DOI 10.12851/EESJ201501C01ART02

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Analysis of the Aspects of Intensity and Metastasis of Breast Cancer to the Lung and Pleura

Key words*: breast cancer, metastases in the lungs and pleura, predictive analytics.*

Annotation: *The paper presents a comparative analysis of clinical findings and laboratory tests in patients differing in terms of remote results of breast cancer treatment. The main group included 40 patients with lung metastases developed within a 5 year follow-up period; the control group included 40 patients with no relapses and metastases over the same period. A set of factors have been identified which significantly affect the probability of development of lung and pleura metastases. These findings help to assess in a comprehensive and exhausting way the probability of metastasizing of the primary tumor without employing any additional expensive techniques.*

The final stage of the development of malignancy is metastasis; theoretically a tumor of any size has metastatic potential. The biological nature of cancer and the characteristics of the organism to the tumor determine the possibility of further development of the disease, even after the treatment radically (1, 3, 6, 7, 8). According to several authors (4, 5, 7, 9) from 12 to 30% of all tumor lesions of the lung and pleura are metastatic.

STUDY OBJECTIVE

The aim of our work was to study the factors affecting metastasis to the lung and pleura of breast cancer (BC).

MATERIALS AND METHODS

To study the factors of metastasis in the lungs and pleura of the primary lesion in patients with breast cancer, a retrospective analysis of 60 case histories of patients who have previously been combined and complex treatment in NCRCMinistry of Health of the Republic of Uzbekistan. The core group - 40 patients with over 5 years after treatment arose lung metastases (LM) and the pleura. The control group consisted of 40 patients surviving more than 5 years after treatment with no evidence of recurrence and metastasis. It was analyzed the dependence of LM and pleura breast cancer patients by age, reproductive function, their

conditions of life, family and financial position; dishormonal presence of breast disease, stage and clinical features of tumor, histological forms and degree of tumor differentiation, presence of concomitant diseases (liver, lung, et al.), these general clinical blood and urine tests; methods, schemes and modes of treatment, their objective effect.

RESULTS AND DISCUSSION

All patients were divided into 4 age groups: 1 (up to 25 years) 1 (3.3%) patients of the main group of patients in the control group - there was; in two age groups (26 - 45 years) included, respectively, 12 (40%) and 12 (40%) patients; Group 3 (46 - 60 years) included 14 (46.7%) patients of the main and 12 (40%) in the control group; 4 (over 60 years) - 3 (10%) and 6 (20%) patients, respectively. Thus the starting age of the patients had no significant effect on the occurrence of LM in patients with breast cancer and pleura.

On the stage of tumor growth (T), the majority of patients in the control group treated T2 - 22 (73.3%) in the study group - 12 (40%). Step T1 marked in 1 (3.3%) patients in the main, and 1 (3.3%) in the control groups, respectively. Stage T3-4 in the main group in the primary treatment was diagnosed in 18 (60%) and in control - in 8 (26.6%) patients (the difference is statistically significant, U = 2,921, p <0.01). N0 lymph node status was observed in 5 (16,6%), N1 - in 14 (46,7%), N2 at - 11 (36.7%) patients of the main group, the control group - in 7 (23.3%), 17 (56.7%) and 6 (20%), respectively. In this primary generalized form of breast cancer was diagnosed in 10 (33.3%) patients of the main group and in 1 (3.3%) patient in the control group, where the metastasis was found in the opposite breast.

Deviation of body weight more than 10% in the study group noted in 23 patients (76.7%) in the control - in 16 (53,3%) (U = 2,345, p <0.05).

The influence of living conditions on breast cancer metastasis to the lung and pleura was evaluated on the basis of indirect data on education and financial position. Patients with higher education in the study group was 11 (36.7%), with an average - 9 (30%), with no education - 10 (33.3%); in the control group - 12 (40%) 5 (16.7%) and 13 (43.3%) (p = 0.05), respectively. A greater number of patients with higher and secondary education in the group with ML and pleura corresponds to more abortions and the small number of births in this group of patients. Income rated as high in 7 (23.3%), medium - y 17 (56.7%) and the lowest - in 6 (20%) patients of the group; in the control group - in 10 cases (33.3%) 14 (46.7%) and 6 (20%), respectively.

To study the effect of endocrine background of patients on the metastatic potential of breast cancer we analyzed data on the beginning of the menstrual function, the number of births, abortions and miscarriages, duration of breastfeeding, early menopause. In most patients, regular menses occurred an average of 13 years. In the study group the number was 9 (30%); those who started menstruating before the age of 14 - 8 (26.7%), up to 15 years - 2 (6.6%), and 16 years - 8 (26.7%) after 16 years - 3 (10%) patients. In the control group - 14 (46.7%) 7 (23.3%) 6 (20%) 3 (10%) (U = 2,049, p <0.05) and 0 (0%) (U = 1.443, p <0.05) patients, respectively. These data allow us to establish the fact that the onset of menstrual function after 15 years is a factor in the occurrence of breast cancer metastasis to the lung and pleura. Chronic diseases of the breast (mastitis, mastalgia, and others.) significantly more often

diagnosed with hormonal instability. This feature in the main group identified more than in controls (62.0 vs. 11.5%), which indicates the fact that he is a poor prognostic (Rt = 0,497, p <0.001).

Also, no less important prognostic is the presence of a history of miscarriages, which were more frequent in the study group (29% versus 11% in the control group) (U = 2,271, p <0.05). On the criterion Kendala share this trait as compared with the control group increased by 3.5 times h (Rk = 0,286, p <0.05).

Breastfeeding is beneficial for women organism. If breastfeeding is continued until 6 months 9 (30%) patients of the study and at 2 (6.7%) in the control group, the feeding of more than 6 months in the study group was 40%, and - in the control 70% of patients, can be regarded as a protective factor (Rt = 0,276, p <0,01; Ras = -0,556). At the time of treatment menstrual function is preserved: in 15 (50%) patients of the study and 20 (66.7%) in the control group (Rt = 0,148, p> 0.05). The clinical picture of the disease symptoms, such as the disintegration of the tumor, hyperemia of the tumor, the most common ailment diagnosed in the group of patients who subsequently emerged LM and pleura. Thus, the collapse of the tumor in the study group were observed in 3 (10%) patients in the control were observed (U = 2,611, p <0,01; F = 3,335, p <0.01). Hyperemia was detected more frequently in patients of the main group (Rk = 8,217, p <0.01); indisposition in 19 (63.3%) patients of the 1 (3.3%) in the control group (p <0.01); complaints of weakness in the study group - 2 (6.7%), loss of appetite - 3 (10%), pain - 27 (81.0%). In the control group a pain syndrome was observed in 8 (26.7%) patients. Pain in the primary treatment significantly more frequent in the study group patients, which can be attributed to it as a sign of significant (U = 6,118, p <0,001; Rt = 0,526, p <0.001). The above allows you to select the listed symptoms as signs indicating a high probability of metastatic breast cancer in the lung and pleura.

From the clinical and biochemical indicators of blood and urine tests, only a few statistically significantly differed depending on the primary tumor metastasis to the lung and pleura. The erythrocyte sedimentation rate (ESR) of less than 15 mm / h in the control group was observed in 80.0%, whereas the main group - only 16.7% of the patients. ESR above 25 mm / h in the control group was observed in the study group revealed high levels in 23.3% of patients. Normal ESR are the warning signs of a favorable course of the disease (p <0.001). Contents in leykoformule segmented leukocytes> 70% (p <0.05), eosinophils> 3% (P <0.001), lymphocytes> 22% (p <0.001) and monocytes <3% (p <0.001) - signs, statistically indicating high antimetastatic body resistance. In general urinalysis most unfavorable sign, indicating a statistically significant probability of LM pleura and breast cancer is the lack of a combination of proteinuria with leukocyturia (p <0.05). Hypocoagulation statistically significantly more frequently in patients who are having a period of observation and LM pleura that allows you to mark it as a sign of affecting metastasis (Rt = 0,230, p <0,05; Ras = 0,714).

Indicators of malignancy are the degree of cell differentiation, invasiveness. In this connection, all the patients depending on the morphological forms of breast cancer were separated according to the degree of differentiation into three groups: low-grade diagnosed in 20 (66.7%), moderately differentiated in 6 (20%) and highly differentiated in 4 (13.3%)

patients the core group; in the control group, respectively - in 11 (36.7%) 9 (30.0%) and 10 (33.3%). The most aggressive in terms of metastatic tumors were poorly differentiated forms (U = 0,763, p <0.001).

Comorbidities in patients with malignant tumors may affect the regulatory system. In the study group patients liver disease is much more frequent in the study group (13 patients) than in controls (patients 1) .This allows them attributed to the factors influencing the formation of LM and pleura (U = 4,753; F = 4,521; x2 = 14.105, p <0.001). Among other comorbidities most unfavorable factors identified chronic anemia. In the control group, only 1 (3.3%) patients showed mild anemia, while more than 50% of patients of the main group diagnosed varying degrees of anemia (23.3%). his feature has expressed a statistically significant association with unfavorable outcome of the disease (Rt = 0,281, p <0,01; Ras = 1,000).

For the growth of secondary tumor nodules requires a favorable "soil" that meets the needs of young tumor cells in the energy and plastic materials. On the side of the healthy lung has all the necessary conditions for the development of secondary metastatic nodes. Among the patients of the group mild chronic nonspecific lung diseases (CNLD) noted only in 2 (6.7%), whereas in the control group, their share (including moderate severity) was 26.7%. Thus CNLD prevents the formation of LM and pleura. This characteristic has a statistically significant and pronounced protective value (Rt = 0,300, p <0,01; Ras = -0,802).

Operations saving organs are executed in the control group, 6 (20%) patients in the main group - 5 (16.7%), which, according to medical histories, a satisfactory noted general condition and the small size of tumor. Radical mastectomy as described Madden, Peity and Blokhin has been applied in the treatment of breast cancer in 25 (83.3%) patients of the study and in 24 (80%) of the control group. According to our data, type of surgery had no significant effect on the prognosis of the disease. Statistically significant differences were observed in terms of postoperative wound healing, because healing by secondary intention in the study group was noted in 14 (46.7%) cases in the control group - in 4 (13.3%), which allows to evaluate this factor as an indication, influence the occurrence of metastases (Rt = 0,425, p <0,01; Ras = -0,798).

In assessing schemes conservative treatment most significant differences between the groups are marked in the application of postoperative 4 courses of polychemotherapy (PCT), which is conducted in 5 (16.7%) patients of the study and 11 (36.7%) patients in the control group (p <0 , 05). A further increase in the number of courses of PCTs do not have effects on the decrease in the percentage of lung disease and metastatic tumors of the pleura, worsening the outlook for emerging toxic effects of chemotherapy.

It is known, preoperative radiotherapy (RT) has a damaging effect on tumor cells, reducing the incidence of tumor, removing concomitant inflammation of the surrounding normal tissues and intoxication symptoms, thereby improving the resectability and reducing the likelihood of metastasis. Postoperative RT provides additional ablation zone operation, thereby preventing the risk of local recurrence of tumor.

Conducted a retrospective analysis of medical records, neoadjuvant course RT in an equivalent dose of less than 30 Gr does not provide the necessary degree of damage to the

tumor and (probably due to the stimulating effect of low doses) impairs long-term results (p <0.05). Preoperative RT in an equivalent dose of 30-40 Gr significantly reduces the risk of LM and pleura (p <0.01). Postoperatively, 8 (26.7%) patients of the study group and 6 (20%) controls received RT at a dose not exceeding 40 Gr, the remaining patients received radiotherapy at a dose of 40 Gr. Conduction mode of postoperative radiation therapy had no significant effect on the development of the RL and the pleura (p> 0.05).

Breast cancer is a hormonally sensitive tumor one and holding of hormone therapy (HT) improves both immediate effects and long-term results. In our observation of 13 (43.3%) patients of the group did not receive HT; 17 (56.7%) patients regularly taking tamoxifen at a dose of 20 mg 2 times per day. In the control group received regular HT 27 (90%) patients, which affects the results of treatment, it can be attributed to this factor as a defense in terms of occurrence of ML and pleura (Rt = 0,330, p <0,01; Ras = -0,734).

Satisfactory condition after treatment was observed in 9 (30%) patients of the group; in 17 (56.7%) rated as moderately condition and in 5 (16.7%) - as severe in the control group, these figures were 19 (63.3%), 9 (30%) and 2 (6, 7%). Satisfactory overall condition at the end of treatment is a favorable prognostic factor preventing the emergence of LM and pleura. Poor general condition of patients at the end of treatment indicates gross regulatory, immunobiological, metabolic changes in the body that require careful correction. Postoperative, the ultimate success of the treatment depends on the adequate correction of disturbed regulation mechanisms of the body.

CONCLUSIONS

1. Among the reasons, resulting in a statistically significant increase in the incidence of LM and pleura, to our knowledge, are: 1) medical history - a violation of the hormonal regulation of the body (the establishment of menstrual function after 15 years, mastopathy, mastalgia, miscarriage (spontaneous abortion) in history); liver disease, general malaise, the presence of pain, a deviation in body weight> 10%; 2) the stage and degree of differentiation - the stage T3-4, low degree of differentiation of tumor cells; 3) local status - the presence of foci decay of the primary tumor, flushing of the skin over the tumor; 4) clinical and laboratory - ESR> 25 mm / h, hypocoagulation blood proteinuria without leykotsiturya, chronic anemia; 5) postoperative status of the patient - the healing of postoperative wounds by secondary intention, poor general condition of patients at the end of the combined treatment.
2. When analyzing aspects and intensity of metastasis of breast cancer to the lung and pleura determine the most important factors influencing the absence of metastasis within 5 years of observation. These include: 1) of the anamnestic data - long-term (more than 6 months) breastfeeding; 2) clinical and laboratory data - ESR <15 mm / h, the content of segmented leukocytes> 70% eosinophils> 3%, lymphocytes> 20% monocytes <3%; 3) the presence of non-specific chronic lung disease; 4) therapy - preoperative radiotherapy (30 Gr <SOD <40 Gr), 4-year postoperative PCT in conjunction with prolonged hormone therapy with tamoxifen.
3. Importance in the outcome of the disease has not only timely diagnosis and treatment of disease, but also the complexity of diagnostic studies, compliance of the treatment and all the features associated with the disease. Direction necessary treatment to eliminate the tumor

focus and correction of the central mechanisms of regulatory systems and sub-systems of the body.

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