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## IMPROVING THE SELECTIVE TREATMENT OF THYMUS TUMORS USING INTRA-ARTERIAL CHEMOEMBOLIZATION

### ABSTRACT:

Epithelial tumors of the thymus occur in the thymus and include thymomas and carcinomas of the thymus. Thymomas are the most common primary tumor in the anterior mediastinum, but are generally rare (1.5 cases / 1,000,000). Although thymomas can spread locally, they are much less invasive than thymic carcinomas. Patients with thymic carcinomas often have metastases. The 5-year survival of patients with thymoma reaches 90%. At the same time, the 5-year survival rate for thymic carcinoma is approximately 55% (NCCN Guidelines. Version 1.2020). Surgical treatment as an independent method can be used only when there are thymus tumors in encapsulated and minimally invasive tumors in the first degree, rarely in the second degree. In all other cases, patients are subject to combined, complex or conservative treatment. In combined and complex treatment, preference should be given to neoadjuvant methods, which allows to achieve regression of the tumor, reduces its volume, limits the invasion of surrounding tissues, as well as to transform the inoperable process into operability. Surgical treatment as an independent method can be used only when there are thymus tumors in encapsulated and minimally invasive tumors in the first degree, rarely in the second degree. In all other cases, patients are subject to combined, complex or conservative treatment. In combined and complex treatment, preference should be given to neoadjuvant methods, which allows to achieve regression of the tumor, reduces its volume, limits the invasion of surrounding tissues, as well as to transform the inoperable process into operability. Endovascular technologies, namely regional chemotherapy, in the preoperative period, as a preparatory stage, will increase the level of ablastics and antiblastics in surgical treatment of thymus and reduce the percentage of cytostatics on the whole body, as in intravenous

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administration. At patients with a paraneoplastic syndrome it is necessary to increase term of regression of displays of these syndromes. Intra-arterial administration of chemotherapeutics has certain advantages: • cytostatics in the arteries that supply blood to the tumor are injected directly into the affected area, which allows you to significantly increase the concentration of the drug in the tumor itself; • reduces the toxic effects of chemotherapy on the whole body; • longer action of drugs allows long-term contact of the cytostatic with tumor cells at all stages of the cell cycle.

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## INTRODUCTION

Epithelial tumors of the thymus occur in the thymus and include thymomas and carcinomas of the thymus. Thymomas are the most common primary tumor in the anterior mediastinum, but are generally rare (1.5 cases / 1,000,000). Although thymomas can spread locally, they are much less invasive than thymic carcinomas. Patients with thymic carcinomas often have metastases. The 5-year survival of patients with thymoma reaches 90%. At the same time, the 5-year survival rate for thymic carcinoma is approximately 55% (NCCN Guidelines. Version 1.2020).

Surgical treatment as an independent method can be used only when there are thymus tumors in encapsulated and minimally invasive tumors in the first degree, rarely in the second degree. In all other cases, patients are subject to combined, complex or conservative treatment. In combined and complex treatment, preference should be given to neoadjuvant methods, which allows to achieve regression of the tumor, reduces its volume, limits the invasion of surrounding tissues, as well as to transform the inoperable process into operability.

## MAIN PART

Endovascular technologies, namely regional chemotherapy, in the preoperative period, as a preparatory stage, will increase the level of ablastics and antineoplastics in surgical treatment of thymus and reduce the percentage of cytostatics on the whole body, as in intravenous administration. At patients with a paraneoplastic syndrome it is necessary to increase term of regression of displays of these syndromes.

Intra-arterial administration of chemotherapeutics has certain advantages:

- cytostatics in the arteries that supply blood to the tumor are injected directly into the affected area, which allows you to significantly increase the concentration of the drug in the tumor itself;
- reduces the toxic effects of chemotherapy on the whole body;



- longer action of drugs allows long-term contact of the cytostatic with tumor cells at all stages of the cell cycle.

Another main detail of treatment is that after the introduction of the cytostatic, it is necessary to introduce special emboli (microspheres) to block the removal of the chemotherapeutic agent.

The analysis of treatment is taking into account the stage, anamnestic data, the development of clinical manifestations, the results of laboratory and instrumental methods of examination.

According to this analysis, intra-arterial chemoembolization was selected from the complex treatment of thymic epithelial tumors, which, as described above, allows to act directly on tumor cells.

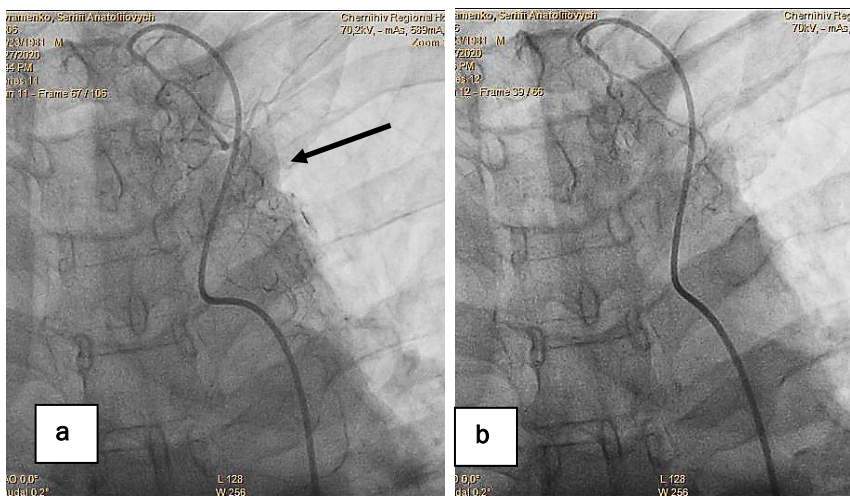
In the surgical thoracic department of the Chernihiv Regional Hospital, which is the clinical base of the Department of Oncology and Pediatric Oncology KhMAPE, we began to use combined and comprehensive treatment of thymic tumors in 2018. We combined systemic and regional chemotherapy (intra-arterial administration of chemotherapy) for patients with cancer of different localizations. We paid the most attention to the results of treatment in patients with thymic tumors.

Firstly, the clinical and radiological picture was positive on the first or second day.

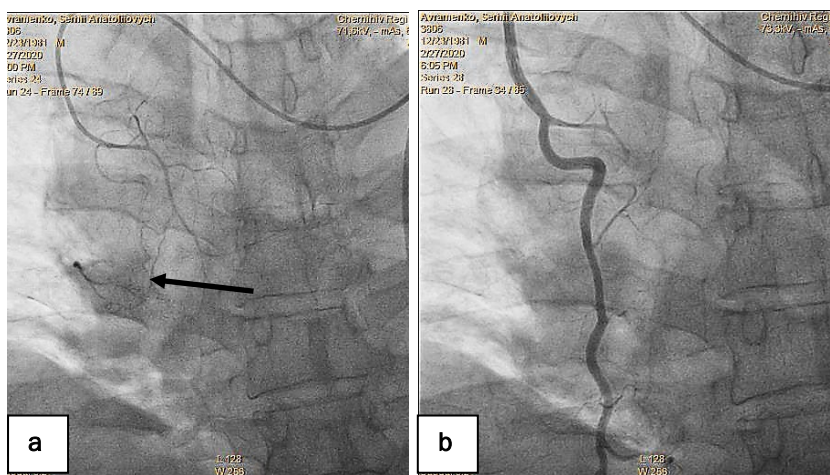
Secondly, observation of these patients after several courses of intra-arterial administration of chemotherapy made it possible to assess the regression of neurological symptoms and the timing of progression, if there is an episode of missing at least one course in the early stages of treatment.

The mechanism of selective chemotherapy of mediastinal tumors, namely intra-arterial chemoembolization, differs from the methods already described in the world literature.

Description of the method: through the femoral artery, by a minimally invasive method, a microcatheter is inserted into the aorta under the control of a special conductor and a hagiographic device. The blood supply to mediastinal tumors is taken into account, namely: a. thoracica interna, truncus brachiocephalicus at a. subclavia. The main purpose and novelty of the method is to enter the microcatheter in all arteries, the introduction of cytostatics in the most found vessels responsible for trophic tumors of the mediastinum, and if possible to embolize all vessels with microspheres, so that the concentration of chemotherapy was maximum in the tumor and did not affect the whole body.



**Fig.1. Angiograms of the branches of the left thyroid-cervical trunk before (a) and after (b) intra-arterial chemoembolization of tumor vessels of the thymus: a) contrasts the tumor formation of the thymus (arrow) ; b) tumor vessels do not contrast.**



**Fig.2. Angiograms of the branches of the right internal thoracic artery of the same patient before (a) and after (b) intra-arterial chemoembolization of tumor vessels of the thymus: a) contrasts the tumor formation of the thymus (arrow); b) tumor vessels do not contrast.**

From 2018 to the present, we have analyzed the preliminary results of work with such patients in the surgical thoracic department of the Chernihiv Regional Hospital. Treated patients during this period were divided into groups according to symptoms, selected treatment and treatment outcomes.

In one group, patients had asymptomatic disease. Thyroid tumor was detected during periodic medical examination. Surgical treatment in the form of thymectomy and thymectomy was performed. Pathohistological examination gave thymomas of type A (spindle cell, medullary), type B (lymphocytic, cortical, epithelial), and AB – mixed.

In a month patient went to our clinic for a follow-up consultation. Patients had no clinical, laboratory, or instrumental manifestations of the disease and were no longer treated.

To patients which have neurological paraneoplastic syndrome, and mostly they are patients with myasthenic syndrome in the acute phase, at first we selected the dose of hormonal drugs (Medrol) and cholinesterase inhibitors (Kalimin), then we conducted a course of intra-arterial chemoembolization. On the first day after intra-arterial administration of chemotherapy, there was a regression of neurological symptoms and subsequent reduction of the dose of hormonal drugs (Medrol) and cholinesterase inhibitors (Kalimin). After several courses of intra-arterial administration of chemotherapy regression in some patients the complete disappearance of neurological symptoms was observed for a long time.

Patients with malignant thymoma, invasive forms, with vena cava syndrome, with symptoms of intoxication and orthopedic, due to invasion were also divided by treatment.

One patient underwent surgical treatment according to the indications and in the early postoperative period the patient died with a diagnosis of "malignant thymoma of the anterior mediastinum with invasion of the heart, aorta, chest wall, diaphragm and lung, complicated by left-sided hydratorax, intoxication, cardiopulmonary insufficiency."

Another patient was admitted with the same symptoms, but we managed to perform intra-arterial administration of chemotherapy and the next day the syndrome of the superior vena cava decreased, orthopedic disappeared (the patient finally was able to sleep on his back), the symptoms of intoxication decreased. The patient underwent several courses of combined chemotherapy (intra-arterial administration of chemotherapy with systemic chemotherapy) and radiation therapy, the dynamics is positive.

## CONCLUSION

According to our evidence, taking into account clinical and anamnestic (complaints), laboratory, instrumental (CT OGK with IV contrast), certain conclusions were made in the treatment of thymic tumors.

According to our observations, a method of complex treatment of thymic tumors was developed. In this technique, we used regional chemotherapy (namely intra-arterial administration of chemotherapy-cytostatics) as the main method.

Evidence on surgical treatment of benign thymus tumors for 2018-2020 (n = 9):

- With myasthenia - 5 patients;

- Without symptoms of illness - 4 patients.

Thoracotomy (thymomectomy, thymectomy) - 5 patients

X-ray endovascular operation – 3 patients

Conservative therapy – 1 patient

In a month after treatment, 7 patients had no symptoms of illness.

One patient had complications in the form of recurrence of myasthenia gravis and cerebral edema, which required tracheotomy and resuscitation.

Evidence on surgical treatment of malignant tumors of the thymus for 2018-2020 (n = 5):

- With superior vena cava syndrome - 4 patients.

Thoracotomy - 1 patient

Operation + intra-arterial administration of chemotherapy – 1 patient

Radiation therapy + intra-arterial administration of chemotherapy – 1 patient

Conservative therapy – 2 patients

Died in the early postoperative period – 1 patient

Died of concomitant complications (brain edema, acute cardiovascular failure) without surgery – 1 patient.

In general died 2 (40.0%) patients.

Object of study. Epithelial tumors of the thymus gland.

Subject of study. Indicators of survival and quality of life of patients with malignant thymoma without surgical treatment. The results of radical surgical treatment after regional chemotherapy. Indicators of ablative and antineoplastic. Indicators of results of patients with paraneoplastic syndrome.

The aim of the study. Increase the effectiveness of treatment of patients with epithelial tumors of the thymus by using intra-arterial chemoembolization as a neoadjuvant therapy to create ischemia and high concentrations of

cytostatics in tumors for a long period of time to achieve devitalization of tumor tissue and reduce overall toxicity of chemotherapy.

Objectives of the study.

1. To determine the causes of unsatisfactory results of treatment of patients with epithelial tumors of the thymus using standard methods
2. Improve the technique of intra-arterial chemoembolization in epithelial tumors of the thymus gland (technology, choice of cytostatics)
3. To study the dynamics of biochemical markers (AFP, HGT) and antibodies to acetylcholine in paraneoplastic syndrome using intra-arterial chemoembolization
4. To study pathomorphological changes in tumor tissue using intra-arterial chemoembolization
5. To compare the clinical efficacy (increased tumor operability) of intra-arterial chemoembolization in the complex therapy of patients with epithelial tumors of the thymus gland.

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