MODERN MEDICINE AND PRACTICE
https://inovatus.es/index.php/ejmmp

EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 4 No. 12 (Dec - 2024) EJMMP ISSN: 2795-921X

MODERN ASPECTS OF THE ETIOLOGY AND PATHOGENESIS OF BREAST CANCER

Kakhhorova Feruza Makhmudovna
Bukhara State Medical Institute

Abstract: The problem of breast cancer is becoming increasingly relevant for oncologists and obstetricians-gynecologists. This article presents information on modern aspects of the risk of development and pathogenesis of breast cancer in women of reproductive age.

Keywords: woman, breast cancer, risk factors, oncology, diagnostics.

Relevance. Breast cancer (BC) is the most common disease among women in developed industrialized countries. The annual incidence of BC in the world is 1,383,000 cases. The share of hereditary BC ranges from 5 to 10%, which is 69,150–138,000 cases, 30% of which are associated with mutations in the BRCA1/2 genes. A family history of accumulation of cases of BC and tumors of the female reproductive system is noted by 25% of affected women. Thus, the number of patients with hereditary and familial forms of BC in total is 345,700 [1]. The etiopathological factor is structural and functional rearrangements of highly penetrant genes BRCA1, BRCA2, TP53, PTEN, MLH1, MSH2 and genes of medium and low probability of manifestation - CHEK2, STK11/LKB1, CDH1, PALB, etc., associated with the development of breast cancer against the background of hereditary oncological syndromes. Hereditary breast cancer is characterized by an autosomal dominant type of inheritance, early age of onset, transmission from both the maternal and paternal sides and pronounced genotypic and phenotypic heterogeneity. In a significant proportion of cases (about 30%), hereditary breast cancer is a component of the so-called breast cancer and/or ovarian cancer syndrome, in 70% of cases associated with mutations in the BRCA genes. The prevalence of carriers of BRCA gene mutations in the general population ranges from 1:800 to 1:1000 [5]. The criteria for establishing a genetic diagnosis of hereditary breast cancer are the presence of 2 or more first- or second-degree relatives in the family suffering from breast cancer and/or ovarian cancer, early age of disease manifestation, bilateral lesions, primary multiple tumors in the patient or his relatives, syndromic pathology.

To confirm the genetic diagnosis, various DNA diagnostic methods and their combinations are used: polymerase chain reaction (PCR) followed by electrophoresis during mutational screening of the entire gene in order to identify structural rearrangements; real-time PCR, which allows for a quantitative assessment of the gene copy number, multiplex PCR and hybridization with oligonucleotide biochips for testing known common mutations.

Automatic sequencing is used to determine the complete nucleotide sequence of the coding part of the BRCA1 and BRCA2 genes. To detect large genomic rearrangements, the MLPA (multiplex ligation-dependent probe amplification) method and others are used.

The most popular and significant today is DNA diagnostics of the BRCA1/2, CHEK2, TP53 genes in order to identify hereditary predisposition to breast cancer. The frequency of mutations of these genes in the general population is 3-5% for women under 40 years of age and 1.1% at the age of 50-70 years [6].

The penetrance of mutations is not complete and depends on both intragenic (mutation type, location, combination with single-nucleotide polymorphisms) and exogenous factors (population and environmental). Lifestyle and reproductive behavior determine the time frame for the implementation of hereditary predisposition.

According to modern concepts, the BRCA1 and BRCA2 genes act as classic tumor suppressors. The functioning of these genes is involved in the repair of double-stranded DNA breaks by homologous recombination, which is involved in the process of maintaining genome stability [7, 8]. Loss of their function entails errors in the repair of DNA damage, as a result of which the cell cycle control genes are activated, inhibiting further growth of cells with the resulting genetic abnormalities and inducing programmed cell death - apoptosis. The accumulation of repair errors, leading to disruptions in the regulation of the cell cycle, apoptosis and cell differentiation and, as a consequence, to genetic instability, is a key event in the process of carcinogenesis.

One study showed that the cumulative risk of developing contralateral breast cancer 25 years after the initial diagnosis of breast cancer in carriers of mutations in the BRCA1 and BRCA2 genes is 47.4%, while in patients with BRCA1 mutations the risk is 1.6 times higher. In the case of manifestation of primary breast cancer in carriers of mutations in the BRCA1 gene at the age of up to 40 years, the risk of developing contralateral breast cancer in the next 25 years is 62.9%, while in those who develop the disease after 50 years, the risk does not exceed 19.6%, which must be taken into account in medical genetic counseling. Recently, much attention has been paid to the search, characterization and determination of the clinical significance of polymorphic DNA variants (single nucleotide polymorphism - DNA sequence variants of one nucleotide (A, T, G or C) in the genome of an individual) in the coding and non-coding regions of genes involved in hereditary and sporadic carcinogenesis. It is assumed that these variants are risk modifiers in patients with a hereditary predisposition, and BRCA gene polymorphisms are important structural and functional components in the development of malignant tumors of the female reproductive system of one or another localization. According to the results of international studies, the homozygous HH allele variant (372H / H) is associated with an increased risk of developing breast cancer by 1.3-1.5 times compared to the average population and, in addition, increases the risk of developing ovarian cancer [49-51]. It has been shown that carriers of the homozygous variant are more often men, and the risk of developing breast cancer is associated with a younger age of disease manifestation [52]. Another well-studied polymorphic variant, the presence of which is associated with an increased risk of developing breast cancer and ovarian cancer, is an amino acid substitution in the 5'-untranslated region (Ex2 + 14G / A, rs1799943) of the 2nd exon of the BRCA2 gene - 203 G / A. Pathomorphological features of breast cancer associated with the germinal haplotype B (BRCA1) are infiltrating ductal carcinoma (66.7%), unicentric growth pattern (81.7%), grade II malignancy (71.7%), positive receptor status (43.3%), low proliferative index, lack of HER-2 / neu gene expression (58.3%) and regional metastasis (53.3%). Rare histological variants of breast cancer are significantly more often detected in the presence of haplotype B (18.3%) compared to BRCA mutations (5.3%) ($p = 0.023$). Breast cancer associated with the presence of the missense variant Q356R in the BRCA1 gene is characterized by a predominantly negative receptor status in 69.2% of cases, in contrast to breast cancer associated with the polymorphic variant N372H in the BRCA2 gene. Tumors with no expression of the HER-2 / neu gene and a high proliferative activity index account for 46.1 and 30.8% of cases, respectively. In the group of patients with breast cancer associated with the presence of the missense variant N372H in the BRCA2 gene, 25% had infiltrative lobular cancer with a unicentric growth pattern, grades II and III malignancy (45 and 40%, respectively), with the presence of cancer emboli in the

lymphatic spaces (65%) and a high frequency of regional metastasis (65%), compared with TP53-associated breast cancer.

With the development of genetic testing over the past 15 years, which allows identifying patients with a predisposition to developing breast cancer and/or ovarian cancer, the need for preventive measures in cancer risk groups has come to the fore. Options for primary cancer prevention for women from the high genetic risk group include drug prophylaxis using tamoxifen or its analogues, preventive surgeries - prophylactic mastectomy or prophylactic oophorectomy.

Literature

1. Олимова А. З., Шодиев У. М. Репродуктив Ёшдаги эркакларда бепуштлик сабаблари: Бухоро тумани эпидемиологияси //Scientific progress. – 2021. – Т. 2. – №. 7. – С. 499-502.
2. Zokirovna O. A., Abdurasulovich S. B. Ovarian Diseases in Age of Reproductive Women: Dermoid Cyst //IJTIMOIY FANLARDA INNOVASIYA ONLAYN ILMIY JURNALI. – 2021. – Т. 1. – №. 6. – С. 154-161.
3. Olimova A. Z. ECHINOCOCCOSIS OF LIVER OF THREE MONTHLY WHITE RAT //Scientific progress. – 2022. – Т. 3. – №. 3. – С. 462-466.
4. Олимова А. З. Морфологические и морфометрические особенности печени белых беспородных трех месячных крыс после тяжёлой черепно-мозговой травмы вызванной экспериментальным путём //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – Т. 1. – №. 6. – С. 557-563.
5. Oglu M. Z. M., Zokirovna O. A. МОРФОЛОГИЧЕСКИЕ И МОРФОМЕТРИЧЕСКИЕ ПАРАМЕТРЫ ПЕЧЕНИ БЕЛЫХ БЕСПОРОДНЫХ КРЫС, ПЕРЕНЕСШИХ ЭКСПЕРИМЕНТАЛЬНУЮ ЧЕРЕПНО-МОЗГОВУЮ ТРАВМУ ПОСЛЕ МЕДИКАМЕНТОЗНОЙ КОРРЕКЦИИ //JOURNAL OF BIOMEDICINE AND PRACTICE. – 2023. – Т. 8. – №. 1.
6. Олимова А. З., Турдиев М. Р. БУХОРО ШАҲРИДА МЕЪДА ВА ЎН ИККИ БАРМОҚЛИ ИЧАК ЯРАСИ УЧРАШ ЭПИДЕМИОЛОГИЯСИ //Oriental renaissance: Innovative, educational, natural and social sciences. – 2022. – Т. 2. – №. 4. – С. 642-647.
7. Zokirovna O. A. Modern Concepts of Idiopathic Pulmonary Fibrosis //American Journal of Pediatric Medicine and Health Sciences. – 2023. – Т. 1. – №. 3. – С. 97-101.
8. Zokirovna O. A. Pathology of Precancerous Conditions of the Ovaries //American Journal of Pediatric Medicine and Health Sciences. – 2023. – Т. 1. – №. 3. – С. 93-96.
9. Зокировна, Олимова Азиза и Тешаев Шухрат Джумаевич. «Морфологические аспекты печени белых беспородных крыс после тяжелой черепно-мозговой травмы, вызванной экспериментально в виде дорожно-транспортного происшествия». *Scholastic: Journal of Natural and Medical Education* 2.2 (2023): 59-62.
10. Zokirovna O. A. Comparative characteristics of the morphological parameters of the liver at different periods of traumatic brain injury //Euro-Asia Conferences. – 2021. – С. 139-142.
11. Zokirovna O. A. Macroand microscopic structure of the liver of threemonthly white rats //Academic research in educational sciences. – 2021. – Т. 2. – №. 9. – С. 309-312.
12. Олимова А. З. Частота Встречаемости Миомы Матки У Женщин В Репродуктивном Возрасте //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2021. – Т. 1. – №. 6. – С. 551-556.

13. Zokirovna O. A., Abdurasulovich S. B. Ovarian Diseases in Age of Reproductive Women: Dermoid Cyst //IJTIMOIY FANLARDA INNOVASIYA ONLAYN ILMIY JURNALI. – 2021. – T. 1. – №. 6. – C. 154-161.
14. Zokirovna O. A. Cytological screening of cervical diseases: pap test research in the bukhara regional diagnostic center for the period 2015-2019. – 2022.
15. Zokirovna O. A., PREVALENCE R. M. M. EPIDEMIOLOGY OF CANCER OF THE ORAL CAVITY AND THROAT IN THE BUKHARA REGION //Web of Scientist: International Scientific Research Journal. – 2022. – T. 3. – №. 11. – C. 545-550.
16. Olimova A. Z. The frequency of occurrence of my uterus In women of reproductive age //JOURNAL OF ADVANCED RESEARCH AND STABILITY (JARS). – 2021. – T. 1. – №. 06. – C. 551-556.
17. Olimova Aziza Zokirovna. (2023). MODERN PRINCIPLES OF THE EFFECT OF HEMODIALYSIS THERAPY ON HEART RATE. *International Journal of Integrative and Modern Medicine*, *1*(1), 80–85. Retrieved from http://medicaljournals.eu/index.php/IJIMM/article/view/28
18. Olimova Aziza Zokirovna. (2023). PATHOMORPHOLOGICAL CHARACTERISTICS OF THE EPIDIDYMIS UNDER IRRADIATION. *International Journal of Integrative and Modern Medicine*, *1*(1), 96–100. Retrieved from http://medicaljournals.eu/index.php/IJIMM/article/view/31
19. Olimova Aziza Zokirovna. (2023). THE INCIDENCE OF CANCER OF THE ORAL CAVITY AND PHARYNX IN THE BUKHARA REGION. *International Journal of Integrative and Modern Medicine*, *1*(1), 86–89. Retrieved from http://medicaljournals.eu/index.php/IJIMM/article/view/29
20. Olimova Aziza Zokirovna. (2023). INFLUENCE OF ALCOHOL INTOXICATION ON THE HEART TISSUE OF RATS IN THE EXPERIMENT. *International Journal of Integrative and Modern Medicine*, *1*(1), 90–95. Retrieved from http://medicaljournals.eu/index.php/IJIMM/article/view/30
21. Olimova Aziza Zokirovna. (2023). Modern Aspects of the Etiology of Gastric Ulcer and Its Complications. *American Journal of Pediatric Medicine and Health Sciences (2993-2149)*, *1*(3), 163–166. Retrieved from http://grnjournal.us/index.php/AJPMHS/article/view/208
22. Zokirovna O. A., Jumaevich T. S. Morphological Aspects of the Liver of White Outbred Rats After Severe Traumatic Brain Injury Caused Experimentally in the Form of a Road Accident //Scholastic: Journal of Natural and Medical Education. – 2023. – T. 2. – №. 2. – C. 59-62.
23. Aziza Zokirovna Olimova GASTRIC ULCER AND ITS COMPLICATIONS // Scientific progress. 2022. №3. URL: https://cyberleninka.ru/article/n/gastric-ulcer-and-its-complications (дата обращения: 28.09.2023).
24. Olimova Aziza Zokirovna. (2022). TECHNIQUE FOR CUTTING BIOPSY AND SURGICAL MATERIAL IN THE PRACTICE OF PATHOLOGICAL ANATOMY AND FORENSIC MEDICINE. *Web of Scientist: International Scientific Research Journal*, *3*(7), 116–120. https://doi.org/10.17605/OSF.IO/PSQ59
25. Zhumayevich N. F., Zokirovna O. A. PATHOMORPHOLOGY OF GASTRIC CANCER //BARQARORLIK VA YETAKCHI TADQIQOTLAR ONLAYN ILMIY JURNALI. – 2022. – C. 330-333.
26. Zokirovna O. A. Epidemiological and Etiological Data of Morphogenesis and Pathomorphology of Congenital Heart Diseases in Children //American Journal of Pediatric Medicine and Health Sciences. – 2023. – T. 1. – №. 4. – C. 88-91.