Research article

Evaluation of the correlation between glioma and a peritumoral edema zone

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ABSTRACT

Introduction and Aim: Peritumoral brain edema (PTBE), which is based on the interplay of vascular and parenchymal components, is the most frequent response that spontaneously arises in brain tumors. The goal of this study was to compare the dynamics of perifocal pathogenesis before and after surgery utilizing medication correction, as well as the relationship between glioma and the peritumoral edema zone.

Methods: 500 patients with gliomas had clinical and morphological evaluations before and after surgery; each patient's operation was based on their unique histogenesis, levels of malignancy, size, and placement.

Results: In this study, big meningiomas and other benign tumors do not exhibit PTBE, whereas gliomas do. However, there is no correlation between the size of the glioma and the severity of PTBE. Malignant brain tumors and benign tumors have a positive link with tumor histogenesis, but benign tumors have a negative correlation with PTBE severity. At the same time, we discovered a substantial inverse relationship between the density of gliomas and the severity of PTBE.

Conclusion: The degree of gliomas and variations in the amount of free and bound water in the red cell mass and density are positively correlated with the severity of the peritumoral edema zone.

Keywords: Peritumoral brain edema; peritumoral edema zone; glioma; red cell mass; correlation.

INTRODUCTION

B ecause of correlation analyses between factors related to morphology, histology, waterelectrolyte, and hydroionic homeostasis, as well as neuroimaging tests including ultrasound dopplerography, computerized tomography, and magnetic resonance imaging (MRI). In neurooncological patients, a correlational connection was formed that enabled researchers to learn more about the tumor's histological characteristics, including its size and density, as well as how severe the peritumoral edema zone (PEZ; 1–5) is.

According to numerous studies, the clinical signs and symptoms of brain tumors vary and are brought on by a variety of factors, including the tumor process itself as well as the responses of the brain tissue surrounding the tumor to abnormalities in the dynamics of the hemo- and cerebrospinal fluid as well as the waterelectrolyte balance. Peritumoral brain edema (PTBE), which is based on the interplay of vascular and parenchymal components, is the most frequent response that spontaneously arises in brain tumors (6– 11).

The clinical course and prognosis of the disease in brain tumor disorders are significantly influenced by the PEZ status. We believe that the comparison of physicochemical and neuroimaging data is of practical significance since it enables us to learn more about the pathophysiology of PTBE as well as the structural features of the tumor. When this occurs, it can more precisely assess the edema's extent and kind, which is crucial for selecting an appropriate decongestant medication during the patients' preoperative care and when organizing surgical operations (3, 9, 11–13). This study used medication correction to assess the relationship between gliomas and the peritumoral edema zone as well as the dynamics of perifocal etiology before and after surgery.

MATERIALS AND METHODS

Between 2016 and 2021, the Department of Neurosurgery of the National Hospital under the Ministry of Health of the Kyrgyz Republic conducted clinical and morphological investigations on 500 patients with gliomas prior to and after surgery.

All patients underwent surgery for gliomas that varied in histogenesis, malignancy, size, and location. The ages of the patients ranged from 18 to 75 years, with 228 females and 272 males averaging 42.49 ± 3.42 years. 220 (44%) of these individuals had malignant brain tumors, while 260 (56%) had benign ones. MRI of the brain by Philips Ingenia 1.5T MRI system (Philips, Amsterdam, Netherlands) with a 15 ml gadolinium-based contrast agent (T1 AX, T2 AX, FLAIR COR, T2 SAG, FLAIR COR, FLAIR SAG, and DWI modes), intraoperative examination of tissue structures of the PEZ and microcirculation vessels of the cerebral cortex over healthy and affected areas using transcranial Doppler examination, Digi-Lite Histomorphological research was conducted using a modular microscope (MIKMED, Russia). At 1.5 cm from the tumor, during a tissue biopsy of the white matter of the brain in the PEZ, prominent alterations were readily washed away by a stream of saline fluid fixed in 10% neutral and acidic formalin fixator. The sections were cut to a thickness of 7-8 microns using standard techniques and stained with conventional stains. The tissue water content was determined by dehydrating to a constant mass, and the sodium, potassium, lipid, and trace element content was determined by ozonation.

The collected data are displayed as the mean standard deviation. Excel.XLSTAT v2020.1 (Microsoft, Addinsoft, France) was employed for the statistical analysis. The Mann-Whitney test was used to determine the significance of group differences. For correlation analysis at the level of statistical significance (p > 0.05), Pearson's chi-squared test,

Spearman's rank correlation coefficient, Student's ttest, and Wilcoxon signed-rank test were undertaken. The collected data were kept confidential, and the I.K. Akhunbaev Kyrgyz State Medical Academy Bioethics Committee endorsed this study (Protocol No. 3 dated May 25, 2020).

RESULTS

The PEZ was split into three zones based on structural, histological, and water-electrolyte changes. The first border zone with the tumor is the zone of apoptosis, the second is the zone of inflammation in the PEZ, and the third is the zone of reactive change. To figure out how bad PTBE is in gliomas, we did an MRI-based association study between the size and density of the tumor and how bad PTBE is.

There was a positive correlation between the severity of the PEZ and the amount of free and bound water in the red cell mass. When there is more free water in the red cell mass of the blood of people with brain tumors, the PTBE goes up to 4–5 points (Fig. 1), and when there is more bound water in the red cell mass, the severity of the PEZ goes down to 1–2 points (Fig. 2). On a range of one to five, one point meant light PTBE, two points meant moderate PTBE, three points meant severe PTBE, four points meant very severe PTBE, and five points meant extensive PTBE.



Fig. 1: Positive correlation between the higher severity of the PEZ and the lower free and bound water content in the red cell mass



Fig. 2: Negative correlation between the higher free and bound water content in the red cell mass and the lower severity of PTBE

In this study, the size of the neoplasm does not associate with the intensity of PTBE. Large

meningiomas and other benign tumors do not show PTBE (Fig. 3), but gliomas do (Fig. 4).



Fig. 3: Large meningiomas and other benign tumors showing no PTBE



Fig. 4: Gliomas showing PTBE

The intensity of PTBE has a relationship with how the tumor grew, and this relationship is positive for malignant brain tumors and negative for normal tumors. At the same time, we found a clear link between the intensity of PTBE and the number of gliomas. Figure 5 shows that imaging studies show that the more severe PTBE is, the less dense the tumors are.



Fig. 5: Imaging studies showing lower the tumor density, the higher the severity of PTBE

An MRI of the brain is widely considered the gold standard in the field of neuroimaging. MRI studies have revealed the existence of a brain mass, as well as accompanying changes in white matter such as PEZ. The relationship between PEZ and the primary infiltrative tumor mass of the hyperintense signal on MRI T2/FLAIR images has been studied extensively. PEZ is characterized as edema, which can manifest as either vasogenic or cytotoxic edema. Vasogenic edema is a medical condition characterized by the expansion of extracellular water volume due to the diffusion of plasma from capillaries with an impaired endothelium vessel. Edema can be observed in cases of metastases or non-infiltrative growth of extracerebral tumors. The T2 MR signals surrounding gliomas are typically a result of both vasogenic edema and the infiltration of brain tissue by tumor cells. This phenomenon is commonly observed in cases of hypertension.



Fig. 6: Boundaries of the glioma and the PEZ

The study found that PTBE had an impact on the echogenicity, structure, and area of white matter. Additionally, the ratio of signal intensity at the border of the gray and white matter of the cerebral cortex in edema was observed to decrease to 0.26 ± 0.01 , which was significantly lower than the normal value of 0.31 ± 0.01 (p <0.05) (Table 1). The study examines the relationship between alterations in the echogenicity of the brain substance in the PEZ and factors such as histogenesis and tumor density. Research suggests that there is a correlation between the malignancy and

density of a tumor and the echogenicity of the white matter surrounding it. Additionally, there is a high emphasis on the boundaries between white and gray matter due to the lack of involvement of gray matter in edema. The pattern of furrows and convolutions may also become smoother as a result of an increase in their area. The study determined the diagnostic informativeness indicators of intraoperative ultrasound in detecting brain tissue edema. The sensitivity was found to be 95.3%, specificity was 80.0%, and diagnostic accuracy was 92.4%.

Table 1. Characteristics of utrasound examination of the FEZ of ghoma						
Variables	Cerebral cortex with PTBE					
	Sulcus tissue	Grey matter	Gyrus of the white matter			
Gyrus size (cm)	0.31 ± 0.19	0.51 ± 0.07	1.5 ± 0.45			
Borders	Clear (100%)	Clear (100%)	Clear (100%)			
Echogenicity	Increased (100%)	Decreased (100%)	Increased (100%)			
Structure	Heterogeneous (75%)	Heterogeneous (100%)	Uniform (58%)			
Signal strength	128.0 ± 13.5	24.1 ± 8.3	91.8 ± 15.9			

Table 1: Characteristics of ultrasound examination of the PEZ of glioma

Pulsed-wave Doppler analysis of blood flow in the PEZ, peri-, and intranodular arteries of unaltered brain tissue was carried out. When compared to similar measures of blood flow in perinodular vessels, the

pulsatile and resistive indices in the arteries of the PEZ were significantly lower (p <0.05). Positive associations and statistically significant variations in linear blood flow rates were not seen (Table 2).

Table 2: Indicators of blood flow velocity in the brain arteries in normal conditions and in the PEZ in tu	umors
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Variables	Intact brain	PEZ	Perinodular	Intra-nodular
	tissue		vessels	vessels
Vmax (m/sec)	0.20 ± 0.10	0.14 ± 0.09	0.23 ± 0.14	0.19 ± 0.14
Vmin (m/sec)	0.07 ± 0.04	0.07 ± 0.04	0.08 ± 0.04	0.09 ± 0.06
Vmean (m/sec)	0.11 ± 0.06	0.09 ± 0.06	0.13 ± 0.08	0.12 ± 0.09
Resistive index	0.62 ± 0.05	0.46 ± 0.06	0.65 ± 0.05	0.55 ± 0.08
Pulsatility index	1.05 ± 0.31	0.70 ± 0.15	1.17 ± 0.21	0.94 ± 0.25

As a result of the study, a correlation was observed between changes in the water-electrolyte balance in cells and the intercellular space. Microscopic examination of the PEZ revealed a decrease in the density of the white matter of the brain due to the rarefaction of tissue of varying severity, with the processes of demyelination and damage to nerve fibers and the presence of drainage forms of oligodendroglia. Morphometry revealed a significant decrease in cells in the PEZ relative to other areas of the brain. In the white matter, the mean number of cells was $(96.7 \pm 1.8) \times 10\text{-}3/\text{m}2$, in the PEZ, the mean cellular index was

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decreased by four times $(21.9 \pm 1.1) \times 10-3/m2$. In different PEZs, an increase in water content by an average of 3.6%, accompanied by an increase in sodium concentration characteristic of extracellular edema, as well as a decrease in lipid content, was revealed when calculating the weight of the fat-free substance.

According to our study, there is a positive correlation in the ratio of water, sodium, and lipids. Changes in the water-electrolyte composition in different PEZs were presented in Table 3.

Table 3: Changes in the water-electrolyte composition in different PEZs

PEZ	Water, %	Sodium, mmol/kg	Potassium, mmol/kg	Lipids (g)
White matter at the focus up to 1 cm	$+4.2\pm0.6$	57.0 ± 2.6	49.0 ± 4.5	0.51 ± 0.06
White matter at a distance up to 1–2 cm	$+3.0\pm0.5$	42.0 ± 3.0	45.9 ± 4.6	0.77 ± 0.08

DISCUSSION

The dilatometric method was used to study the fractions of water in whole blood and its components to study the role of PTBE in the clinical manifestations of brain tumors in the pre-and postoperative periods. It is quantitative and can provide a high degree of accuracy in detecting minimal deviations in the ratio of water fractions in body fluids, which objectively reflects the state of brain tissue (8, 14).

The results of this study showed that in the adjacent PEZs to the tumor nodes, there was a significant rarefaction of tissue with the development of large leaf spongiosis up to microcystic transformation, which was accompanied by showing demyelination, fragmentation of axons with a disorderly arrangement of convoluted fragments of myelin fibers with ring-shaped formations.

Vascular Doppler ultrasound was performed in patients with glioma, regardless of histological origin, in this group there were astrocytomas, oligodendrogliomas, glioblastomas, and other gliomas, they were not divided by histological degrees of malignancy. The severity of PTBE was considered according to an MRI of the brain, all patients had PEZ.

Studying the PEZ is important not only for morphologists but also for clinicians, especially neurosurgeons, for successful surgical intervention to remove a glioma. PEZ is a pathological area that performs the same brain functions and, with the wrong approach, creates complications before and after surgery. Some studies describe the migration of tumor cells at the distance of the tumor node in the PEZ and multiple vascular convolutions (14, 15).

In addition to the negative sides, PTBE has several positive useful functions for healthy areas of the brain. PEZ acts as a buffer between the tumor and brain tissue, and performs a drainage function, eliminating the waste products of the tumor tissue (1, 9, 16, 17). Thus, changes in the brain substance in the PEZ of glioma have a complex multicomponent reactive-destructive character, they are represented by axon damage, demyelination, death of glial elements, and rarefaction of the neuropil which was correlated.

CONCLUSION

The degree of gliomas and variations in the amount of free and bound water in the red cell mass and density all positively correlate with the severity of the PEZ. For the selection of a sensible decongestant therapy in the preoperative care of the patient and the planning of surgical intervention, a thorough investigation and evaluation of the extent of edema and its type are of utmost significance.

CONFLICTS OF INTEREST

None.

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