Gynecology and Reproductive Endocrinology

Circulating tumor cells (CTCS) as a marker of the radicality of surgical treatment of breast cancer

Ya A Shliakhtunou

Vitebsk State Medical University, The Republic of Belarus

Abstract

Objective: To determine the clinical significance of circulating tumor cells expressing the targeted genes BIRC5 and HER2-neu - markers of minimal residual disease, as markers of the "purity" of the surgical stage of breast cancer treatment, Methods. The study involved 230 patients with verified primary non-metastatic breast cancer (BC) stage I-IIIC at the age of 58.2 ± 9.9 years. All women underwent surgery in the amount of radical mastectomy in Madden (group 1) – 113 (49.1%), oncoplastic radical resection of the breast (group 2) – 49 (21.3%), and 68 (29.6%) women underwent bilateral subcutaneous mastectomy with regional lymph node dissection on the affected side with simultaneous implant reconstruction (group 3). In all patients on the day of surgery, as well as on day 2 after surgery, peripheral blood was examined for the presence of circulating tumor cells (CTCs). To identify the CTCs, the expression of the BIRC5 and HER2-neu genes was studied using real-time PCR. Results: Positive BIRC5 mRNA and HER2-neu mRNA CTCs before surgery in the total sample were found in 158 of 230 women (68.7%). Before the operation, in the group of patients subject to radical mastectomy in Madden, the target CSCs were found in 81 women (71.%), in the group of oncoplastic resection subject in 34 (69.4), in the group of subject subcutaneous mastectomy with reconstruction in 43 (63.2). After surgery, targeted CTCs were identified in venous blood samples of 99 patients (43.0%). After radical mastectomy according to Madden (group 1) CTCs were identified in 46 patients (40.7%), in group 2 after oncoplastic resection of CTCs were identified in 22 women (44.9%), in group 3 after subcutaneous mastectomy with reconstruction of CTCs were identified 31 patients (45.6%). There were no significant differences in the frequency of identification of CTCs expressing the BIRC5 and HER2-neu genes after surgery, depending on its size ($p > 0.05$). Accordingly, the risk of disease return in patients of these three groups, regardless of the extent of surgical treatment, is comparable. However, the dynamics of decrease in targeted CTCs depending on the volume of the operation is significantly different. In group 1, the proportion of reduction in patients who were positive for CTCs was 31.0%, in group 2 – 24.5%, in group 3 – 17.6% ($p = 0.019$, ANOVA). In the general sample, the frequency of preservation of targeted CTCs after surgery was significantly higher in the early stages (I-IIA) without regional lymph nodes, 66.2%, than in the more advanced stages (IIB – IIIC), 45.0%. A significant change in the frequency of identification of the CTCs in the downward direction after the operation was established with luminal A and luminal B HER2 non-expressing cancers. However, in a comparative analysis of the frequency of preservation of CTCs in peripheral blood, depending on the tumor subtype, no significant differences were obtained. Conclusion: The definition of CTCs expressing the BIRC5 and HER2-neu genes in enriched peripheral blood samples after radical surgery for breast cancer is a reliable marker of the "purity" (radically) of the surgery. In the present study, the most "cleaning" operation was radical Madden mastectomy, which allows removal of CTCs from peripheral blood in 31.0% of patients, compared with oncoplastic resection (24.5%) and subcutaneous mastectomy with implant reconstruction (17.6%). However, the mean frequency of maintaining CTCs in peripheral blood at the level of 43.7±1.9% (M±SD) after the operation in all groups, which is not significantly different, does not significantly differ from the volume of the surgical operation. the amount of surgery does not affect the frequency of return of the disease. Early dissemination of tumor cells contributes to their preservation in the peripheral blood in the form of the CTCs in spite of the surgical intervention.

Biography

He is the author of more than 100 scientific papers, including one monograph, 6 patents for invention, 3 instructions for use. He is the developer of four unique test systems for the diagnosis of minimal residual disease in solid tumors. He was a project manager and executive in charge of the international project LLB-2-242 «Improving the quality of medical care through the use of information technologies for the diagnosis of skin cancer and lung cancer (Lithuania-Latvia-Belarus 2012–2015)». The direct scientific leadership, such scientific programs of the Belarusian Republican Foundation for Basic Research as «Breast Cancer and Epstein-Barr Viral Infection» (2013–2015), «Molecular Genetic Diagnosis of Minimal Residual Disease in Breast Cancer» (2015–2017) , the scientific theme of the State program of scientific research «Assess the expression of tumor progression genes in order to identify the minimum residual disease in breast cancer» (2016–2017).

At present, Yauheni A Shliakhtunou is the scientific director of the research topic «To study the prognostic and predictive significance of miRNA expression in circulating tumor cells in patients suffering from breast cancer with overexpression of the epidermal growth factor receptor Her2-neu» (2019–2020).

Publications

1. Clinical Importance of Expression of BIRC5 and HER2-Neu Genes in Circulating Tumor Cells as Markers of Minimum Residual Disease in Surgical Treatment of Breast Cancer, August 2018, Novosti Khirurgii 26(4):457-464, DOI: 10.18484/2305-0047.2018.4.457
2. Adjuvant cytostatic therapy of minimum residual disease in breast cancer, August 2018, Vestnik of Vitebsk State Medical University 17(4):64-71, DOI: 10.22263/2312-4156.2018.4.64
3. Pantel K, Alix-Panabières C, Riethdorf. Cancer micrometastases. Nature Reviews Clinical Oncology. 2009;6(6):339-51. doi:10.1038/nrclinonc.2009.44
4. Onstenk W, Gratama JW, Foekens JA, Sleijfer S. Towards a personalized breast cancer treatment approach guided by circulating tumor cell (CTC) characteristics. Cancer Treat. Rev. 2013;39(7):691-700. doi:10.1016/j.ctrv.2013.04.001
5. Tonak J, Gall FP, Hohenberge W, Hermanek P, Mühe E, Angermann B. Prinzi pien der chirurgie maligner tumoren. In: Gall FP, Hermanek P, Tonak J, editors. Chirurgische Onkologie. Springer Link; 1986. p. 131-53

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