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Original article

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Using cytological rapid method in biopsy diagnostics of sentinel lymph nodes in breast cancer patients

Vladislav Yu. Barsukov [1] ✉, Lyudmila F. Zhandarova [1], Sergey V. Kapralov [1], Olga M. Konopatskova [1], Olga A. Kalmykova [2], Natalia G. Volodina [2], Liliya A. Mescheryakova [2], Yulia I. Orlova [2], Liliya S. Tomashevskaya [3,4]
✉522942@mail.ru

[1]Saratov State Medical University, Saratov, Russia
[2]Russian Railways Clinical Hospital of Saratov, Saratov, Russia
[3]Regional Oncology Clinical Dispensary, Penza, Russia
[4]Penza Institute for Further Training of Physicians (Penza Branch of the Russian Medical Academy of Continuing Professional Education), Penza, Russia

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Abstract:
Objective: to assess the informativity of using the cytological rapid method for examining sentinel lymph nodes in patients breast cancer.
Materials and Methods. Our included 46 patients 30-85 years of age with verified breast cancer. On the day before the surgery, approximately 150-200 MBq of the 99mTc-NanoTop radiopharmaceutical were injected peritumorally into the parenchyma of the affected mammary gland. After 1.5-2 hours, lymphoscintigraphy was performed, followed by SPECT/CT. The latter helped visualizing sentinel lymph nodes. The next day after the administration of the radiopharmaceutical, during surgery, sentinel lymph nodes were identified using a gamma detector. Further on, the surgeon removed the lymph node(s) and sent it/them for the examination by the cytological rapid method. To assess the informativity of this method, we compared its results the gold standard of morphological diagnostics: histological examination of postoperative material.
Results. The cytological rapid method revealed the presence of metastases in sentinel lymph nodes in 12 patients, which substantially influenced their further treatment tactics. We therefore conformed that this method is not inferior to the histological examination of the tumor. The sensitivity and specificity of the cytological rapid method are 100%. When comparing the results of cytological rapid method and planned histological examination, we revealed no discrepancies in diagnoses based on the state of the lymph nodes.
Conclusion. Cytological rapid method is an informative method for sentinel lymph node detection in breast cancer patients.

Keywords: breast cancer, sentinel lymph nodes, cytological examination

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Introduction

Breast cancer (BC) remains among the most common malignant neoplasms worldwide. In recent years, its diagnostics and treatment methods improved significantly. The number of patients with early-stage BC progressively increased. E.g., while the prevalence of BC in the Russian Federation increased from 380.5 to 526.4 (per 100 thousand population) from 2012 to 2022, and the accumulation index augmented from 9.7 to 11.2, patient detection with stages I and II BC increased from 64.5% to 73.7%, respectively [1].

Early detection of cancer naturally involves the performance of organ-preserving surgeries, since radical dissection of lymph nodes (LN) can lead to an undesirable postoperative effect in the form of lymphostasis. The search for diagnostic criteria regarding metastatic lesions of LN still remains relevant. Such diagnostic methods as sonography (SG), computed tomography and magnetic resonance imaging cannot give a clear answer about the presence or absence of metastases in the LN. A fairly noteworthy technique for detecting metastases in the LN is the cytological method (CM). The information content of fine-needle aspiration biopsy of the LN in the axillary region, carried out under SG control, ranges from 72.6% to 100% [2-4]. According to various authors [5, 6], the information content of examining LN via cytological rapid method (CRM) is 77.6-88.7%.

Preoperative scintigraphy of sentinel lymph nodes (SLN) is a less traumatic and fairly informative diagnostic method that allows objectively and reliably visualizing the LN and confirming the presence of metastases in them [5, 6]. The frequency of SLN detection reaches 85-91%. This method helps detecting hidden regional metastases, predict the

routes of metastasis of the primary lesion, but most importantly, it allows determining the degree of radicality of LN dissection and elucidating the stage of the disease, which is a major criterion for prognosis and planning of further treatment [4, 5, 7, 8].

Therefore, when searching for ways to optimize the degree of LN dissection, it is necessary to examine the removed LN in a short time to decide on the advisability of expanding the scope of the surgery. In this regard, simple to perform, safe, low-traumatic and reliable research methods should be used already at the stage of primary diagnostics. First of all, these include CM. While the standard technique for studying the SLN visualizes the LN, the implementation of the CRM for examining the removed LN allows studying its morphological substrate and advising the operating surgeon in a short time on further tactics of intervention.

Objective – to assess the information content of using the CRM for examining the SLN in BC patients.

Materials and Methods

The informativity of the CRM study of SLN was analyzed on 46 female patients aged 30 to 85 years with verified BC. All patients were treated in the Division of Mammalogy at the private healthcare institution, Russian Railways Children's Clinical Hospital, Saratov, Russia, from July through October 2023. The tumor was most often localized in the upper outer quadrants of the mammary gland (MG). In 16 patients (34.8%), the stage of the disease according to the international TNM (tumor, node and metastasis) classification of malignant neoplasms corresponded to T1N0M0, while 30 patients (65.2%) had T2N0M0 stage of the disease. Inclusion criteria were as follows: verified diagnosis of BC, tumor size no more than 5 cm (T1-T2), and absence of axillary LN, both palpable and based on SG data (N0). All patients underwent standard examination including mammography in two projections, SG of regional LN, abdominal and pelvic SG, computed tomography of the chest, and core needle biopsy of the MG tumor with immunohistochemical examination.

Diagnostic stages were as follows. On the eve of the operation, approximately 150-200 MBq of the 99mTc-NanoTop radiopharmaceutical was injected peritumorally into the parenchyma of the affected breast. Then, after 1.5-2 hours, lymphoscintigraphy was performed followed by the use of SPECT/CT imaging, which visualized the SLN and assesses their number, anatomy and topography. The data were recorded in the protocol. The next day after the introduction of the radiopharmaceutical, during the surgery, the SLN were localized using a gamma detector, which generated an audio signal with a simultaneous display of the pulse magnitude digital value on the screen. This helped correctly identify and localize these SLN. The surgeon removed the LN(s) and sent it/them for examination by the CRM. The LN were incised in one plane and scrapings were taken from the incision surface in the laboratory located directly in the operating room. In the case of macroscopically suspected metastases on the incision surface, scrapings were taken specifically from these areas with subsequent staining with Leukodif-200 and their CRM examination (10 min). Rapid examination by the histological method (HM) was not performed.

Statistical data processing was carried out using the Statistica v. 10 software. The digital data in this article is presented as counts and relative values (frequency of occurrence). The nonparametric Pearson's chi-squared test was used for data processing. The sensitivity and specificity of CRM (CRMsens. and CRMspec., respectively) were calculated using the following formulas:

$$CRM_{sens.} = \frac{\text{Number of patients diagnosed using CRM} \times 100\%}{\text{Number of patients diagnosed using HM}};$$

$$CRM_{spec.} = \frac{\text{Number of healthy people diagnosed with CRM} \times 100\%}{\text{Number of healthy people diagnosed with HM}}.$$

Results

Of the entire group of observations of SLN mapping (46 women), 1 SLN was detected in 9 (19.6%) patients, 2 SLN in 19 patients (41.3%), 3 SLN in 8 patients (17.4%), 4 SLN in 6 patients (13%), and 5 SLN in 4 women (8.7%).

With CRM used for SLN study, metastases were not detected in 34 patients, which constituted 73.9% (*Figure 1*). This made it possible to perform organ-preserving surgeries without axillary LN dissection, thereby reducing the possible risk of developing postmastectomy syndrome and a consequent significant improvement in the patient's quality of life.

Metastases in SLN were detected in 12 (26.1%) women (*Figure 2*). All these patients underwent extended LN dissection, during which grade III metastases in LN were additionally revealed in 3 patients.

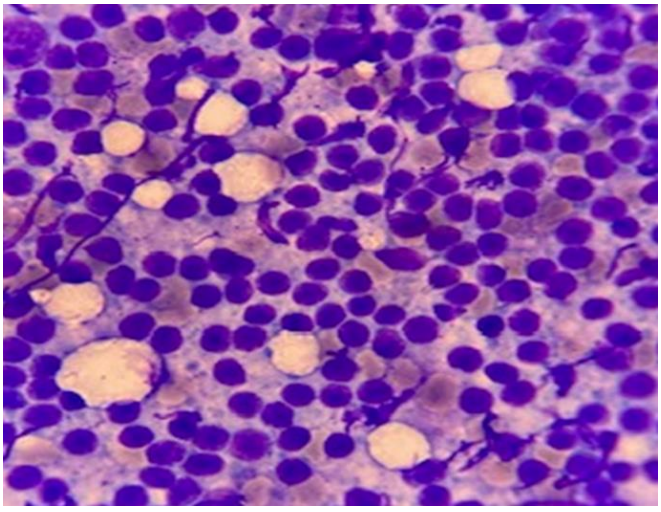

Figure 1. Hyperplasia of lymphoid tissue in the lymph node. Staining by the Leukodif-200, ×1000

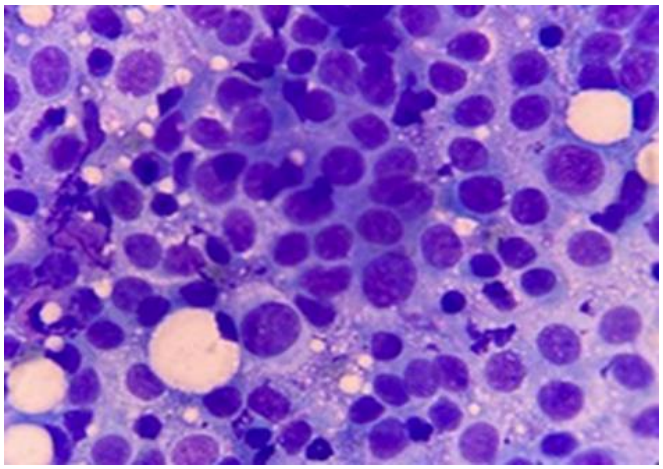

Figure 2. Metastasis of breast cancer to the lymph node in the form of small clusters. Staining by the Leukodif-200, ×1000

All removed tissues were sent for a planned study via the HM to eliminate the presence of micrometastases. When comparing the results of CRM studies with HM studies, we established no discrepancies in diagnoses regarding the state of the LN.

To verify the or informativity of the CRM, a comparison was made with the gold standard of morphological diagnostics, which is a study of postoperative material by the HM. Considering the small sample of patients, the specific criteria for including patients in the study, and the fact that binary categorical data were used in the assessment (the presence/absence of metastases in the LN), we revealed that the CRM is not inferior to the HM ($\chi 2=0$; $p=1$), and its sensitivity and specificity are 100%.

Discussion

Early diagnosis and effective treatment of all types of cancer are critical for a favorable prognosis of the disease. Patients with small tumor sizes at diagnosis exhibit a significantly higher survival rate and a significantly lower probability of a fatal outcome due to cancer. That is why many new technologies are currently under development for the early detection of primary tumors. Such technologies for the early detection of distant metastases and relapses of the disease are essential for the effective treatment of BC [9]. Early detection of metastases in the LN draining the tumor, i.e. in the SLN, should improve the assessment of the BC stage and facilitate the choice of the most suitable treatment [10].

Since one of the leading current directions in BC surgery is the preservation of regional LN, the importance of SLN biopsy is beyond doubt. Urgent examination by HM is a conventional strategy of morphological verification, but this method requires a long time, which is especially important to consider during a surgery [8]. Our experience in using CRM of examination during surgery for marking SLN demonstrated its high information content (absence of both false positive and false negative conclusions), which is supported by the data of other authors, e.g., by M.V. Starkova et al. The latter study examined 101 patients with invasive (T1-T2) BC and discovered that using CRM for examination allows assessing the SLN status with an accuracy of up to 94% [11]. Using CRM over a short period of time (10 min), it is possible to obtain data on the nature of SLN changes without destroying the material for a routine examination by the HM, since a scraping is taken from the cut surface. It is also important that this verification method does not result in loss of LM tissue, which affects the further preparation of tissue samples for the examination by the HM. Another advantage is that the time is also saved, which is important for patients.

Conclusion

CRM examination of surgically removed SLN in BC patients is a simple and quickly performed method that is not inferior to HM. Its sensitivity and specificity according to the results of our study are 100%.

Author contributions: All authors made equal contributions to the preparation of the manuscript.

Compliance with ethical standards. The authors confirm that the rights of study participants were respected, including obtaining informed consent whenever necessary.

Conflict of interest. None declared by the authors.

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Authors:
Vladislav Yu. Barsukov – DSc, Professor, Department of Surgery and Oncology, Saratov State Medical University, Saratov, Russia, https://orcid.org/0000-0002-6135-9223;
Lyudmila F. Zhandarova – PhD, Associate Professor, Department of Surgery and Oncology, Saratov State Medical University, Saratov, Russia, https://orcid.org/0000-0002-6286-4504;
Sergey V. Kapralov – DSc, Associate Professor, Chair of the Department of Faculty Surgery and Oncology, Saratov State Medical University, Saratov, Russia, https://orcid.org/0000-0001-5859-7928;
Olga M. Konopatskova – DSc, Professor, Department of Faculty Surgery and Oncology, Saratov State Medical University, Saratov, Russia, https://orcid.org/0000-0003-2123-4730;
Olga A. Kalmykova – Head of the Laboratory of Cytology, Russian Railways Clinical Hospital of Saratov, Saratov, Russia, https://orcid.org/0009-0009-3329-0351;
Natalia G. Volodina – Physician, Laboratory of Cytology, Russian Railways Clinical Hospital of Saratov, Saratov, Russia, https://orcid.org/0009-0004-0229-5428;
Liliya A. Mescheryakova – Physician, Laboratory of Cytology, Russian Railways Clinical Hospital of Saratov, Saratov, Russia, https://orcid.org/0009-0008-9513-5288;
Yulia I. Orlova – PhD, Chief Physician, Russian Railways Clinical Hospital of Saratov, Saratov, Russia, https://orcid.org/0009-0007-8210-5779;
Liliya S. Tomashevskaya – Radiologist, Department of Radiotherapy, Regional Oncology Clinical Dispensary, Penza, Russia; Instructor, Department of Oncology and Urology, Penza Institute for Further Training of Physicians (Penza Branch of the Russian Medical Academy of Continuing Professional Education), Penza, Russia, https://orcid.org/0000-0002-4814-7269.