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CLINICOMORPHOLOGICAL ANALYSIS IN OSTEOMEDULLARY TUMORS

Abstract: *Considering the histogenetic closeness of Ewing's sarcoma and PNET, proved based on molecular-genetic and cultural studies, as well as the uniformity of therapeutic approaches in the diagnosis of these tumors, the need for differential diagnosis of them has not been sufficiently justified [1]. The only real morphological feature that distinguishes PNET from Ewing's sarcoma is the expressed rosette formation [7].*

Key words: *Osteomedullary tumors, Ewing's sarcoma, PNET, pseudorosettes, rosette formation*
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Introduction

Osteomedullary tumors include Ewing's sarcoma, malignant bone lymphoma (reticulosarcoma), and primitive neuroectodermal tumors of the bone [2, p79; 4,p.68;7,p.464]. Some of the representatives of this group – Ewing's sarcoma and primitive neuroectodermal tumors (hereinafter PNET) are localized mainly in bones and soft tissues [5,p.214; 6,p.343]. These tumors were reported long before the introduction of electron microscopy and immunohistochemistry [1,p.532; 3,p.174; 8,p.295].

Purpose of the study.

Analysis of clinicomorphological signs in osteomedullary tumors.

Materials and Methods.

This work, following the tasks set, includes data on bone marrow tumors of patients who underwent treatment at the Oncology Clinic of AMU from 2007 to 2020.

To solve the set tasks, the following research methods were used in the work: clinical, radiological, cytological, histological, histochemical, and statistical.

Cytological research methods - routine cytological analysis of punctates, imprint smears, stained with hematoxylin-eosin and thionine,

followed by histological verification of the diagnosis and comparison of cytological and histological findings [3,p.294-299].The histological research methods included cases in which archival material was preserved (histological preparations, paraffin blocks, or material fixed in formalin), as well as current observations.

Material for histochemical analysis was fixed in 80% alcohol. Staining with iodic acid and Schiff's reagent (SHIK or PAS reaction) was used to identify glycogen; Kreiberg stain was used to identify chondroid and myxomatous degeneration of the stroma.

All histological and histochemical research methods used in this work were repeatedly tested, modes were worked out, errors were measured, and described in detail in manuals on histochemistry.

All digital data obtained during the experiments were statistically processed taking into account modern requirements. The data obtained were statistically analyzed by nonparametric methods according to Wilcoxon-Mann-Whitney.

Results and Discussion

We found Ewing's sarcoma in 114 cases. In most patients with this pathology, the disease began either in full health, for no apparent reason, or sometime after the trauma. According to our data, a trauma preceded the appearance of a tumor in 40% of cases. The average time of tumor emergence after the injury was 5 months. The shortest period was a few days, the longest was 12 months. A trauma in anamnesis was noted in 30 of our patients (26.3%). Clinical manifestations of the disease occurred at various time intervals - from several days to 2 years.

In most cases, the disease began slowly, gradually: mild, quickly subsiding pains appeared in the affected part of the bone with significant light gaps between attacks. The described course of the disease was observed in 85 (74.5%) of 114 (100%) of our patients. Like in other malignant neoplasms of the skeleton, the characteristic triad of symptoms was repeated with the greatest constancy in Ewing's sarcoma: pain in the affected part of the skeleton, swelling, dysfunction. According to our research, pain in Ewing's sarcoma never reached the acute "skeletal" pain characteristic of osteosarcoma. Another permanent symptom of the disease is swelling. In our observations, the tumor was detected in 70 (61.4%) of 114 (100%) patients; as the first sign of the disease - in 31 (27.2%) patients. The sizes of the tumors varied - from a small localized swelling to extensive deformity of the affected limb. We detected an increase in body temperature at different periods of the disease in 40 patients (35.0%); however, we did not find a direct relationship between the degree of malignancy of the tumor and temperature response.

The cytological picture of Ewing's sarcoma is characterized by the presence of a large number of tumor cells, which are scattered or form structures in the form of rosettes and complexes. The cells are of the same type in shape and size, the background of the preparation is formed by erythrocytes. Tumor cells are predominantly round in shape, oval-shaped cells also occur. The cytoplasm is stained weakly basophilic, it's borders are not always clear, vacuoles are often visible. The nuclei are large, mostly rounded, located in the center of the cell, monomorphic or weakly polymorphic. The structure of chromatin is fine-grained, uniform. Nucleoli (1-2) of a rounded shape are visible in the nuclei. The presence of blood vessels is sometimes noted. Cells with a polymorphic structure are quite rare.

According to the results of microscopic examination, the cell mass with an almost invisible stromal component dominates in the tumor [4, p.214]. Secondly, it is generally accepted that the cells of Ewing's sarcoma are relatively small in size, round in shape, and monomorphic. A part of the tumor cells is concentrated around small (capillary type) vessels, forming irregular strands in the longitudinal section, and pseudorosette structures in the transverse section. Fibrous elements of the stroma in the tumor tissue are almost undetectable. The argyrophilic carcass is present only in the vessels and to a very small extent in the perivascular spaces. In the histochemical study, the differential diagnosis should be carried out for malignant bone lymphoma, from which the Ewing's sarcoma cells differ in less polymorphism and usually a significantly lower number of atypical mitotic figures [5, p.2436-2449]. After fixation in alcohol under the influence of Schiff's reagent (SHIK-PAS reaction) and using amylase as control, a significant content of glycogen is always detectable in Ewing's tumor cells, which is absent in the cells of malignant bone lymphoma.

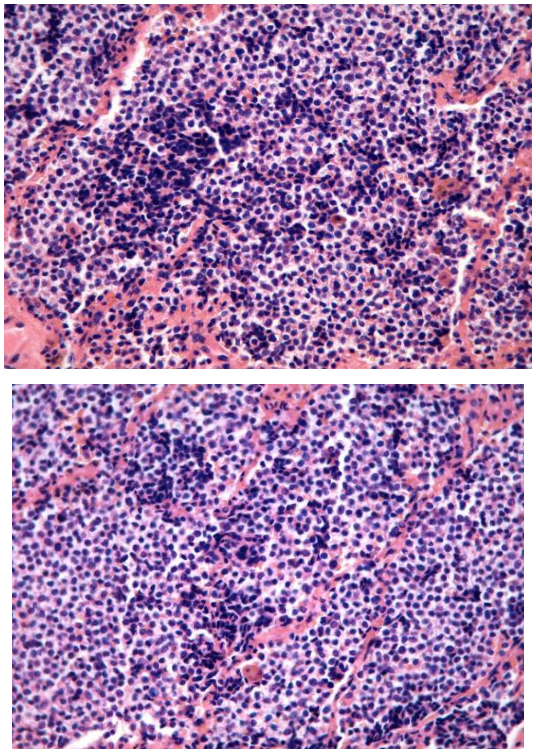

Figure. 1. Patient D., 16 years old. Ewing's sarcoma of the humerus. The diffuse variant of the structure of the tumor with the presence of two variants of cells. The bulk of the tumor is represented by cells with an enlightened cytoplasm, in which the same type, rounded or oval nuclei are located. The second variant of hyperchromic, smaller cells. Staining with hematoxylin and eosin. Magnification 200x.

We detected PNET in 42 cases. In the majority of patients, clinical signs of the disease appeared during the first 4 - 5 months after a trauma, immediately after a trauma, or shortly after it. Some patients (10 observations - 23.8%) denied the role of trauma in anamnesis. In the majority of the patients studied by us (37 observations-88.1%), the symptoms of this pathology were noted for no apparent reason or sometime after the trauma. We believe that the frequent definite coincidence in time and localization of the trauma with the subsequent development of the tumor suggests that the damage in some cases triggered the acceleration of the growth of a malignant tumor, which had been without symptoms until that time. Like in Ewing's sarcoma, characteristic triads of symptoms are repeated: pain in the affected part of the skeleton, swelling, dysfunction of the limbs. The tumor was detected in 35 (83.3%) of 42 patients (100%); as the first sign of the disease in 9 (21.4%) patients. The sizes of the tumors varied - from a small localized swelling to extensive deformity of the affected bone.

A characteristic feature of PNET was an extremely aggressive clinical course of the tumor process [2, p. 79-80]. Life expectancy in 32 (76.1%) patients averaged 8 months, in the remaining 10 (23.9%) patients averaged 12 months after diagnosis.

Tumor tissue in PNET is characterized by diffuse growths of the same type of rounded and oval cells with barely distinguishable cytoplasm. The cells are usually tightly adjoined. With good blood supply, especially with a developed capillary network, the formation of pseudorosettes (such as Homer Wright) and pseudoalveoli, which are clusters of tumor cells around the capillaries, is noted. At high magnification, in the center of such a pseudorosette or pseudoalveolus, a lumen formed by an endotheliocyte is always seen. In the presence of vessels of a larger caliber (venules, veins, arterioles) confluent fields of hemorrhagic necrosis are formed in the tumor with the simultaneous underdevelopment of the capillary network. In this case, the cells are preserved only in the form of sleeves around the wide-walled vessels, forming the so-called pericytic structures. Returning to the question of pseudorosettes,it should be noted that they are still rare in Ewing's sarcoma and, in a total study of a tumor section, make up less than 10% of its area. Besides, in PNET, practically the only specific morphological feature at the light level is pronounced rosette formation (more precisely, pseudorosette formation), which makes up the majority of the tumor area (about 80%)[6, p.174]. Thus, based on literature data and our research, we can conclude that in the presence of this symptom (taking into account, of course, all clinical and radiological information), the diagnosis is in favor of a primitive neuroectodermal tumor.

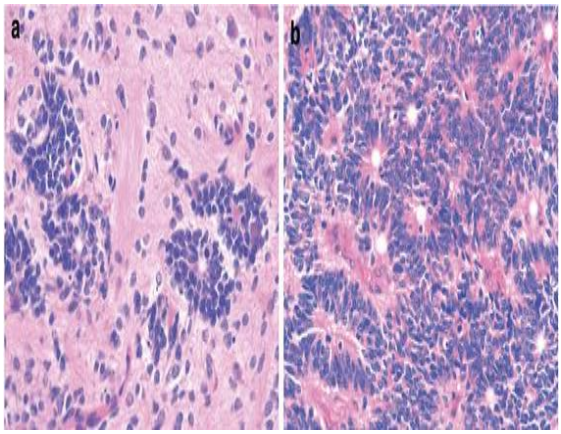

Figure 2. Patient D. 12 years old. PNET, femoral. Diffuse growths of the same type of rounded and oval cells with barely distinguishable cytoplasm. The cells are usually tightly adjoined. Formation of pseudorosettes (like Homer Wright) and pseudoalveoli, which are clusters of tumor cells around the capillaries. At high magnification, in the center of such a pseudorosette or pseudoalveolus, a lumen formed by an endotheliocyte is always found (b). Staining with hematoxylin and eosin. Magnification 200x.

Conclusion: Thus, the basic light-optical signs for the diagnosis of PNET are: diffuse nature of growth, pronounced monomorphism of cells and nuclei (among the nosological units considered in the work, this feature is most characteristic of Ewing's sarcoma and PNET), the presence of a perivascular nature of necrosis by the formation of pericytic cell sleeves. Considering the histogenetic proximity of Ewing's sarcoma and PNET, proven on the basis of molecular-genetic and cultural studies, as well as the uniformity of therapeutic approaches for these tumors, the need for differential diagnosis of them has not been justified yet. The only significant morphological feature that distinguishes PNET from Ewing's sarcoma is pronounced rosette formation.

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