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DEFIRENCED TREATMENT OF LUNG MALIGNANT TUMORS COMPLICATED WITH PLEURITIS

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Abstract:

This article provides information, treatment for malignant lung tumors and what drugs are used. The purpose of this study was to 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.

Keywords: chest, methods of nonspecific therapy, lung diseases, specific therapy of the pleural cavity and lungs, primary tumor.

INTRODUCTION.

Pathological processes in the pleura and pleural cavity, including pleurisy, are usually secondary, most often they are complications of lung diseases, chest injuries, diseases of the mediastinum and abdominal cavity. At the same time, the symptoms of pleural effusion are often leading in the clinical picture of the disease.

The history of the doctrine of pleurisy is centuries old. In the XVIII century. Some clinicians tried to isolate pleurisy into an independent nosological form. For decades, the etiology, pathogenesis of pleurisy and the most appropriate methods of their treatment have been studied.

An effusion in the pleural cavity should not be considered an independent disease, since it is only a peculiar manifestation of various common diseases: tumors, pneumonia, allergic conditions, tuberculosis, syphilis, heart failure, etc. (Table 1).

The accumulation of fluid in the pleural cavity due to heart failure and pneumonia occurs 2 times more often than in malignant tumors.

MATERIAL AND METHODS:

To achieve this goal, a prospective analysis of the results of diagnosis and treatment of 38 patients with malignant lung tumors complicated by hydrothorax was carried out.

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 (73.3%). 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.

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.

Pleural effusion may be transudate or exudate. The cause of transudate formation is usually congestive heart failure, mainly in patients with left ventricular failure and pericarditis. With the accumulation of transudate (hydrothorax), the pleura are not involved in the primary pathological process.

Hydrothorax is observed in cases where systemic or pulmonary capillary or oncotic plasma pressure changes (left ventricular failure, liver cirrhosis).

Pleurisy (accumulation of exudate in the pleural cavity) is most often formed in patients with malignant neoplasms. The most common cause of exudative pleurisy is metastasis to the pleura and lymph nodes of the media. Pleural effusion in tumors has a complex origin: fluid accumulation is due to an increase in capillary permeability due to inflammation or rupture of the endothelium, as well as deterioration of lymphatic drainage due to obstruction of the lymphatic tract by the tumor and tumor invasion into the pleura. The accumulation of effusion in oncological patients can be facilitated by malnutrition and a decrease in the content of protein in the blood serum.

Tumor (metastatic) pleurisy is a common complication in lung, breast, ovarian cancer, as well as in lymphomas and leukemias. Thus, it occurs in 24–50% of patients with lung cancer, up to 48% with breast cancer, up to 26% with lymphomas, and up to 10% with ovarian cancer. In other malignant tumors, tumor pleurisy is detected in 1-6% of patients (cancer of the stomach, colon, pancreas, sarcomas, melanomas, etc.). The most

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common cause of exudative pleurisy is metastasis to the pleura and mediastinal lymph nodes. Pleurisy, as a rule, indicates a far advanced tumor process and is a consequence of tumor eruptions along the pleura.

DIAGNOSTICS.

Cytological examination of the pleural fluid for tumor cells (the content of erythrocytes is more than 1 million/mm3) is an important diagnostic method. Obtaining hemorrhagic exudate during pleural puncture with a high degree of probability indicates a tumor etiology of the effusion. The frequency of detection of tumor cells in this case reaches 80–70%. Based on a cytological examination of the pleural fluid, it is often possible to determine the morphological type of the primary tumor.

Table 1
The frequency of effusions of various etiologies

Diseases	Frequency of effusions, %
Heart failure	37
Bacterial and viral infections	30
Malignant tumors	15
Pulmonary embolism	11
Diseases of the gastrointestinal tract (liver cirrhosis, pancreatitis, subphrenic abscess, etc.)	6
Mesothelioma	0.5
Vascular collagenoses	0.3
Tuberculosis	0.2

The accumulation of fluid in the pleural cavity leads to compression of the lung, displacement of the mediastinum, which in turn causes increased shortness of breath, impaired respiratory and cardiac activity. Often pleurisy, being the only manifestation of the tumor process, can be the cause of death of the patient. Treatment. Treatment of patients with effusion into the pleural cavity consists primarily in the evacuation of fluid, intrapleural administration of drugs in order to stop the accumulation of fluid in the pleural cavity and resorption of the exudate. This leads to an improvement in the patient's condition, a decrease in shortness of breath, pain, pulmonary heart failure, and thus to a lengthening of life. The algorithm for the diagnosis and treatment of tumor pleurisy is shown in the diagram.
Before deciding whether to administer certain drugs intrapleurally, it is necessary to clarify the localization of the primary process, since in case of breast cancer, ovarian cancer, small cell lung cancer, lymphomas, systemic chemotherapy can lead to the elimination of pleural effusion in 30–60% of patients.

Table 2
Drugs used for pleurodesis (summary)

Class	A drug	Doses
Cytostatics	Embihin	10-30 mg
	Thiophosfamide	30-50 mg
	5-fluorouracil	750-1000 mg
	Adriamycin	30 mg
	Cisplatin	50 mg
	Vepezid	200 mg
	Bleomycin	15-30 mg
Radioisotopes	Au-198	50-100mCu
	Phosphorus-32	
	Chromium	
	Yttrium-90	
Immunomodulators	Corinbacterium parvum	7 mg
	Interleukin + LAK cells	500 thousand IU + 10 million cells

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Nonspecific sclerosing drugs	Talc	2-4 mg
	Quinacrine	100 mg
	Tetracycline	1.2-1.6 g

In cases where systemic chemotherapy is not indicated or it was ineffective, intrapleural administration of drugs is necessary. The indication for pleural punctures and intrapleural administration of drugs is the presence of effusion in the pleural cavity above S level of the II–III rib in front, severe dyspnea with symptoms of pulmonary or pulmonary heart failure, with a life expectancy of more than 2 weeks. In the presence of effusion without clinical symptoms, it makes no sense to perform pleural punctures and administer certain drugs.

Thus, the following indications for pleurodesis can be noted:

1. The presence of subjective symptoms of pleurisy (severe shortness of breath, pain, cough).
2. The presence of effusion, refractory to modern chemotherapy and hormone therapy.
3. The presence of bronchial obstruction.

In tab. 2 presents the drugs currently used for pleurodesis.

The method of administration of cytostatics, their single and total doses, as well as the treatment regimen:

1. Embihin 10–30 mg once every 7–14 days, 3–4 injections, total 40–120 mg.
2. Thiophosfamide 30–40 mg once every 7–14 days, 3–4 injections, total 120–160 mg.
3. Fluorouracil 500–1000 mg once every 7 days, 3–4 injections, total 2000–3000 mg.
4. Bleomycin 15–30 mg once every 7 days, 4–5 injections, total 60–150 mg.
5. Adriamycin 30–40 mg once every 7 days, 3–4 injections, total 90–120 mg.
6. Cisplatin 50–60 mg once every 7 days, 2–3 injections, total 100–180 mg.
7. Mitoxantrone (novantrone) 20–25 mg, 2–3 injections.
8. Vepezid 100-150 mg 2 times in 7 days, 3-4 injections, total 600 mg.
9. Thiophosfamide 30-40 mg + fluorouracil 500 mg once every 7 days, 3 injections.

The effectiveness of intrapleural administration of individual cytostatics in lung and breast cancer ranges from 60 to 80%. In tab. 3 presents the data of the Russian Cancer Research Center. N.N. Blokhin of the Russian Academy of Medical Sciences on the effectiveness of chemotherapy for tumor pleurisy .

Particularly noteworthy are the methods of non-specific therapy using various sclerosing agents to obtain chemical serositis, gluing the pleural sheets and thus eliminating the effusion in the pleural cavity. These substances include talc, quinacrine (Akrikhin), delagil and tetracycline. The effectiveness of the introduction of talc, quinacrine, delagil reaches 55-60%, and tetracycline – 80-70%.

The method of administration of tetracycline. Tetracycline hydrochloride is most effective at high doses (20 mg/kg or 1200–1600 mg -12–16 100 mg ampoules). In a patient under local anesthesia, a puncture of the pleural cavity is performed with the introduction of a thin silicone tube, through which fluid is evacuated using a vacuum suction. After that, the tube is clamped and, under x-ray control, they are convinced that the lung has expanded. If the lung has not expanded or there is a shift of the mediastinum towards the pleural effusion, tetracycline should not be administered because of the possibility of the formation of a T-armored lung U. Since the administration of tetracycline may be accompanied by pain, it is first diluted in 50 ml of a 0.5% novocaine solution and then injected into the drainage tube. The latter is pressed for 2 hours, and the patient is asked to change the position of the body several times. After 2 hours, the clamp is removed and the drainage tube is connected to a constant pressure vacuum suction (15 to 20 cm of water column). Aspiration is continued for at least 24 hours until the volume of excreted fluid is less than 150-200 ml per day. After that, the drain tube is removed.

Table 3

The effectiveness of chemotherapy for tumor pleurisy

Process localization	Number of patients	Complete remissions, %	Partial remissions, %	No effect, %
Mammary cancer	62	39	39	22
Lung cancer	77	45	34	21
Pleural mesothelioma	79	33	33	33

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Other tumors	12	50	33	17
Total	16	40	35	25

The procedure is considered successful if the patient developed acute pleurisy as a result of the administration of tetracycline, and with the help of drainage, the convergence of the visceral and pariental pleura was ensured and obliteration of the pleural cavity was achieved. The failures of this technique are mainly associated with insufficiently complete drainage of the pleural cavity. This technique of drainage of the pleural cavity can also be used for the introduction of cytostatics.

A meta-analysis conducted by C. Belani et al on the effectiveness of individual drugs in various studies showed that the most effective drugs are tetracycline, talc and bleomycin.

FINDINGS:

Pleural effusion is a fairly common complication of lung cancer, breast cancer, and other malignant processes; its manifestation often complicates the problems of treating cancer patients.

Many patients with tumor pleurisy live, hoping for a cure, for months and even years. Therefore, effective palliative therapy of tumor pleurisy is an important aspect of the treatment of patients with a common malignant process to improve their quality of life. For intrapleural administration, both individual cytostatics (bleomycin, cisplatin, etc.) and drugs of nonspecific sclerosing action (tetracycline, talc, etc.) can be used.

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