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PATHOMORPHOLOGICAL FEATURES OF DIFFUSE AND ANAPLASTIC ASTROCYTOMAS

H. A. Rasulov.
Tashkent Institute of Pediatric Medicine. The head of the anatomy department is professor of DSc

D. A. Nishanov.
Director of the Republican Pathological Anatomy Center DSc. professor

Х. Ж. Бекназаров
Republican Specialized Scientific Practical Medical Center of Neurosurgery,
Head of the Department of Pathological Anatomy. PhD

Abstract: In the analysis of the conducted studies, the main attention is paid to the morphological characteristics of astrocytomas of medium and high risk, which occupy an important place among neuroepithelial neoplastic processes in the central nervous system, while attention is paid to the morphological features of diffuse and anaplastic astrocytomas, and based on the results obtained, lays the foundation for making a correct diagnosis. And this can serve for further treatment of patients with this disease and prognosis of the course of the disease.

Keywords: neuroepithelial, glial, diffuse astrocytoma, anaplastic astrocytoma, blood vessel, histochemistry.

Introduction:

MNT glial or neuroepithelial tumors occur in almost all sexes and ages, and their pathomorphological characteristics are fundamentally different from each other. According to the data presented in the literature, among primary nervous system tumors, neuroepithelial tumors account for 80-85%, while astrocytomas occur in almost 65-70% of cases. If we consider age indicators, it was found that astrocytomas with a risk level of G-I are more common in children (35-40%), astrocytomas with a risk level of G-II are more common in middle-aged people (up to 55-60%) in the main indicators around 30-40 years of age, and astrocytomas with a risk level of G-III are more common in the age group of 40-55 years (60-65%). By gender, it was also found that men are affected by astrocytomas in a ratio of 1.8:1 compared to women. A 5-year analysis of the epidemiology and prognostic significance of central nervous system tumors in Asia up to 2020 (GLOBOCAN), age-standardized incidence and mortality rates (ASIR), and the overall mortality and morbidity ratio (MIR) were used to predict the epidemiology and prognostic significance of the disease for the period from 2025 to 2040 (S. E. Mousavi -2024). According to the results of the 5-year analysis, the incidence per 100,000 population is 9.40, and the mortality rate per 100,000 population is 6.20 in Armenia, 6.20 in Iran, and 5.10 in Turkey, which is the highest mortality rate due to central nervous system diseases compared to other regions. By 2040, it is predicted that new cases of central nervous system tumors in Asia will reach 232,000, and deaths will reach 200,000. The analysis of pathomorphological types of primary

MNS tumors showed that 60% are astrocytomas, including diffuse astrocytoma (23.6%), anaplastic astrocytoma (4.4%), oligodendroglioma (4.4%) and pilocytic astrocytoma - 0.4%, pleomorphic xanthoastrocytoma - 0.7% and other types (Milyukov S. M. 2016). Based on the literature and observations of a number of authors, we can conclude that glial tumors account for more than 60% of primary MNS tumors, and astrocytomas account for 45-50% of glial tumors. Astrocytomas are tumors arising from astrocyte cells and occur in all ages and genders. Among them, several types of diffuse and aplastic astrocytomas are listed in the WHO (2007, 2016) classifications. Diffuse astrocytomas are infiltrative growth boundaries are unclear. Sometimes the boundaries are clear, they can meet in the form of knots. Morphologically, diffuse astrocytomas are divided into 3 types: fibrillar, protoplasmic, fibrillar-protoplasmic, fat (large) hemistocytic cells. It occurs in all ages and genders. Astrocytomas in the cerebral hemispheres are more common around the age of 20-45, and in the cerebellum, they are more common around the age of 7-18. Sometimes it can occur in early infancy and in rare cases around 55-65 years of age. Anaplastic astrocytoma is a tumor characterized by a pronounced diffuse atypical astrocyte cell proliferation and the preservation of typical astrocytes. Anaplastic astrocytoma occurs in the cerebral hemispheres - up to 60%, less often in the cerebellum - 15%. In 70% of cases, benign astrocytomas are transformed into malignant astrocytomas. Morphological heterogeneity of astrocytic tumors: heterogeneity of varying degrees was detected in the same tumor tissue. In particular, in 62% of cases, areas with a different morphological picture were detected in one type of glial tumors. This leads to errors in diagnosis with small fragments of tumors. As a result, the probability of error among pathologists in the diagnosis of astrocytic tumors increased to 20%. In studying the morphological picture of astrocytic tumor processes, it is important to study them based on several criteria.

Research and methods:

150 patients with different histologically dangerous astrocytic tumors (diffuse astrocytoma (fibrillary, protoplasmic, gemistocytic), anaplastic astrocytoma) who underwent surgery at the Republican Center for Neurosurgery between 2016 and 2020 were randomly selected, their histological results were analyzed, and tumor tissues from 40 patients were studied for their characteristics using traditional histological and histochemical methods. In this case, astrocytomas with a degree of danger II (G) (n=20) and with a degree of danger III (G) (n=20) were analyzed.

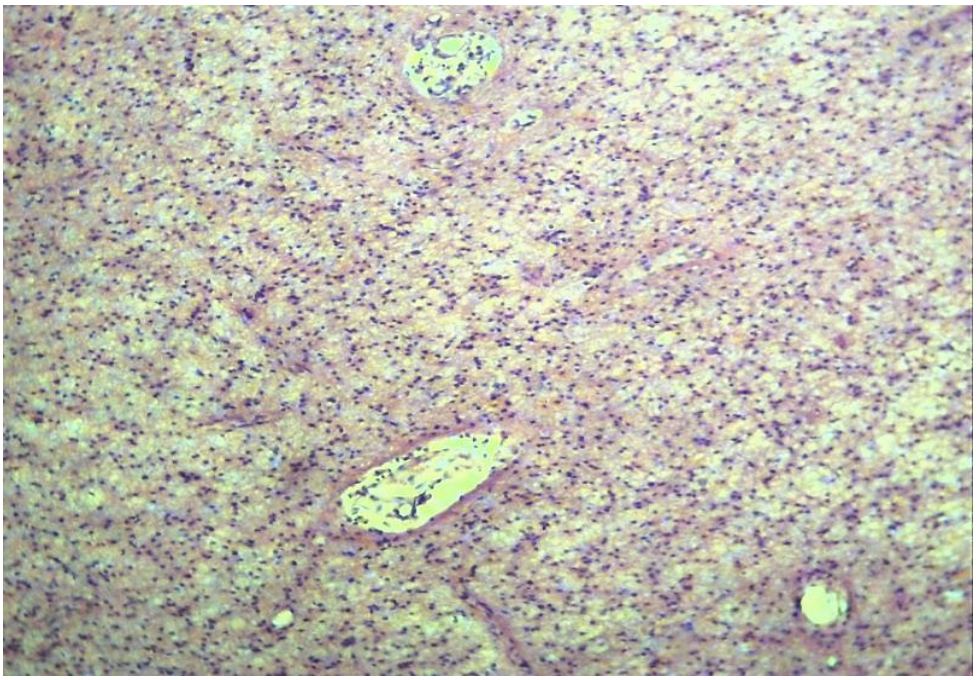
For general morphological examination - hematoxylin and eosin staining, morphological features of the tissue composition - atypia, proliferative and mitotic activity, hyperplasia, morphological characteristics of blood vessels, and methods for assessing the degree of tumor risk according to the Grades (G) criterion were used.

Histochemical method - staining of sections obtained by the Nissl method with toluidine blue - This method allows you to assess changes in nerve cells in normal and pathological conditions (tigroid flocculation, tigrolysis, cytoplasmic vacuolization, etc.), as well as the state of glial elements. Sections with a thickness of approximately 6-8 μm were taken from the embedded paraffin blocks. The obtained sections are processed from deparaffinization to the final rinsing stage with distilled water. In this case, the samples are kept in 3 xylenes, 3 960 ethyl alcohols and 1 700 ethyl alcohols for 3-5 minutes each, and then in distilled water for 1-2 minutes. In the next stage, the sections are immersed in a 0.1% toluidine blue solution and heated to +50+55C0 until steam is formed, but it should not boil. After the formation of colors in the sections, they are rinsed in distilled water, dried through filter paper, and a drop of vitrogel liquid is applied and the coverslip is closed. Result: the cytoplasm of ganglion and glial cells is light blue, the fibrous structures of the brain substance are not stained.

Histochemical method - Azan staining according to the Heidenhain method - This technique is carried out using two dyes: azocarmine and aniline blue. In this case, the prepared sections were mounted on glass slides and then placed in distilled water. Reagent A was incubated in a flask at +55°C for 45 minutes, cooled

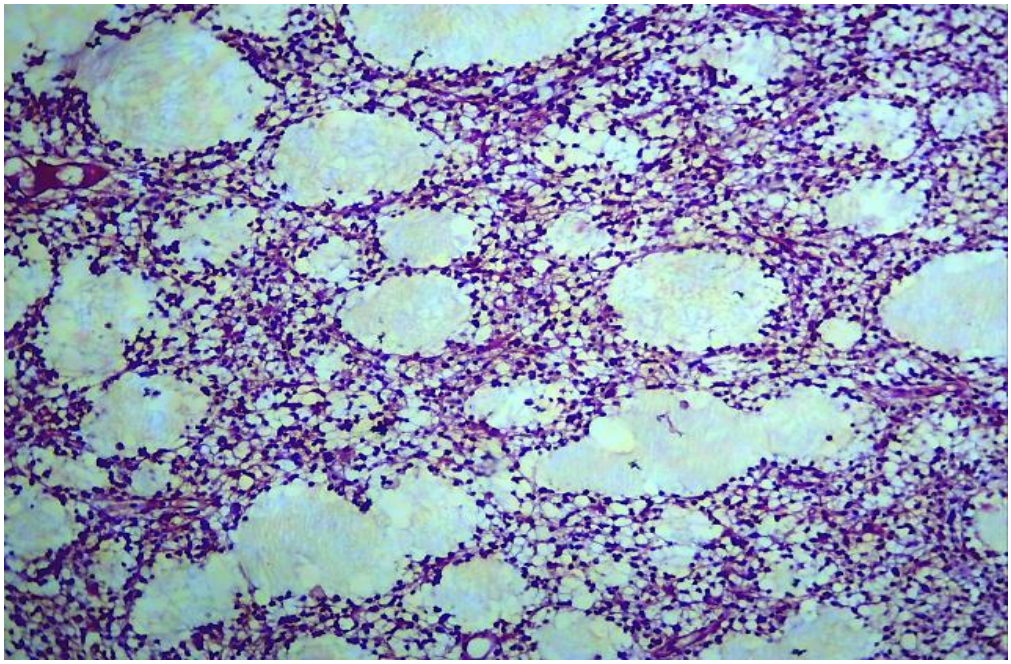
to room temperature and poured back into the flask, the sections were washed again in distilled water. 10 drops of reagent B were poured onto the sections and left for 1 minute, 10 drops of reagent C were poured onto the sections and waited for another 1 minute, the glass slides from which the sections were taken were placed in a container with reagent D for 1 hour and dried through filter paper and placed in reagent E, the sections were washed in a 96% solution of ethyl alcohol, the colors were clarified with xylene, vitrogel liquid was added and the coverslip was closed. The obtained result was a dark red neuroglial tissue.

Results and their discussion: Morphological features of diffuse astrocytomas in general morphological examinations by hematoxylin and eosin staining: The morphological picture of fibrillar astrocytomas is a fibrillar mesh-shaped and oval or irregular shape of various sizes, monomorphic, hyper or hypochromic nuclei are scattered, the cell body is located in various positions and mitosis is absent, proliferation of blood vessel endothelium is observed, small cystic spaces, in rare cases calcification foci are scattered or focal, the cytoplasm is dim and poorly expressed. (Pic. 1).



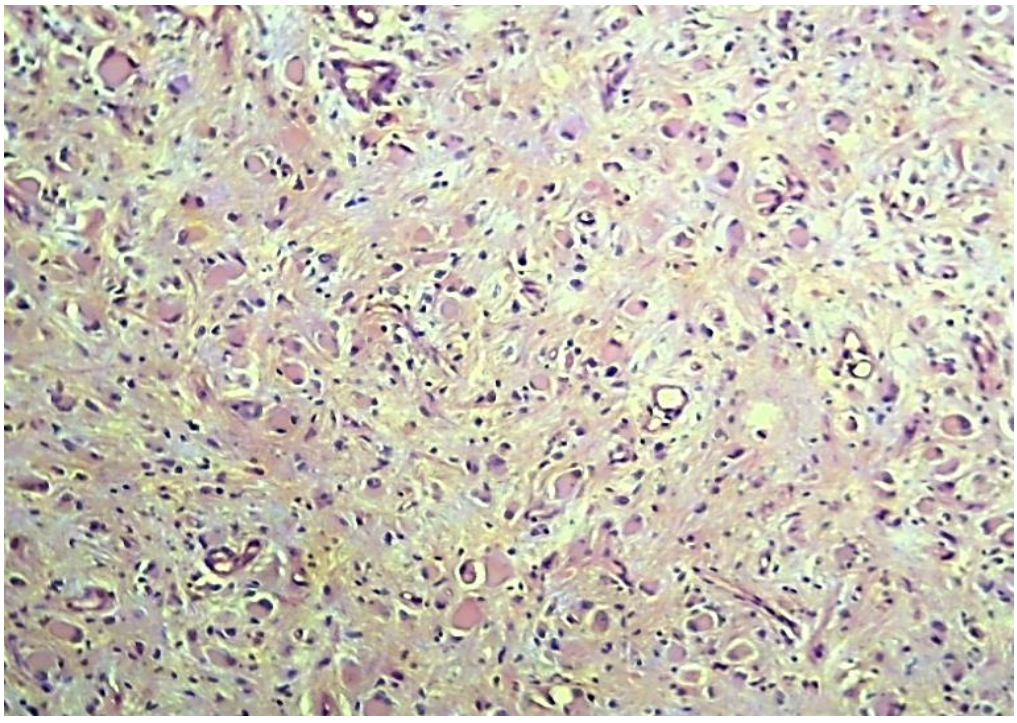
Pic. 1. Fibrillary astrocytoma - astrocytes are hypertrophied, oval or irregular in shape, monomorphic, hyper or hypochromic nuclei of various sizes are scattered, the cytoplasm is poorly expressed (Grade -II). Hematoxylin-eosin. Ob10. Ok 10.

Protoplasmic astrocytoma - arising from protoplasmic astrocytes, located mainly in the gray matter, that is, in the area of neurons. Contains a large amount of glycogen in the cytoplasm. The cells are close to normal or hypertrophied, with cystic spaces of various sizes, presenting a morphological picture (Pic. 2).



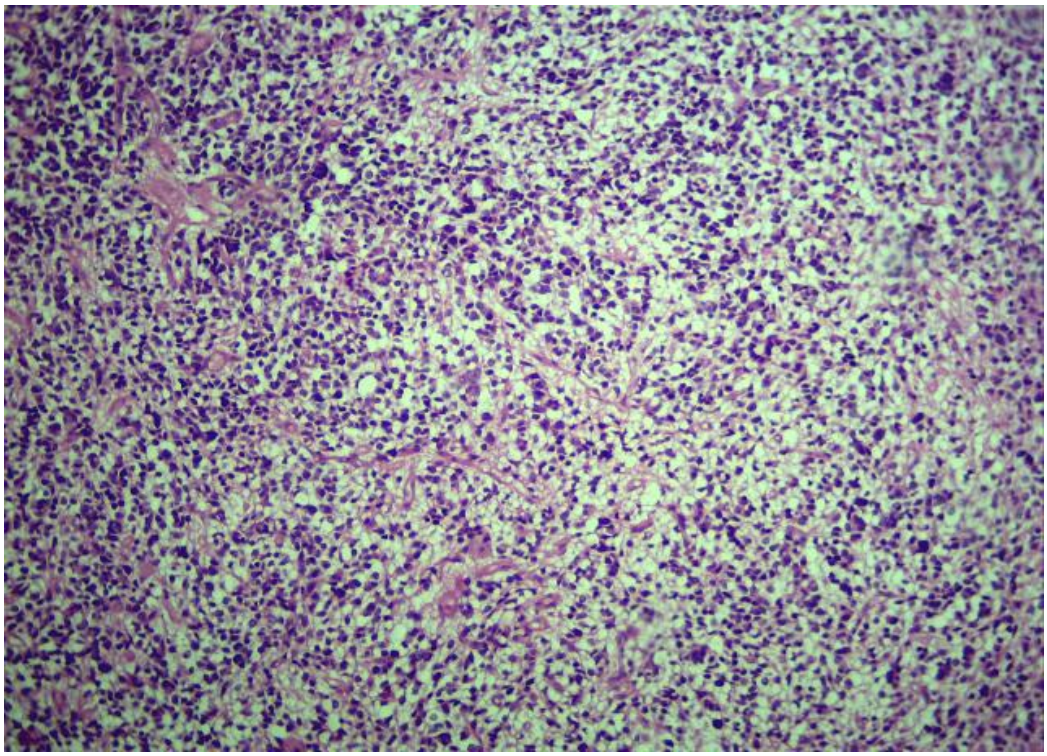
2. Pic. Protoplasmic astrocytoma - astrocytes are close to normal or hypertrophied, expressed by cystic spaces of various sizes (Grade -II). Hematoxylin-eosin. Ob10. Ok 10.

Fat (large) gemistocytic astrocytoma - A tumor arising from protoplasmic astrocytes, more often fibrillar - protoplasmic astrocytes. In the morphological picture, the astrocyte is characterized by a significant enlargement of the cell body, eosinophilic staining and hypertrophy of the cytoplasm, normal or slightly enlarged and eccentric location of the nucleus (Pic. 3).



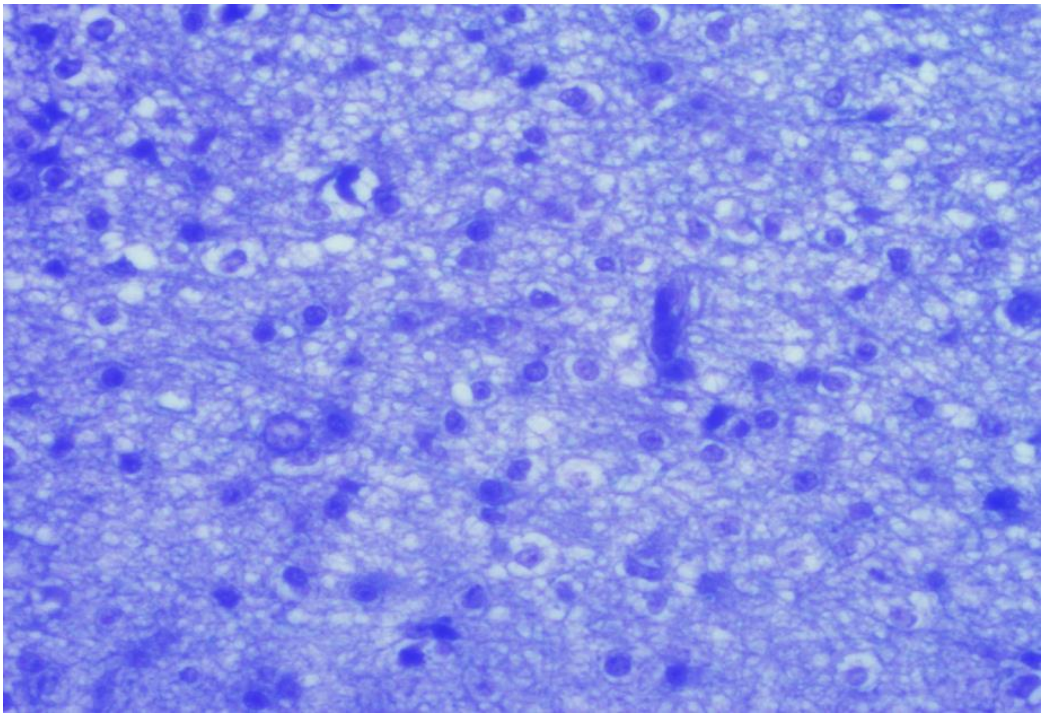
Picture 3. Fat (large) gemistocytic astrocytoma - hypertrophy and hyperplasia of astrocytes with eosinophilic staining of the cytoplasm and eccentric location of the astrocyte nucleus (Grade -II). Hematoxylin-eosin. Ob10. Ok 40.

Anaplastic astrocytoma - characterized by diffuse expression of atypical astrocyte cells and preservation of typical astrocytes. Polymorphism of astrocytes and hyperchromia of the nuclei, atypical mitoses, proliferation of the vascular endothelium, focal necrosis in the form of "pseudopolysade", small papillary structures, and in some cases lymphocytic infiltration are observed. The morphological picture of anaplastic astrocytoma resembles fibrillary or protoplasmic astrocytoma, but differs from them in that it is characterized by dense clusters of atypical cells and an increase in the appearance and number of nuclei, hyperchromia, chromatin dispersion, various sizes, irregular shapes, and an abundance of glial fibers. In some cases, the cytoplasm is dim, the cytoplasmic-nuclear ratio is shifted towards the nucleus, and in some cells, the nucleus occupies the entire cell (Pic. 4).



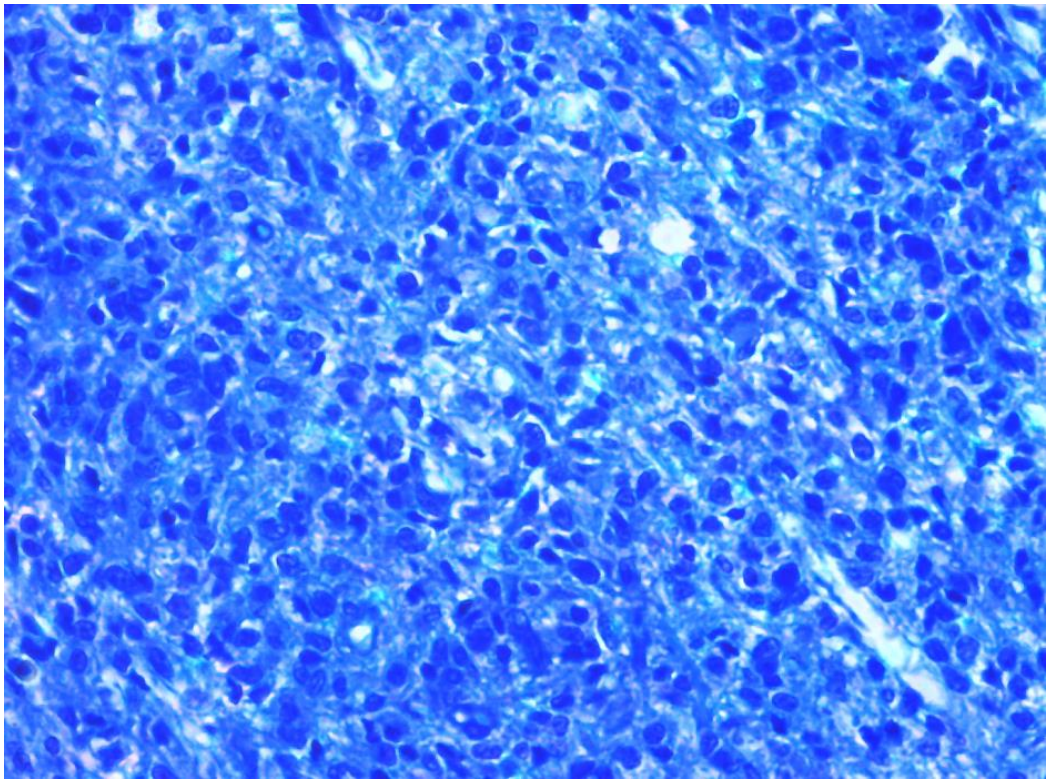
Pic. 4. Anaplastic astrocytoma - astrocyte polymorphism and hyperchromia of the nuclei, proliferation of the microvascular endothelium. (Grade -III). Hematoxylin-eosin. Ob10. Ok 10

According to the results of histochemical methods, diffuse astrocytomas have well-formed fibrous structures and scattered cell locations, while neuroglial structures are relatively unchanged, less vacuolization is observed at the periphery of neurocytes, and significant hyperplasia is formed in glial cells (Pic. 5).



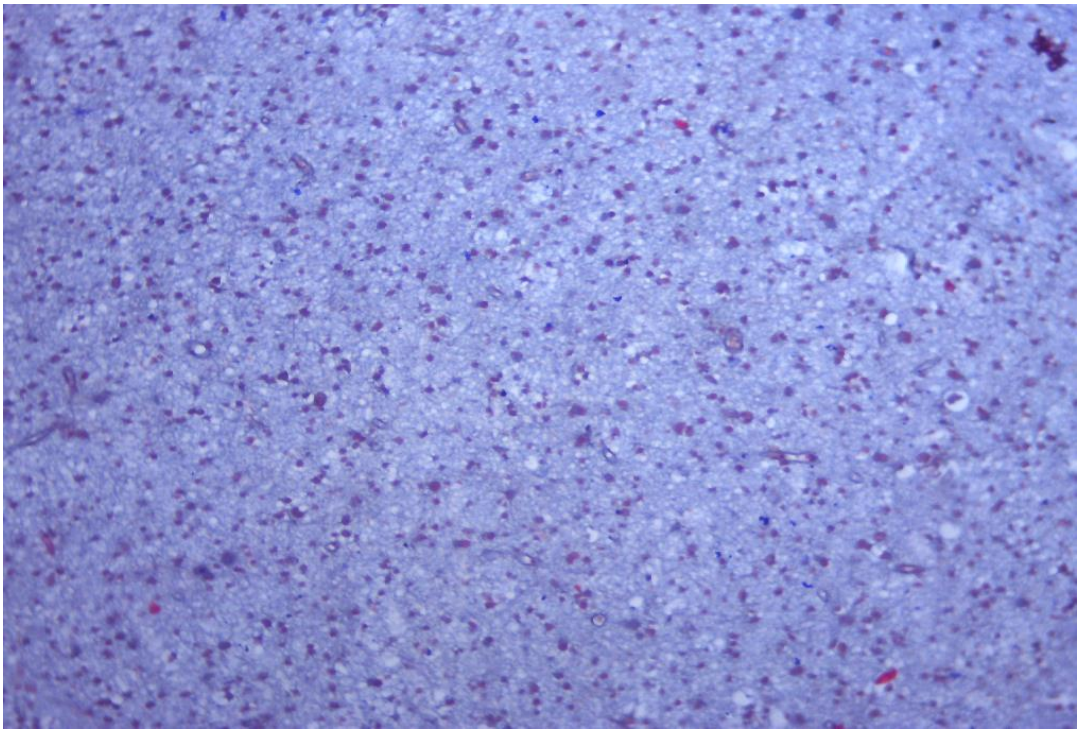
Picture 5. Diffuse astrocytoma. Toluidine blue. Ob10. Arrow 10.

In anaplastic astrocytomas, fibrous structures are hardly detected, polymorphism, hyperplasia and hypertrophy of astrocyte cells, eccentric arrangement of nuclei, cytoplasm is light blue, nucleus is dark blue. Around the atypical astrocyte cell, small undifferentiated cells of dark blue color with undifferentiated cytoplasm are detected (Pic. 6).

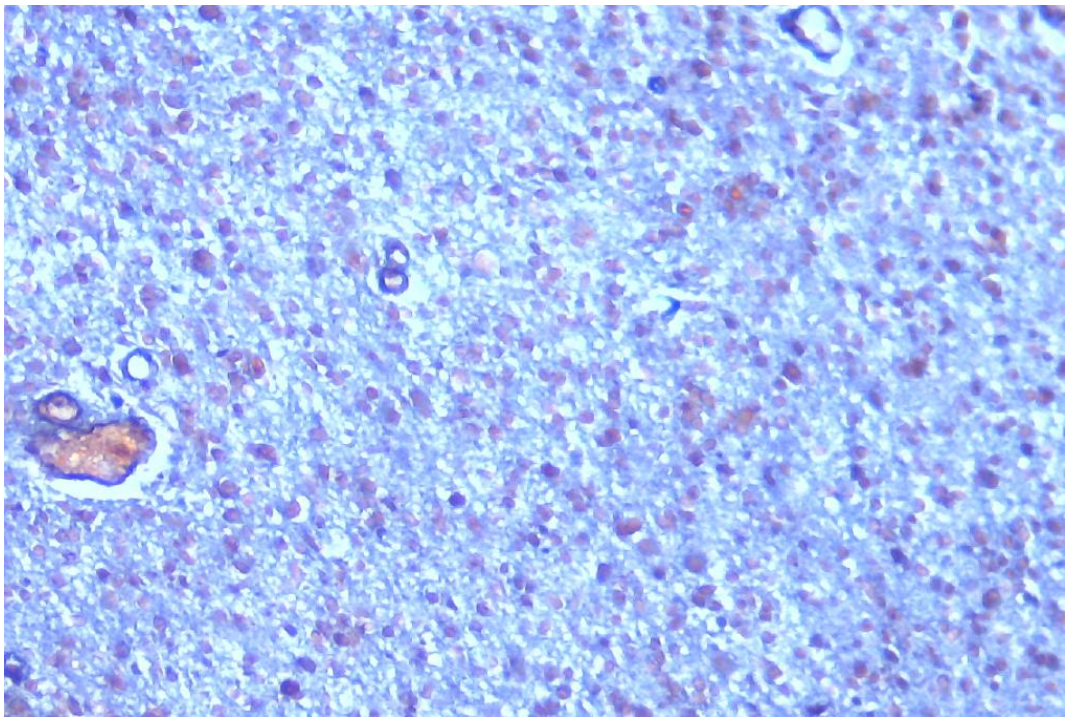


Pic. 6. Anaplastic astrocytoma. Toluidine blue. Ob10. Ok 40.

On Azan staining, morphological changes in astrocytomas presented an almost uniform picture, with a predominance of microvessels in diffuse astrocytomas, glial cells in a reddish color, fibrous structures in a light blue color, and the formation of dark blue fibroblast cells in the walls of some blood vessels (see Fig. 7-8 for Azan staining of astrocytomas).



Pic. 7. Diffuse astrocytoma. Azan paint. Ob10. Arrow 10



Pic. 8. Anaplastic astrocytoma. Azan Ob10. Arrow 10

The types of blood vessels in the anaplastic astrocytoma tissue were as follows: the predominance of the capillary vascular system along the periphery of the tissue was 55-60%, the ratio of vascular clusters and vascular groups in the peritumor zone was alternating, in the center of the tissue there was a high prevalence of vascular clusters and vascular groups (75%), the appearance of vascular wreaths around the foci of necrosis, as reported in the literature, was 60%, while vascular clusters and vascular vessels were detected in small quantities (25%). Considering that morphologically AAs represent the picture (heterogeneity) of other astrocytoma tumors of the glial series, in the AAs that expressed the picture of diffuse astrocytoma (Grade) in the analyses - high mitotic activity and pronounced atypia in the cell nucleus in 80% of cases, pronounced atypia in the cell nucleus marked necrosis foci and proliferation of vascular endothelium was found in 17%, low proliferative activity, clearly expressed necrosis foci and proliferation of vascular endothelium - 2%, high mitotic activity - up to 3%. In AAs of hemistocytic and plemorphic astrocytoma, mitotic activity and atypia in the cell nucleus is 90-95%, the ratio of the nucleus to the cytoplasm is 3/1, and the proliferation of necrosis and vascular endothelium was almost not observed.

Conclusion: According to the results of traditional staining methods, in the morphological heterogeneity of anaplastic astrocytoma, a high proportion of diffuse astrocytomas was found, followed by pleomorphic and hemistocytic astrocytomas. The use of histochemical methods in conjunction with traditional methods in astrocytomas can lead to some convenience in assessing their cellular composition. The peritumorality of the tumor tissue and the occurrence of spheroid blood vessels in the center of the tissue are associated with neoangiogenesis, i.e. the formation of new blood vessels. Blood vessel wreaths are more often visible around the foci of necrosis, and the initial stage of proliferative processes in the endothelium was detected.

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