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Features Of Exudate Accumulation In The Pleural Cavity In Patients With Malignant Neoplasms

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Annotation

The main clinical sign of malignant pleural effusion is shortness of breath. We have studied the degree of shortness of breath Evaluation of shortness of breath on the Medical Research Council Scale (MRC) Dyspnea Scale. The degree of shortness of breath did not depend on the primary localization of the lesion. Most patients had a moderate degree of dyspnea. Patients with a very severe form of shortness of breath, who urgently had to aspirate the effusion from the pleural cavity, were observed in 8 cases. Aspiration of exudate in this group of patients, contrary to expectations, did not lead to rapid relief of shortness of breath. The reason for this was a relatively small amount of aspiration (no more than 1.5 l), long-term accumulation of effusion. Prolonged accumulation of effusion lead to a chronic decrease in the vital capacity of the lungs, due to the development of fibrotic and inflammatory changes in the compressed areas of the lungs.

Keywords: LDH, CEA, pleural effusion, products of fibrinogen, orosomucoid, CEA, hyaluronic acid, mucoproteins, LDH activity, Ultrasound makes it possible

Introduction

Obvious fact in the progression of malignant neoplasia is the localization and histological type of the tumor. Until now, one of the main prognostic factors, confirmed by many studies, is undoubtedly the stage of the pathological process. The high metastatic potential of the tumor is certainly associated with the size of the tumor, the degree of involvement of regional and distant lymph nodes, and the presence of metastases in other organs. Different sizes of tumors in different organs do not have the same degree of aggressiveness. If the peculiarity of the course and prognosis of the primary tumor process is well studied, in the available literature of the last 50 years, we could not find a study on the influence of the primary tumor on the clinical variant and the intensity of accumulation of exudate in the pleural cavity. Considering this fact, we presented the results of the study, the characteristics of the correlations between the above factors, the likelihood of the influence of the characteristics of the primary tumor on the intensity of accumulation, the clinical features of the course of hydrothorax. We have evaluated the most important relationships that exist between signs and conditions that affect the progression of the process. Only highly significant correlation coefficients ($p<0.001$) were selected for analysis and had values of more than 0.3 (moderate and average) in absolute value (modulo). In most cases (88.9%), hydrothorax was accompanied by visible lung metastases. Since the lung parenchyma is an ideal environment for the growth and development of metastatic tumors, this fact is not unexpected. This

organ is well supplied with blood, has a strong protein and enzymatic environment, and is richly supplied with energy and plastic materials. The most common type of lung injury was multiple, miliary type of metastases and lymphangitis (70.8%). In the course of the pathological process, the miliary lesion had a more aggressive character. Solitary lesions were rarely complicated by pleural effusion. With a single type of lesion, metastatic foci were large, more often located in the subpleural or basal region. Hydrothorax in lung cancer is often accompanied by a decrease in lung volume, due to atelectasis or replacement of lung tissue by a tumor. The decrease in lung volume is compensated either by the displacement of the mediastinum towards the lesion, or by the accumulation of fluid in the pleural cavity. Reducing the volume of the lungs and in the presence of a conglomerate of lymph nodes in the root, the mediastinal organs are not enough to compensate for the volume, are shifted towards the pathology, which in turn leads to compensatory accumulation of effusion. A decrease in lung volume occurs not only with solitary formations, but also with multiple and miliary lesions of the lung parenchyma. In breast cancer, more than (50.6%) half of the cases had a miliary lesion. In tumors of the urogenital zone, the miliary nature of metastatic lung damage occurred in 66.7% of cases. Solitary metastasis in lymphoma is rare. In our observation, one patient with suspected lung cancer underwent an incisional biopsy from supraclavicular lymph node metastasis. Histological examination revealed Hodgkin's lymphoma (mixed cell variant). Often, a metastatic lesion against the background of hydrothorax was not immediately detected. Thus, most often, with secondary tumor lesions of the lung parenchyma, the accumulation of exudate in the pleural cavity is characteristic of multiple and miliary lesions of the lungs. In our opinion, with solitary and single metastases, a necessary condition for the accumulation of pleural effusion is the involvement of the pleura or elements of the lung root in the pathological process. As is known, the histological structure, the localization of the lesion significantly affects the intensity of the development of the pathological process. We wanted to analyze whether this tendency is preserved and in malignant pleural effusements, whether the primary focus of the defeat on the intensity of the exisudate accumulation in the pleural cavity does not affect. The pre-conducted study shows the possibility of the existence of this type of communication, since, with breast cancer, the accumulation of liquid more than 1.5 liters was observed in patients with double negative infiltrative cancer, no more than 30 daily doubling time of the tumor. Also, with the location of the primary tumor in the lungs, the accumulation of exudate with high intensity was observed at a low-differentiated adenocarcinoma tumor. The same trend was observed in the tumors of the urogenital zone, but due to not a large amount of research, the accuracy of statistical data was moderate ($p < 0.05$), and for the unequivocal confirmation of our assumption is insufficient. Since, before us did not stand the study of the prognostic significant signs of malignant pleural effusion. To establish patterns, we consider further research in this direction. With metastatic lesions of tumors of the skin, bone, soft tissues and other tumors, the intensity of fluid accumulation in the pleural cavity was moderate, but in statistical analysis this sign was not significant due to the small number of observations. Statistically significant, small or moderate (90.8%) accumulation of fluid in the pleural cavity was observed in the majority of patients, and only in some patients with breast cancer, tumors of the urogenital zone, lungs, intensive accumulation of fluid was observed (9.2%). Thus, intensive accumulation of exudate is more typical for cancer of the breast, urogenital area and lungs. There is a moderately significant ($p<0.05$), statistically significant, relationship between the histological variant of the tumor and the intensity of exudate accumulation in the pleural cavity. We assumed that the determining factor for the intensity of exudate accumulation in the pleural cavity, in addition to the area of damage to the lungs and pleura, is the change in the main homeostatic parameters and pronounced regulatory disturbances, both of the central mechanisms and the main subsystems associated with the main functions of the body. One of

the indicators of a violation of regulatory mechanisms, along with other disorders, is the presence of protein, glucose and LDH in the pleural fluid. Given the fact that our treatment is aimed at restoring lung excursion and did not aim to affect biochemical and molecular disorders, these changes also affected the outcome of the disease. For many years, differentiation of pleural effusions was made on the basis of protein content in the pleural fluid; so, the exudate is characterized by a protein content above 3 g / 100 ml. However, later it was found that in malignant pleural effusions, the protein content is higher than in other etiologies of hydrothorax. To detect the relationship between the biochemical composition of exudate and the intensity of accumulation of pleural fluid, we studied the content of protein, glucose and LDH in the pleural effusion in 154 patients (Table 3.3.). The amount of protein in the pleural fluid significantly affects the intensity of accumulation of the latter (11%; $p<0.01$). As is known, the protein in the pleural fluid in malignant tumors mainly consists of the breakdown products of fibrinogen, orosomucoid, CEA, hyaluronic acid, and mucoproteins. A high protein content is a sign of the aggressiveness of the tumor process, since such products as orosomucoid and hyaluronic acid are intensively produced by some forms of the tumor, and the very existence of protein in the exudate increases its oncotic pressure and contributes to the accelerated accumulation of the latter. In this connection, for the treatment of malignant effusions in the anatomical cavities of the body, the use of diuretics is not recommended, since they contribute to an even greater accumulation of protein in the residual fluid. Given this fact, we decided to use drugs such as hyaluronidase (Lidase) and heparin in the treatment of pleural effusions. Glucose is an ideal nutrient substrate for a malignant tumor. For the growth and development of any cell, including a tumor cell, two indispensable materials are needed: 1) energy, provided by carbohydrates, and 2) plastic (proteins). It is obvious that the tumor cell intensely absorbs carbohydrates to compensate for its energy costs. Features of the enzymatic processes of the tumor cell do not allow to fully break down glucose, as a result of which the products of incomplete glucose breakdown accumulate in the tumor cells, the osmoticity of the cell increases with swelling of the cell cytoplasm, the acid-base balance is disturbed, which can create unfavorable conditions for further growth and development of the tumor. One effective treatment, artificial hyperglycemia, relies on this fact. In the study of blood glucose concentrations in 147 (95.6%) patients, carbohydrate metabolism disorders were not observed, only 7 patients (4.4%) had high blood glucose levels, of which 5 patients were under the supervision of an endocrinologist about diabetes mellitus. For the examination of glucose in the pleural fluid, no additional conditions (analysis on an empty stomach, etc.) are needed. An analysis of the glucose content in the pleural fluid that we carried out showed a clear relationship between the content of the latter and the intensity of exudate accumulation. In our study, in 133 (86.4%) patients, the glucose content in the pleural fluid was less than 4 mmol/l, superintense accumulation of fluid (more than 2.0 liters per week) was statistically significantly observed only in patients with a glucose content of less than 2.0 mmol /L (04, 07, 1.2; $p<0.001$). Large and superintense accumulation of fluid was observed only at low levels of glucose in the pleural fluid. The explanation for such a low level of glucose in the pleural fluid of patients, apparently, may be increased uptake of glucose with the tumor and selective blockade of the entry of glucose into the pleural fluid. An increase in LDH activity in the blood is observed in many malignant neoplasms; with effective treatment, it decreases. This phenomenon is sometimes used for dynamic monitoring of cancer patients. The amount of LDH activity is often used to determine the activity of tumor growth and to determine the prognosis in a number of cancer patients. Although in the early works it was reported that an increase in the level of LDH in the pleural fluid is observed only in cases of malignant disease of the pleura, later it was shown that the level of LDH is elevated in most exudative pleural effusions, regardless of their origin, and cannot be used in differential diagnosis. However, the level of LDH in the pleural fluid can be a reliable

indicator of the intensity of involvement in the process of the pleura. To test our hypothesis, we analyzed pleural fluids for the presence of LDH in 90 patients. Large and superintense fluid accumulation was observed only at high LDH activity (15.5%). With an LDH index of less than 1000 U/l, the accumulation of fluid in the pleural cavity was less intense ($p<0.005$), which indicates less involvement of the pleural layers in the tumor process. Also, a high content of LDH is not only the result of an extensive lesion of the pleura by a tumor, but also of paracancrotic pneumonia and the presence of migrating leukocytes in the pleural effusion. We did not find a relationship between the histological type of malignant neoplasm and the content of LDH in the pleural fluid. Also, an increase in the activity of these enzymes can be the result of an acceleration of the processes of their synthesis, cell necrosis (with increased growth, and tumor decay). Hypoxia caused by many reasons (in this case, hydrothorax) can increase the permeability of the membrane for proteins, cause a «leakage» of intracellular enzymes. From the point of view of formal logic, the relationship between the area of damage to the pleural sheets and the intensity of accumulation of exudate in the pleural cavity is natural. Measurement of the area of the lesion was carried out in 84 patients with solitary, single and multiple tumor metastases in the lungs, with miliary lesions of the lungs and with lymphangitis, it was impossible to objectively judge the true size of the area of the lesion. All available imaging methods were used to determine the relative area of the pleural lesion. The most effective, in our opinion, was the combination of ultrasound with CT. Given the different anthropometric data in different patients, we decided to calculate the area of the lesion as a percentage. Specialists in ultrasound diagnostics and computed tomography carefully measured the pathological areas on the surface of the pleura. The ultrasound and CT data were summarized and the average value was taken. Of course, the true area of the lesion may differ from the size calculated by us. Therefore, we can only talk about relative data. X-ray semiotics of the pleural lesion does not present great difficulties. Extensive, subtotal and total darkening of the pulmonary field (after evacuation of the effusion) with or without displacement of the mediastinal organs in the opposite direction of the lesion indicates a likely lesion of the pleura and makes it possible to visually assess its area. The disadvantage of conventional X-ray examination is the difficulty in differentiating pleural thickening, lung compaction and the presence of exudate. Ultrasound makes it possible to distinguish the zone of thickening, compaction and effusion. With ultrasound, the boundaries of pleural thickening were marked with a marker, after which the area of the probable lesion was measured. The use of CT technologies greatly simplifies this task, since it not only makes it possible to differentiate clinical and anatomical formations, but also to more accurately assess the area of the lesion. The disadvantage is the high radiation exposure to the patient during the study. From the above data, the effect of the area of the lesion on the intensity of accumulation of exudate in the pleural cavity becomes clear. Only with extensive lesions of the pleural surface (66.6%) was the accumulation of more than 1.5 liters of effusion ($p<0.001$). With relatively small affected areas, the maximum accumulation did not exceed 1.5 liters per week. According to our assumption, this fact may affect the intensity of effusion accumulation in the pleural cavity. To test our assumption, we conducted a correlation analysis of this fact. To do this, we compared the intensity of effusion accumulation with the site of the greatest pleural lesion in 154 patients. Conducted analysis of the data in Table 3.7. established a statistically weakly significant correlation between the affected area and the intensity of accumulation of pleural effusion ($p<0.5$). The intensity of exudation was more influenced by the localization of the affected area. This table shows that among the patients included in our study, the main contingent had a total lesion (39.6%), lesions of the lower sections with accumulation of effusion in the hemithorax were observed in only 11.7% of cases. One of the most informative studies is a cytological analysis of pleural effusion, since it allows more than 50% of cases to accurately diagnose a malignant process involving the pleura.

Before staining the pleural exudate, it is useful to obtain a cell concentrate. This is easily accomplished by centrifuging 10 ml of the liquid pellet. The detection of tumor cells in the exudate indicates the involvement of the visceral pleura in the tumor process. With intensive accumulation of exudate, intensively tumor cells must be intensively washed off into the pleural fluid. To test our hypothesis, we compared the intensity of pleural fluid accumulation with the presence and absence of tumor cells in the exudate. Cytological analysis of the pleural effusion revealed tumor cells in 95 cases, which is 61.7% and corresponds to the diagnostic value of the data indicated in the literature. As the data analysis showed, the presence or absence of tumor cells in the pleural fluid does not affect the intensity of exudate accumulation in the pleural cavity.

Conclusion

An effusion in the pleural cavity prevents the full expansion of the lungs, thereby not only reducing the volume of the lungs, but also limiting the excursion of the latter. The small amount of the fourth degree of shortness of breath is explained by the fact that patients often seek medical help after the onset of signs of lack of air, however, in some patients, too rapid accumulation, or prolonged unsuccessful treatment, leads to the loss of a large amount of lung capacity.

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