancing the patient's prognosis. The patient's immediate relatives also underwent *BRCA1* mutation testing for preventive purposes. They were advised to undergo regular medical examinations for early cancer detection and risk reduction if the mutation was detected.

These findings emphasize the value of a personalized approach and highlight the need for further research into genetic factors as essential tools for developing preventive and therapeutic strategies in oncology.

Conclusions: Integrating *BRCA1/2* mutation analysis and PARP inhibitor therapy significantly improves clinical outcomes in ovarian cancer management. Advances in molecular biology and clinical oncology have increased survival rates in *BRCA*-associated ovarian cancer. Furthermore, the introduction of combination therapies, such as PARP inhibitors with antiangiogenic agents, has expanded treatment options.

However, challenges remain, including therapy resistance, limited efficacy in non-*BRCA*-mutated patients, and the need for further investigation into PARP inhibitor interactions with other therapeutic agents. Addressing these issues requires additional studies to optimize clinical practice and improve patient outcomes.

References:

1. Sung H., Ferlay J., Siegel R., Laversanne M., Soerjomataram I., Jemal A., Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries // CA Cancer J. Clin. – 2021. – Vol. 71. – P. 209-249. https://doi.org/10.3322/caac.21660

2. Jelovac D., Armstrong D.K. Recent progress in the diagnosis and treatment of ovarian cancer // CA Cancer J. Clin. – 2011. – Vol. 61 (3). – P. 183-203. https://doi.org/10.3322/caac.20113

3. Kaidarova D, Bolatbekova R, Kukubassov Y, Sadykova T, Aidarov A, Satanova A. Ovarian cancer in Kazakhstan for 15 years (2005–2020) // Int. J. Gynecol. Cancer. – 2021. – Vol. 31. – Art. no. A276. https://doi.org/10.1136/ijgc-2021-ESGO.475

4. Konstantinopoulos P.A., Ceccaldi R., Shapiro G.I., D'Andrea A.D. Homologous Recombination Deficiency: Exploiting the Fundamental Vulnerability of Ovarian Cancer // Nat. Rev. Clin. Oncol. – 2015. – Vol. 12(7). – P. 417-428. https://doi.org/10.1158/2159-8290.CD-15-0714

5. Moore K., Colombo N., Scambia G., Kim B.G., Oaknin A., Friedlander M., Lisyanskaya A, DiSilvestro P. Maintenance Olaparib in Patients with Newly Diagnosed Advanced Ovarian Cancer //

N. Engl. J. Med. – 2018. – Vol. 379(26). – P. 2495-2505. https://doi.org/10.1056/NEJMoa1810858

6. Gonzalez-Martin A., Pothuri B., Vergote I., DePont Christensen R., Graybill W., Mirza M.R., McCormick C., Lorusso D., Hoskins P., Freyer G., Baumann K., Jardon K., Redondo A., Moore R., Vulsteke C., O'Cearbhaill R., Lund B., Backes F., Barretina-Ginesta P., Haggerty A., Rubio-Pérez M., Shahin M., Mangili G., Bradley W., Bruchim I., Sun K., Malinowska I., Li Y., Gupta D., Monk B. Niraparib in patients with newly diagnosed advanced ovarian cancer // N Engl. J. Med. – 2019. – Vol. 381 (25). – P. 2391-2402. https://doi.org/10.1056/NEJMoa1910962

7. Coleman R.L., Oza A.M., Lorusso D., Aghajanian C., Oaknin, A., Dean A., Colombo N., Weberpals J., Clamp A., Scambia G., Leary A., Holloway R ., Amenedo Gancedo M., Fong P., Goh J., Malley D., Armstrong D., Garcia-Donas J., Swisher E., Floquet A ., Konecny G., McNeish I., Scott C ., Cameron T., Maloney L., Isaacson J ., Goble S., Grace C., Harding T., Raponi M ., Sun J ., Lin K ., Giordano H ., Ledermann J. Rucaparib maintenance treatment for recurrent ovarian carcinoma // Lancet. – 2017. – Vol. 390 (10106). – P. 1949-1961. https://doi.org/10.1016/S0140-6736(17)32440-6

8. Ray-Coquard I., Pautier P., Pignata S., Pérol D., González-Martín A., Berger R., Fujiwara K., Vergote I., Colombo N., Mäenpää J., Selle F., Sehouli J., Lorusso D., Alía E., Reinthaller A., Nagao S., Lefeuvre-Plesse C., Canzler U., Scambia G., Lortholary A., Marmé F., Combe P., Gregorio N., Rodrigues M., Buderath P., Dubot C., Burges A., You B., Pujade-Lauraine E., Harter P. Olaparib plus bevacizumab as first-line maintenance in ovarian cancer // N Engl J Med. – 2019. – Vol. 381 (25). – P. 2416-2428. https://doi.org/10.1056/NEJMoa1911361

9. Banerjee S., Kaye S.B. New strategies in the treatment of ovarian cancer: current clinical perspectives and future potential // Clin. Cancer Res. – 2013. – Vol. 19 (5). – P. 961-968. https://doi.org/10.1158/1078-0432.CCR-12-2243

10. Lheureux S., Gourley C., Vergote I., Oza A.M. Epithelial ovarian cancer // Lancet. – 2019. – Vol. 393 (10177). – P. 1240-1253. https://doi.org/10.1016/S0140-6736(18)32552-2

11. Matulonis U.A., Sood A.K., Fallowfield L., Howitt B.E., Sehouli J., Karlan B.Y. Ovarian cancer // Nat. Rev. Dis. Primers. – 2016. – Vol. 16061. – P. 53. https://doi.org/10.1038/nrdp.2016.61

12. Pujade-Lauraine E., Ledermann J.A. Maintenance strategy for newly diagnosed advanced ovarian cancer: A European perspective // Oncologist. – 2020. – Vol. 25 (11). – P. 899-907. https://doi.org 10.1016/j.annonc.2023.09.3110

13. Franzese E., Centonze S., Diana A., Carlino F., Guerrera L.P., Di Napoli M., De Vita F., Pignata S., Ciardiello F., Orditura M. PARP inhibitors in ovarian cancer // Cancer Treat. Rev. – 2019. – Vol. 73. – P. 1-9. https://doi.org/10.1016/j.ctrv.2018.12.002

АҢДАТПА

BRCA-БАЙЛАНЫСТЫ АНАЛЫҚ БЕЗ ҚАТЕРЛІ ІСІГІ: ЖЕКЕ ЕМДЕУ ТӘЖІРИБЕСІ. КЛИНИКАЛЫҚ ЖАҒДАЙ

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Өзектілігі: *Аналық без қатерлі ісігі-жыл сайын мыңдаған әйелдердің өмірін қиатын ең қауіпті гинекологиялық ісіктердің бірі. Кеш диагноз (III-IV сатыдағы жағдайлардың 70% - дан астамы) нақты белгілердің болмауына және скринингтің төмен тиімділігіне байланысты. Емдеуге жекелендірілген тәсіл, соның ішінде BRCA1/2 мутациясын талдау және PARP ингибиторларын қолдану маңызды жетістік болды. BRCA1/2 мутацияларын анықтау тәуекелді ерте болжауға және өлімді азайтуға ықпал ететін маңызды болжамдық мәнге ие. Тұқым қуалайтын бейімділігі бар науқастарға генетикалық кеңес беру ерте диагностика, мақсатты терапия және алдын алу шаралары арқылы алдын алуға мүмкіндік береді.*

Мақсаты *– терапияны жекелендіру мүмкіндігі және мутацияның сирек түрі бар BRCA-мен байланысты аналық без қатерлі ісігі бар науқасты емдеудің клиникалық жағдайын талдау және сипаттау.*

Әдістері: *Бұл зерттеуде сирек кездесетін BRCA1 мутациясымен байланысты аналық бездің қатерлі ісігі бар науқастың клиникалық жағдайы келтірілген. Мутацияларды анықтау реттілік арқылы жүргізілді және емдеудің тиімділігі КТ және СА-125 деңгейін өлшеу арқылы бағаланды.*

Нәтижелері: *Ісік процесі үш жылдан астам тұрақтандырылды. Кешенді емдеу (диагностикалық лапароскопия, химиотерапия, хирургия, мақсатты және қолдау терапиясы) ісік процесін тұрақтандырды. Генетикалық тестілеу болжамды жақсарту арқылы терапияны бейімдеуге мүмкіндік берді. Алдын алу үшін жақын туыстарына тестілеу жүргізілді.*

Қорытынды: *BRCA1/2 мутациясын және PARP ингибиторларын талдаумен жекелендірілген тәсіл клиникалық нәтижелерді жақсартады. Молекулалық онкологиядағы жетістіктер пациенттердің өмір сүруін арттырды. Алайда, кемшіліктер бар: терапияға төзімділік, BRCA мутациясы жоқ науқастарда тиімділігі шектеулі, PARP ингибиторларының басқа препараттармен өзара әрекеттесу механизмдерін одан әрі зерттеу қажеттілігі.*

Түйін сөздер: *аналық без қатерлі ісігі, BRCA1 жен BRCA2 мутациясы, химиотерапия, PARP ингибиторлары, клиникалық жағдай.*

АННОТАЦИЯ

BRCA-АССОЦИИРОВАННЫЙ РАК ЯИЧНИКОВ: ОПЫТ ПЕРСОНАЛИЗИРОВАННОГО ЛЕЧЕНИЯ. КЛИНИЧЕСКИЙ СЛУЧАЙ

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Актуальность: *Рак яичников – одна из самых смертоносных гинекологических опухолей, ежегодно уносящая жизни тысяч женщин. Поздняя диагностика (более 70% случаев на III-IV стадии) обусловлена отсутствием специфических симптомов*

и низкой эффективностью скрининга. Значительным достижением стал индивидуальный подход к лечению, включающий анализ мутаций BRCA1/2 и использование ингибиторов PARP.

Выявление мутаций BRCA1/2 имеет важное прогностическое значение, способствуя раннему прогнозированию риска и снижению смертности. Генетическое консультирование пациентов с наследственной предрасположенностью позволяет проводить профилактику с помощью ранней диагностики, таргетной терапии и профилактических вмешательств.

***Цель исследования** – проанализировать и описать клинический случай лечения пациентки с BRCA-ассоциированным раком яичников с редкой формой мутации с возможностью персонализации терапии.*

***Методы:** В данном исследовании представлен клинический случай пациентки с распространенным раком яичников, ассоциированным с редкой мутацией BRCA1. Выявление мутаций проводилось с помощью секвенирования, а эффективность лечения оценивалась с помощью компьютерной томографии и измерения уровня CA-125.*

***Результаты:** Опухолевый процесс был стабилизирован более чем на три года. Комплексное лечение (диагностическая лапароскопия, химиотерапия, хирургическое вмешательство, таргетная и поддерживающая терапия) стабилизировало опухолевый процесс. Генетическое тестирование позволило адаптировать терапию, улучшив прогноз. Ближайшие родственники прошли профилактическое обследование.*

***Заключение:** Индивидуальный подход с использованием анализа мутаций BRCA1/2 и ингибиторов PARP улучшает клинические результаты. Достижения в области молекулярной онкологии позволили увеличить выживаемость пациентов. Однако проблемы остаются: резистентность к терапии, ограниченная эффективность у пациентов без мутаций BRCA и необходимость дальнейших исследований механизмов взаимодействия ингибиторов PARP с другими лекарственными средствами.*

***Ключевые слова:** рак яичников, мутации BRCA1 и BRCA2, химиотерапия, ингибиторы PARP, клинический случай.*

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