HISTOLOGICAL AND IMMUNOHISTOCHEMICAL CHARACTERISTICS OF PARASAGGITAL MENINGIOMAS OF THE BRAIN

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Abstract. *Meningiomas, a group of tumors originating from the meninges, have a wide range of morphological characteristics that determine the type and grade of malignancy. The study of anaplastic meningiomas is challenging because they resemble soft tissue malignancies. Immunostaining makes it possible not only to determine the cytogenetic source and the degree of malignancy of the tumor, but also to detect pathological proteins - transcription products of damaged DNA sections and give recommendations on the appointment of targeted therapy.*

Keywords: *meningioma, benign, typical, atypical, anaplastic, immunohistochemistry, markers.*

Meningiomas are slow-growing, mostly benign tumors arising from arachnoendothelial detachments of the dura mater [2]. In the adult population, meningiomas are observed in 18-34% of cases of all intracranial neoplasms, confidently occupying the 2nd place among all brain tumors and second only to gliomas. The incidence is 4-6 per 100 thousand population. Most often, meningiomas occur in the 4th-6th decade of life. The frequency of their occurrence is much higher in women, especially among middle-aged people [3, 12].

To the occurrence of meningiomas. They often develop in patients with neurofibromatosis type 2. In addition, there is evidence of families with an increased tendency to form meningiomas that do not suffer from neurofibromatosis. The occurrence of meningiomas is associated with exposure to ionizing radiation, hormonal imbalance, trauma, and magnetic field [3].

The cytogenetic source of meningiomas is transformed arachnoid meningothelial cells [1]. Prior to microscopic examination, it is very important for a pathologist to clarify the localization of the tumor, the location of its matrix bed, the involvement of surrounding structures, and the presence of a capsule. Most meningiomas are clearly demarcated from the surrounding nervous tissue, more often they grow as a single encapsulated node (they push back and compress the surrounding tissues). However, meningiomas are also capable of invasive growth, sprouting the substance of the brain, dura mater, adjacent bone with the formation of hyperostoses and extracranial nodes. In addition, due to the frequent involvement of the cavernous sinus and the main cerebral vessels in the tumor process, the frequency of continued growth of meningiomas is up to 45% [3, 6, 14].

CLINICAL CHARACTERISTICS AND HISTOLOGICAL CLASSIFICATION OF MENINGIOMAS BY WHO (2007)

Despite the fact that most meningiomas are benign, this group of tumors is characterized by certain clinical signs and histological variants that are associated with a high risk of recurrence. Rarely, malignant types of meningiomas occur.

The proposed WHO histological classification suggests a clinical prognosis for patients with meningiomas based on statistically significant clinicopathological correlations [10].

According to this classification, it is customary to distinguish between three grades of meningiomas: benign or typical (WHO grade 1), atypical (WHO grade 2) and anaplastic meningeal tumors (WHO grade 3)

TYPICAL OR BENIGN MENINGIOMAS (WHO GRADE 1)

Approximately 80% of all meningiomas are slow-growing, benign, WHO grade 1 tumors. Most of the histological variants of meningiomas correspond to WHO grade 1, with the exception of chordoid, clear cell, rhabdoid, and papillary meningiomas, which are characterized by a rapidly progressive and invasive growth pattern [23]. The most common in clinical practice are meningotheliomatous, fibrous and transitional meningiomas. The meningotheliomatous variant of meningiomas consists of homogeneous tumor cells in the form of lobules separated by thin collagen fibers. Inside the lobules, the cell boundaries are indistinct, resembling a syncytial structure. The shape of tumor cells varies from polygonal to epithelioid. The contours of the nuclear membrane are even, the chromatin structure is fine-grained, uniform, the nucleoli are not visualized [7]. Fibrous meningioma is a group of spindle-shaped cells resembling fibroblasts that form intertwining bundles embedded in a matrix rich in collagen and reticulin fibers. The transitional or mixed variant of meningiomas combines the features of meningotheliomatous and fibrotic variants. In this case, meningotheliomatous bodies are often found with fibroblast-like cells located along the periphery. The meningotheliomatous variant of the tumor is characterized by concentric meningotheliomatous structures, sometimes with a vessel fragment in the central part. Much less often, such structures are determined in other types of meningiomas. With hyalinosis and calcification of concentric structures, the so-called psammoma bodies (rounded layered calcified bodies) are formed (Fig. 1c). It should be noted that smears of meningioma with a predominance of psammoma structures should be interpreted as a psammoma variant of the tumor [18, 22]. When stained with hematoxylin-eosin, small or large psammoma bodies have a pinkish-violet tint. Meningothelioma bodies are often found in a psammoma- free smear, however, psammoma bodies are usually associated with a concentric cellular structure. It is important to distinguish psammoma from the smallest bone fragments, which can sometimes get into the histological material during its sampling.

Typical meningiomas are capable of invasive growth, sprouting the dura mater, cerebral sinuses, the main vessels of the brain, and also spread beyond the cranial cavity. All this leads to great difficulties in performing microneurosurgical resection of the tumor and reduces the degree of its radicalization. However, the invasive growth potential of WHO grade 1 meningiomas should not be considered equivalent to atypical or malignant types.

ATYPIC AND OTHER HISTOLOGICAL OPTIONS OF WHO GRADE 2 MENINGIOMAS

Atypical meningiomas account for 15-20% of all types of meningiomas. Atypical meningiomas are prone to aggressive growth and frequent recurrence. So, after a radical resection of a benign meningioma, the percentage of recurrence in the next 5 years is about 5%. As for atypical meningiomas, the percentage of their recurrence in the next 5 years is more than 40% and increases over time [6]. Therefore, when verifying a patient with an atypical form of meningioma, the timing of his next follow-up after surgery should be no later than 3 weeks [17].

The most reliable prognostic risk factor for meningioma recurrence in histopathological examination is the number of mitoses. Four or more mitoses per 10 visual fields is a reliable sign of a high risk of meningeal tumor recurrence [18]. However, the absence of a high degree of mitotic activity of tumor cells does not exclude a high risk of meningiomas recurrence. According to the 2000 WHO criteria, pathological confirmation of atypical meningioma (Fig. 2a) requires at least three of the five proposed criteria: a large number of cells, a high nuclear-cytoplasmic ratio (small cells), visualization of the nucleoli, leaf-like growth, foci of spontaneous necrosis (not induced by embolization or radiotherapy).

As already mentioned, atypical meningiomas, along with chordoid and clear cell variants, are more aggressive tumors and have a 2nd degree of malignancy according to the WHO classification. Clear cell meningioma is characterized by leaf-like aggregations of polygonal cells rich in glycogen, nuclear atypia, enlarged perivascular spaces, and the absence of meningothelioma bodies. The cells have a light vacuolated cytoplasm (often vacuoles occupy most of the cytoplasm), the formation of syncytium-like structures of 6-8 nuclei takes place. chordoid meningioma got its name for the similarity of some of its parts with chordoma and is represented by an abundance of oxyphilic extracellular matrix around tumor cells, this matrix braids individual cells in the form of thin strands. The cytoplasm is wide, polygonal, with irregularly shaped processes in the form of "thorns", the edges of which are sometimes poorly distinguishable (tumor cells resemble cells of the thorn-like layer of squamous epithelium). Most of the cell nuclei have a uniform chromatin structure, contain nucleoli with fuzzy contours. The presence of such properties as pronounced nuclear polymorphism, enlarged hyperchromic nuclei with uneven contours and larger, clear nucleoli allows this variant to be classified as an aggressive meningiomas. A feature of the localization of these variants of meningiomas was noted: clear cell meningioma is often located in the spinal cord and in the region of the posterior cranial fossa, for chordoid meningiomas are characterized by supratentorial location [24].

ANAPLASTIC (MALIGNANT) MENINGIOMAS AND OTHER MENINGIOMAS WHO STAGE 3 MALIGNANCE

Anaplastic meningiomas account for 1 to 3% of all types of meningiomas. This type of tumor has a number of clinical and histological properties similar to other malignant tumors (cancers and sarcomas): aggressive infiltrating growth and the ability to metastasize. The recurrence rate of anaplastic meningiomas after microneurosurgical resection ranges from 60% to 80%, and the median survival is less than two years [9, 10].

A histological feature of anaplastic meningiomas that determines a high degree of malignancy is a high index of mitotic activity of tumor cells - twenty or more mitoses per 10 fields of view. Often, anaplastic meningiomas can resemble sarcoma, cancer, or melanoma in their picture, which makes it difficult to determine the cytogenetic source of the tumor and its affiliation. However, for anaplastic meningioma, the presence of peripheral tissue shreds and fragments is uncharacteristic, in contrast to soft tissue malignant tumors [11]. In addition, the presence or absence of melanin pigment will also help in determining the correct diagnosis. In histological sections, signs of sharp polymorphism, an abundance of mitoses, and necrosis are noted. As a rule, there are continuous cell fields of small monomorphic tumor cells with areas of cavities of the epithelial-embryonic type [16]. Along with anaplastic meningioma, high-grade meningiomas also include papillary and rhabdoid meningiomas. Papillary meningioma is characterized by invasive growth, persistent recurrence, and frequent metastasis. This variant is very difficult to distinguish

from the papillary variant of metastatic cancer. The age of the patient (usually younger than 15 years) and the localization of the tumor (usually in the posterior cranial fossa) testify in favor of papillary meningioma. Histologically, this variant of meningiomas is represented by monomorphic cells with relatively large hyperchromic nuclei. Tumor cells form papillary structures without pronounced papillary fibrovascular stroma. Necrosis is not typical. rhabdoid meningioma consists of round-shaped tumor cells with a large nucleus. When stained with hematoxylin-eosin in a histological preparation, the cytoplasm is eosinophilic, the cells resemble skeletal muscle myoblasts. Under light microscopy, there is no transverse striation in the cytoplasm; under electron microscopy, organelles and Z-bands characteristic of skeletal muscle myocytes are not detected, but complexes of vimen -tin-positive intermediate filaments are found. Since the cells resemble rhabdomyocytes, but are not, the tumor was called " rhabdoid " [14]. It is a very aggressive malignant tumor with a high recurrence rate and frequent metastasis.

IMMUNOHISTOCHEMISTRY OF MENINGIOMAS

Immunohistochemical examination plays an important role in the diagnosis of meningiomas, especially in cases of anaplastic forms. However, in some cases of anaplastic forms of meningiomas, even when using immunohistochemical markers, it is extremely difficult to determine the type of tumor and its cytogenetic source [4, 21].

The most common immunohistochemical marker of meningiomas is epithelial membrane antigen (EMA), which is detected in most types of meningiomas [12, 15]. The use of such a marker as vimentin also helps in making a diagnosis, since many variants of meningiomas contain this neurofilament [5]. Unfortunately, EMA and vimentin are not pathognomonic markers for this group of tumors, and additional immunohistochemical markers are needed for full verification.

Another important sign of meningiomas, determined by immunohistochemistry, is the proliferative index, which is traditionally determined in clinical pathology using antibodies to the nuclear antigen MIB-1 (Ki-67). Expression of Ki-67 makes it possible to isolate tumor cells that are in the active phase of the cell cycle throughout its entire length (G1-, S-, G2- and M-phases). Ki-67 is absent only in the GO period. Actively proliferating tumor cells represent the “growth fraction” of the neoplasm. Proliferative activity is a leading factor both in the mechanism of malignant transformation of cells and in the biological behavior of tumors that have already arisen. The index of proliferative activity in different tumors has different values, while being an independent prognostic sign that determines the clinical course and prognosis of the disease. For meningiomas, with a Ki-67 index of more than 5%, the tumor is considered aggressive and has a high risk of recurrence [8]. Recently, the expression of progesterone receptors in meningioma cells has been increasingly determined. At the same time, the degree of expression of receptors for this steroid hormone is inversely related to the degree of malignancy of meningioma, but so far this marker has not entered into wide clinical practice [19].

A completely new immunohistochemical marker that allows determining the degree of malignancy of meningiomas is an antibody to mitosis- specific phosphohistone-H3. Staining preparations with these antibodies allow the pathologist to clearly visualize mitotic figures and distinguish them from apoptotic nuclei, which are almost identical in conventional examination [20].

CONCLUSION

Thus, meningiomas have a wide range of morphological characteristics that ultimately determine the type and degree of malignancy of this group of brain tumors. Of particular difficulty

in the study are anaplastic meningiomas. This type of tumors has a number of similarities with soft tissue malignant neoplasms (cancer, sarcoma, melanoma) and it is not possible to distinguish them from each other without immunohistochemistry. At present, the immunohistochemical method continues to develop actively, having taken a strong place among the diagnostic methods in oncology. Thanks to immunostaining a pathologist can not only determine the cytogenetic source and the degree of malignancy of the tumor, but also detect pathological proteins - transcription products of damaged DNA sections and give recommendations on the appointment of targeted therapy.

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