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Results of the Study of Proliferative Activity (Ki-67) of High-Quality Soft Tissues Sarcomas

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ABSTRACT

The article presents data on certain indicators of proliferative activity (Ki-67) in high-grade soft tissue sarcomas. Analysis of Ki-67 expression showed that in high-grade soft tissue sarcomas, Ki-67 expression in most cases depended on the histological structure of the tumor and the degree of malignancy. The rate of recurrence and metastasis was higher in synovial sarcoma and rhabdomyosarcoma compared with angiogenic sarcoma and leiomyosarcoma.

Relevance.

Soft tissue sarcomas account for up to 1% in the structure of oncological diseases and have an unfavorable prognosis compared to other malignant tumors. [1]

Since the anatomical localization and appearance of sarcomas in patients is quite diverse, surgeons of any specialty may sooner or later face the problem of their differential diagnosis [2]. Soft tissue sarcomas are characterized by aggressive course and high resistance to chemotherapy and radiotherapy [3]. The high resistance of the tumor is due to the molecular biological features and instability of the genetic apparatus, as well as the heterogeneous cellular structure of the tumor. In addition, it has been established that such molecular biological factors as Bcl-2, HER2/neu, Bax, VEGF, p53 suppressor gene mutation, and others play a leading role in tumor chemoresistance. But these factors alone cannot affect the prognosis of the disease, if the proliferative activity of tumor cells would not exist. Therefore, the proliferative activity of the tumor can have a leading influence not only in determining the chemoresistance of the tumor,

but also in the choice of tactics for the treatment of soft tissue sarcomas. According to the literature [4], there are more than 50 types of soft tissue sarcomas. The proliferative activity of soft sarcoma cells in most cases depends on the histological structure, the degree of malignancy and differentiation, and the molecular genetic features of the tumor [5]. Therefore, the determination of proliferative or mitotic activity (Ki-67 gene) in tumor cells is essential in the development of soft tissue sarcomas.[6] The index of proliferative activity is low in less aggressive tumors, and high in highly aggressive ones. Based on the study of proliferative activity, one can judge the possible response of the tumor process to therapy and evaluate the effectiveness of the treatment already performed. The index of proliferative activity in various tumors has different values, being an independent prognostic sign that determines the clinical course and prognosis of the disease. At Ki-67 + 5%, the tumor is considered less aggressive, with a value of more than 30%, the tumor is considered highly aggressive. With a high level of Ki-67, the tumor is more likely to respond to chemotherapy treatment. [7]. Ki-67 is a nuclear protein highly expressed in the proliferative state of the somatic cycle [8].

Proliferative activity is valuable in the treatment of patients and in assessing their quality of life and survival rates [9]. Tumor size and Ki 67 are strong independent predictors of disease-free survival [10].

Among all sarcomas of malignant neoplasms of the connective and soft tissues, the best survival rate is for liposarcoma (>70%) and leiomyosarcoma (>40%), the lowest is for sarcoma without a specified diagnosis [11].

The purpose of the study: to study the role and evaluation of Ki-67 expression in high-grade soft tissue sarcomas, their influence on the course and choice of treatment method.

Material and research methods

Studies of the proliferative activity of Ki-67, a marker of tumor cells. It is carried out using special reagents according to the antigen-antibody principle. It is estimated as a percentage and shows what percentage of tumor cells are actively dividing. The Ki-67 antigen is a specific protein found in the nuclear material of a tumor cell and is an indicator of proliferation or division. The detection of Ki-67 indicates tumor cells that are in the division phase of the cell cycle. This allows you to understand how actively and quickly the division of tumor cells occurs, the rate of tumor growth, to assess the risk of metastasis. A joint histological and immunohistochemical study of the tumor tissue allows you to first obtain a morphological confirmation of the diagnosis, and then determine its proliferative activity - the degree and rate of cell division. After determining the histological characteristics of the tumor, an immunohistochemical study is carried out on the image of the pathological tissue, which has cells with Ki-67 antigens in its composition, specially synthesized labeled antibodies are added. During the reaction, antigen-antibody complexes are formed, the proportion of which indicates the number of cells in the active phase of division. We observed 16 patients with highly aggressive malignant soft tissue tumors. Of the 16 sick men, there were 10 (62.5%), and women - 6 (37.5%). The age of the patients ranged from 0 to 60 years, the average age was -36.7 years. In most cases, soft tissue sarcoma occurred at the age of 30-39 years - 6 patients less often up to 18 years - 3 patients and 20-29 years - 3 patients. In other age groups, patients were rare (Table No. 1).

Table №1

Gender	Number of patients	Age					
		0-19	20-29	30-39	40-49	50-59	Over 60
Men	10	2	2	5	1	1	1
Women	6	1	1	1			1
Total	16	3	3	6	1	1	2

Upon admission to the clinic, out of 16 patients, 10 complained of the presence of a tumor, 6 - of the presence of a tumor and pain, dysfunction of the limb. Of the 16 patients, in 3 (18.75%) the tumor was localized in the soft tissues of the femoral region, in 1 (6.25%) - in the gluteal region, in 2 (12.5%) - in the lower leg, in 2 (12.5%)) - in the shoulder region, in 1 (6.25%) - in the forearm, in 2 (12.5%) - in the scapular region, in 1 (6.25%) - foot, in 3 (18.75%) - head and neck and in 1 (6.25%) - retroperitoneal space (Table No. 2).

Table №2

Tumor localization	Number of patients	Histological structure			
		CC	AC	PMC	JIMC
Hip	3	1	1		1
Gluteal region	1			1	
Shin	2		1		1
Shoulder	2	1		1	
forearms	1	1			
scapular region	2	1		1	
Heads and necks	3	1		2	
Foot	1	1			
Abdomen	1			1	
Total	16	6	2	6	2

All patients underwent cytological and histological examination by performing puncture, trephine biopsy and open biopsy. In addition, all 16 patients underwent an immunohistological study with the determination of indicators of the proliferative activity of Ki-67. When analyzing the histological structure of the tumor, it was found that out of 16 patients, 6 (37.5%) had synovial sarcoma, 2 (12.5%) had angiogenic sarcoma, 6 (37.5%) had rhabdomyosarcoma, and 2 (12.5%) had synovial sarcoma. .5%) leiomyosarcoma (table No. 3).

Table №3

Frequency of recurrence and metastasis	Number of patients	Histological structure			
		CC	AC	PMC	JIMC
relapse	5	3		1	1
Metastasis	4	1	1	2	
Did not have	7				
Total	16				

In 2 (12.5%) patients, grade I malignancy was detected, grade II - in 3 (18.75%), grade III - in 11 (68.75%), grade IV malignancy was not registered. 6.8% of patients had low-grade differentiated tumors. This is to say that the tumor is highly malignant. (table No. 4)

The degree of malignancy of the tumor depending on the histological structure of the tumor

Table №4

The degree of malignancy of the tumor	Number of patients	Histological structure			
		CC	AC	PMC	JIMC
G1	2	2			
G2	3	2	1		
G3	11	2	1	6	2
G4	-	-	-	-	-
Total	16	6	2	6	2

Result and discussion: The results of the study of the Ki-67 expression index depending on the histological structure showed that in synovial sarcoma out of 6 patients in 3 (50%) patients it was up to 30%, in 2 (33.3%) from 30% to 50% and 1(16.7) has more than 50%. With angiogenic sarcoma, out of 2 patients, 1 (50%) had 20% and 1 (50%) had 30%. With rhabdomyosarcoma out of 6 patients, in 1 (16.7%) patients, the Ki-67 index was up to 20%, in 2 (33.3%) up to 30%, in 2 (33.3%) 30-50% and in 1 (16.7%) more than 50 %. With leiomyorsarcoma, out of 2 patients, in 1 (50%), the Ki-67 index was up to 30% and in 1 (50%) more than 30%. As can be seen from the presented data, out of 16 patients with highly aggressive soft tissue sarcomas, 3 (18.75%) had a Ki-67 index of more than 50%. This indicates a high proliferative activity of the tumor, which requires the start of specialized treatment with the appointment of chemotherapy. Accordingly, these patients have a poor prognosis. In relation to recurrence and metastases of the tumor. Indeed, among patients with the presence of tumor metastases, the Ki-67 index was significantly higher compared to patients without metastases. In addition, we found that in highly aggressive soft tissue sarcomas, the Ki-67 index was high and the sensitivity to chemotherapy largely depended on the expression of Ki-67. Patients were followed up for 11 months to 5 years. During these observation periods, out of 16 patients, 5 (31.25%) patients had a tumor recurrence, on average, the time for the appearance of relapses was 8 months. At the same time, out of 6 patients in 3 (50%), the histological structure was synovial sarcoma in 1 (16.7%) of the femoral region, in 1 (16.7%) in the shoulder region and in 1 (16.7%) in the head region. and neck. In addition, in 1 (16.7%) patients with rhabdomyosarcoma, tumor recurrence was detected and in 1 (50%) patient with leiomyosarcoma. Of the 16 patients, 4 (25%) had metastases in separated organs. At the same time, metastases appeared in the lungs and were of a multiple nature. The timing of the appearance of metastases ranged from 2 to 60 months, on average 18.5 months. Separated metastases appeared in 1 (16.6%) patient with synovial sarcoma, in 1 (50%) with angiogenic sarcoma, and in 2 (33.3%) with soft tissue rhabdomyosarcoma. In terms of observation up to 60 months, out of 16 patients, 3 died from recurrence and tumor metastases, 1 is a relapse and 2 with tumor metastasis.

Of the 16 patients, 3 (18.75%) underwent surgical treatment, 5 (31.25%) - combined treatments, 8 (50.0%) - complex treatment. 5 patients who had tumor recurrence underwent complex treatment. 4 patients who had tumor metastases, 1 underwent chemotherapy, 3 patients underwent symptomatic treatment due to the spread of the tumor. The authors studied the indices of Ki-67 depending on the histological structure and degree of malignancy of the tumor, as well as the indices of tumor recurrence and metastases in various types of high-grade soft tissue sarcomas. It was found that in malignant soft tissue tumors, especially in synovial sarcoma and rhabdomyosarcoma, Ki-67 expression was significantly higher than in angiogenic sarcoma and leiomyosarcoma.

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