ejpmr, 2020,7(5), 639-642

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

THE ASPECTS OF DIAGNOSIS, TREATMENT AND PROGNOSIS FOR METASTATIC BREAST CANCER

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Article Received on 19/03/2020 **Article Revised on 09/04/2020** **Article Accepted on 29/04/2020**

SUMMARY

The main prevention of relapse, the identification of distant metastases and pathological changes in regional lymph nodes is fundamental in the prognosis and choice of treatment methods for breast cancer. In this case, combinations of various methods of radical therapy (surgical, radiation, chemotherapeutic and radiation) can be successfully used. Dissection of the sentinel lymph node is not currently the standard in the treatment of breast cancer patients, but further study of this technique is promising in order to exclude the execution of axillary lymphadenectomy in the absence of its metastatic lesion.

KEYWORDS: Breast Cancer, Lymph Nodes, Distant Metastases, Lymphadenectomy, Adjuvant Chemotherapy, Morphological Verification.

Diagnosis of breast metastases presents certain difficulties. Many research methods have been proposed, ranging from general clinical examination and palpation to nuclear magnetic resonance and computed tomography.[10] Radiothermometry is actively used in the algorithm for the comprehensive study of mammary glands. Russian scientists (Nechushkin MI and others, 2003) have proposed modern research methods, such as video thoracoscopic parasternal lymphadenectomy in the diagnosis of the prevalence of breast cancer.[15] Recently, molecular and histochemical methods of research using tumor and tissue markers have been proposed, which make it possible to clarify the prevalence of the tumor process, conduct an adequate assessment of the treatment, and trace long-term results.[1,11] Nevertheless, X-ray methods for the study of breast cancer and other tumor lesions of the breast remain fundamental and significant types of diagnosis.

An important link in the process of metastasis is the state of regional lymphatic collectors. The identification of pathological changes in regional lymph nodes is fundamental in the prognosis and selection of treatment methods for breast cancer.

Talakhadze N.T. et al. provided an overview of the methods of radiation examination of parasternal lymph nodes. The method of scintimammography with 99tTc - technetril is considered in detail. In the observations of the authors, the sensitivity of the method was 96.5% and the specificity was 95.4%.[12]

Over the past 5 years, various methods have been developed for identifying sentinel lymph nodes, which are the first in the path of lymph outflow from a primary tumor in the mammary gland. Thus, injections of a dye or radioisotopes into the periareolar zone of a tumor directly into the tumor itself before its removal, or in the tumor bed after its removal, are proposed. Using these injections, it became possible to determine axillary and / or parasternal "sentinel" lymph nodes in 95% of patients with primary breast cancer.[5] Sometimes it is one node, sometimes two or more sentinel lymph nodes. If these nodes are removed and do not contain tumor elements, then with a probability of 95-97% it can be argued that the axillary lymph nodes do not contain tumor metastases and thereby refuse axillary lymphadenectomy.[7] Speaking about the role of the sentinel lymph node, it was noted that some tumors have "sentinel" nodes, both in the axillary zone and in the chest cavity. The possible role of removing the sternal nodes in the event that they are the only way out of the lymph from the tumor is currently under discussion. However, most experts believe that these nodes should not be removed or biopsy.

It goes without saying that surgeons must have some experience in applying this technique under the guidance of specialists who have mastered this method before they can use it in everyday practice. It is recommended that at least 30-40 biopsy procedures of the "sentinel" node be performed followed by complete axillary dissection before it can be concluded that the surgeon has even minimal competence in this matter.[8] This minimum

number of observations should have 5% or less false-negative results and an acceptable level of identified "guard" nodes.

Another ALMANAC study (axillary lymphatic marking versus axillary dissection) evaluated the ability of mammologist surgeons to master new biopsy techniques for a sentinel lymph node. According to a study by ManselC.D. biopsy of a sentinel lymph node followed by axillary dissection in case of detection of its metastatic lesion or removal of axillary lymph nodes was performed in patients with operable breast cancer without clinical signs of metastases to axillary lymph nodes.[5] All surgeons participating in the study underwent an audit stage, when during the treatment of the first 40 patients they were all identified and sentenced by a sentinel node biopsy followed by axillary dissection, regardless of the biopsy results. Sentinel nodes were identified using an injection of a radiopharmaceutical around the tumor, as well as intraoperative administration of a blue dye and a manual gamma sensor. According to the study protocol, each surgeon should achieve 90% localization and 5% false-negative results in the audit phase. 400 patients in the audit phase 10 surgeons performed a biopsy of the sentinel lymph node, the detection rate of the sentinel lymph node was 96.6%, the false-negative rate (when there were no metastases in the lymph node, and muscle lymph nodes, they were detected) amounted to 5%.[10,13] Thus, 10 surgeons met the requirements and were able to participate in the randomization phase.Despite the various results shown by the surgeons during the first phase, most surgeons needed 40 procedures to meet the audit criteria.

Further, Mansel R. E., (2004) reported potential risk factors for errors in the localization of the axillary "sentinel" lymph node. A high body mass index (above 30), a tumor in the inner quadrants of the breast, invasive lobular cancer are regarded as statistically significant risk factors for errors in determining the location of the sentinel lymph node. Tumor size and lymph node status are not factors that influence localization.

Another interesting report (Louis-Sylvestre S., 2001) was an update of a prospective randomized study comparing lumpectomy with radiation therapy to the axillary region and lumpectomy with axillary lymphodissection.[7] For the period 1982-87. 657 patients after surgery for breast cancer

T <3 cm, N0 or Nia, were randomized into two groups, one of which received irradiation to the axillary zone, and the other received lymphodissection. All patients received postoperative breast irradiation. The average age of these women was 51.2 years. Metastatic lesion of one lymph node was noted in 57% of patients, from 2 to 3 lymph nodes in 34% and 3 or more lymph nodes in 9% of patients who underwent axillary lymph node dissection. Updating the study data showed that patients with axillary dissection reliably less frequently observed relapse in the axillary zone, however, there were no differences in the incidence of distant metastases, relapse-free and overall survival, even with an extension of the observation period. It has been suggested that with a positive sentinel lymph node, the use of both axillary dissection and irradiation of the axillary zone can equally be recommended.

A large number of researchers are looking for factors that can predict with a high degree of probability the absence of metastatic damage to axillary lymph nodes. Sharp S. and others reported that tumors with a high degree of differentiation (grade I) with sizes <1 cm have a very low probability of damage to the lymph nodes and they should not undergo axillary lymphadenectomy.[2] Seavolt and colleagues analyzed the results of treatment of 111 patients older than 70 years and the size of the primary tumor less than 1 cm. They concluded that it was possible to refuse to perform axillary lymphadenectomy in this group of patients.

Elangovan A.E. et al. showed that lymphovascular invasion of the primary tumor is combined with the detection of a metastatic lesion of the sentinel lymph node and concluded that patients with lymphovascular invasion and tumor sizes greater than 2 cm are shown to perform axillary lymphadenectomy without prior biopsy of the sentinel node.[3]

PeitingerF. with colleagues made a report on comparing the quality of life and mobility of the upper limb after axillary dissection and after a biopsy of the sentinel lymph node.[5] It was noted that patients after a sentinel biopsy had less severe pain and more active movements of the shoulder and the entire upper limb than patients after lymphadenectomy. The quality of life, based on the European Organization for the Study of Cancer Research and Treatment (EPRTC) questionnaire, the McGill questionnaire, and the visual analogue pain scale, was better in patients after biopsy.

Thus, dissection of the sentinel lymph node is not currently the standard in the treatment of breast cancer patients, but further study of this technique is promising in order to exclude the performance of axillary lymphadenectomy in the absence of its metastatic lesion.

The goal of preoperative chemotherapy (CT) in a knownly operable patient is to reduce the size of the tumor to perform organ-preserving treatment and to influence the primary focus and micrometastases to improve the prognosis of the disease. In the literature (WolffA.C., DavidsonN.E, 2000), several randomized trials have been reported on the role of preoperative CT.[8] In most of them, it was shown that preoperative CT does not improve treatment outcomes for patients with operable breast cancer compared with adjuvant CT. To illustrate this work, we used the results of the most representative study (Fisher B., 1998) of NSABP B-18. In this study, 1,500 women with operable breast cancer

received 4 CT courses with a combination of AS (doxorubicin 60 mg / m and cyclophosphamide 600 mg / m every 3 weeks) before or after surgery.[4]

As a result of the study, the following answers were received. The effectiveness of preoperative CT is not inferior (but not superior) to the results of adjuvant CT. Relapse-free and overall survival rates were the same for both groups. Further, during preoperative CT, the full effect was recorded in 36% of patients, partial in 43%, stabilization in 18%, and progress only in 3%. A morphological study in 13% of patients confirmed complete resorption of the tumor tissue. The effect of chemotherapy was correlated with the duration of the relapse-free period, but did not have a significant effect on life expectancy. Only patients with morphologically confirmed complete regression showed significantly better results of both 5-year relapse-free and overall survival. And finally, preoperative chemotherapy made it possible to reduce the stage of the disease, both by reducing the size of the primary tumor (the frequency of the objective effect of the primary tumor on chemotherapy was 80%) and axillary lymph nodes (complete clinical regression was observed in 73% of patients with previously palpable nodes, from 32% of them are morphologically confirmed). The detection rate of metastases in axillary lymph nodes was 41% in the preoperative chemotherapy group and 57%> in the adovant chemotherapy group. All this made it possible to slightly increase the frequency of organ-preserving operations, which was 67% and 60% in the preoperative and adjuvant chemotherapy groups, respectively.[13]

Does this mean that the use of preoperative chemotherapy has no prospects? Not at all. Preoperative chemotherapy can be used primarily in patients for whom organ-sparing surgery at the first stage is not possible. In this case, a successful preoperative chemotherapy may allow a similar operation to be performed. The B-18 study convincingly showed that achieving morphologically confirmed complete tumor regression significantly improves long-term treatment outcomes. Complete morphological regression is an indicator of high sensitivity to ongoing chemotherapy of not only the primary focus, but also distant micrometastases. It is the successful elimination of distant micrometastases that leads to an improvement in relapse-free and overall survival. It becomes apparent that the goal of preoperative CT is to morphologically confirm the complete destruction of the primary tumor. All other clinical effects are not critical.

It has now been shown that an increase in the effectiveness of preoperative chemotherapy is possible due to an increase in the number of courses of preoperative chemotherapy, the use of modern effective antitumor drugs, such as taxanes, more careful selection of patients with factors predicting the high efficacy of preoperative chemotherapy and early assessment of the effectiveness of preoperative chemotherapy. preoperative chemotherapy.

Winer E.R. and colleagues (2004) compared the efficacy of paclitaxel in standard and high doses in the treatment of patients with advanced breast cancer. The study included 474 patients who had not previously been given chemotherapy or had received first-line chemotherapy for breast cancer. All patients were prescribed 3-hour infusions of paclitaxel once every 28 days at different doses of 175 mg / m2, 210 mg / m2 and 250 mg / m2. All patients filled out a questionnaire on quality of life at the beginning of treatment and after 3 courses of chemotherapy.[6]

An increase in the dose of paclitaxel did not affect the frequency of the objective effect (23%, 26%, and 21%, respectively), time to progression, and life expectancy. In groups with an increased dose of the drug, hematological toxicity and neurotoxicity were more often noted. The quality of life in the three groups was the same. An increase in the dose of paclitaxel does not improve the results of treatment of patients with disseminated breast cancer. 175 mg / m2 paclitaxel should be considered a standard chemotherapy regimen.

Burstein H. and his colleagues (2003) determined the efficacy and tolerability of weekly docetaxel infusions in women with metastatic breast cancer. Treatment was carried out for 29 patients who received weekly docetaxel at a dose of 40 mg / m / week. in the form of a one-hour infusion. Each cycle consisted of 6 weeks of therapy followed by a two-week break. Treatment was carried out until the disease progressed, the development of unacceptable toxicity or patient failure.[6] Adjuvant chemotherapy was previously performed in 52% of patients; 21% of those included in the study received chemotherapy for the metastatic process. Almost a third of patients (31%) had previously used anthracyclines. 66% of patients had liver metastases. Toxicity was evaluated in all patients, efficacy - in 27. The average number of infusions was 18 with a total total dose of docetaxel 720 mg / m2. No full effects were observed, in 12 (41%) patients a partial tumor regression was observed, achieved in all of them during the first two courses. Similar efficacy was observed in patients who had previously received anthracyclines. In 17% of patients, stabilization of the disease lasting more than 6 months was observed. In general, the regimen was well tolerated. Toxicity 4 degrees is not marked. Only 28% of patients developed grade 3 toxicity, mainly neutropenia and weakness. Acute toxicity, including myelosuppression, was unexpressed. The severity of weakness, fluid retention and conjunctivitis increased with an increase in the number of administrations, but rarely exceeding 2 degree. Dose reduction was carried out in 8 out of 29 patients, mainly due to the development of weakness.[9] Thus, the weekly use of docetaxel was effective in patients with metastatic breast

cancer. The toxicity of this regimen differs from that with the "normal" (every 3 weeks) use of docetaxel.

The goal of Levin A.M. and his colleagues (2004) studied the response to chemotherapy as a predisposing factor in the treatment of metastatic breast cancer. A total of 1,430 patients were examined from 1977 to 1992 who received chemotherapy based on anthracycline antibiotics. Using statistical methods of multivariate analysis and a regression model, it was shown that an objective response to chemotherapy was observed in 60% of patients. About 15 biological parameters were used. It was noted that the main prognostic factors are: adjuvant chemotherapy, the presence of lung metastases, the primary status of patients and pleural effusion. The authors hope that with the widespread introduction of taxanes into chemotherapy schemes, more encouraging results can be obtained.[13,14]

According to some data on the study of phase 3 chemotherapy, Avastin or Bevacizumab with Paclitaxel is the first chemotherapy line for breast cancer. It was shown that relapse-free survival from such chemotherapy is two times more effective than using Paclitaxel alone. The overall survival rate also increases.[4,7]

Some researchers (Hartmann L.C., et al., 1999) consider the possibility of prophylactic mastectomy of the opposite breast in order to prevent metastasis in it.[5]

Thus, a review of literature data showed that there is a rather high incidence of metastatic forms of breast cancer. According to most authors, especially in developing countries, from 50 to 70% of patients already have advanced forms of the disease upon admission (locally common forms, in the form of lesions of regional lymph nodes and distant metastases to various organs). The nature and frequency of distant breast cancer metastases is very diverse. In 40-80% of cases, breast cancer metastasizes to bone. However, it can metastasize other organs and systems, for example, to the liver, lungs, ovaries, brain, and others. Diagnosis and treatment of distant breast cancer metastases is an urgent problem in oncommammology, since mortality in these forms remains very high, and the long-term and immediate results of treatment are still very unsatisfactory.

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