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MECHANISMS OF DEVELOPMENT OF CENTRAL AND PERIPHERAL NERVOUS SYSTEM DAMAGE IN HERPESVIRUS INFECTION

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Abstract:
Today, a serious increase in human viral diseases is observed all over the world, which makes pathological changes in the nervous system one of the common problems. Improving the effective treatment of patients with epilepsy due to post-viral encephalitis by diagnosing the clinical-neurological and neurophysiological features of this disease helps to improve the quality of life of patients and prevent disability, and indicates the urgency of this problem.

Keywords: Viral diseases, herpes infection, human herpes virus, papillomavirus Infections.

Introduction

The urgency of the problem. In order to improve the clinical, neurological and neurophysiological characteristics of acute viral encephalitis complicated by symptomatic epilepsy and the effective treatment procedure, a number of scientific studies have been conducted in the world. In this regard, to determine the pathogenesis of the development of seizures in epilepsy after herpesvirus encephalitis, to assess the severity level and the factors causing pharmacoresistance; to determine the pathogenetic role of the immune state in the development of neurological diseases that occur in different periods; A number of scientific studies are being carried out on the development of algorithms for the diagnosis of neurovisualization changes and comparative diagnostic criteria. Early detection of clinical and neuroimaging features of symptomatic epilepsy in herpesvirus encephalitis and the development of an effective method of treatment of the disease are of particular importance.

Wide introduction of modern methods of neuroimaging in clinical practice (EEG and MRI) in determining the severity of epileptic patterns in patients with

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symptomatic epilepsy after herpesvirus encephalitis (Drobni M., 2020) and in determining the expansion of the internal and external subarachnoid spaces in the brain and the localization of demyelination foci have been assessed (Wanhui Lin et al., 2020). Treatment of herpesvirus infection itself (Shaheen E.L., 2021) and pharmacoresistant epilepsy developed in these patients has been shown to be a serious problem in patients with herpesvirus encephalitis with symptomatic epilepsy (Kaufmann E. et al., 2020).

According to the World Health Organization (WHO), herpes virus infection ranks second among human viral diseases after influenza. Herpes simplex virus type 1 infects about 67% of the world's population, or about 3.7 billion people. About 13% of the world's population is infected with herpes simplex virus type 2.

Human herpesvirus types HHV-6A, HHV-6V and HHV-7 have been shown to cause severe encephalitis or encephalopathy, leading to death due to organ dysfunction, including damage to the limbic system, brainstem and hippocampus (Ongrádi J. et al., 2017) . The causative factor of febrile seizures and febrile status epilepticus is often the human herpes virus type 6, in which neurospecific proteins are shown as markers of brain cell damage in various central nervous system diseases (Alekseev L.A., 2021).

An increase in TsMV infection was found with immunosuppression and (or) immunosuppressive therapy (Gizem K.S. et al., 2021). It has also been proven that herpes simplex viruses (OGV) have a large DNA genome, more than 50 HSV-1 or HSV-2 genomes, and are important in early detection due to the difficulty of isolation (Greninger A.L. et al., 2018).

Materials and Methods

100 patients with GVE SE and 20 patients with symptomatic epilepsy of post-traumatic origin who were treated in the neurology departments of the Urganch Branch of the Khorezm Region Multidisciplinary Medical Center and the Republican Emergency Medical Research Center were observed as research material. 70 (58.34%) of the patients selected for the study were women, 50 (41.67%) were men.

The EEG study was carried out in the EEG equipment of the emergency medical hospital of the multidisciplinary medical center of the Khorezm region. For a more

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detailed study, patients underwent EEG examination using Neurosoft (Russia) equipment at the "Umid Shifo" clinic in Urganch (Professor I.A. Kilichev's clinic). Registration of bioelectrical activity of the brain was carried out according to the generally accepted method (Zenkov L.R., 2013). The research was carried out on Neurosoft (Russia) electroencephalographs. The equipment made it possible to record EEG in 16 channels. Recording of background EEG and recording of brain bioelectrical activity was performed with different functional stimuli (opening-closing eyes, hyperventilation, photostimulation with rhythmic light in the range of 3-21 Hz). EEG was evaluated according to the modified classification of patterns. EEG assessed depth-frequency spectra of biopotentials, their manifestation, localization, stability of basic rhythms, identified pathological EEG-activity, paroxysmal forms of EEG activity, assessed brain excitability, determined lateralization and localization of epileptic focus. The electrophysiological study started with regular EEG, and in case of unclear, questionable data, long-term video-EEG monitoring was performed. The correlation of EEG data with the structure of epileptic seizures was studied. Video-EEG monitoring was used to investigate the epileptic nature of seizures, to determine the type and characteristic patterns of seizures. Clinical manifestations of epilepsy were compared with the characteristics of EEG manifestations (localization and structure of epileptic activity). Video-EEG monitoring was performed in 8 patients.

Results and Discussion of Results

Patients with GVE SE were divided into 3 groups, mild, moderate and severe, according to the frequency of epileptic seizures and the severity of the disease. In addition, to compare clinical neurological, immunoenzymatic (IFA) and neurophysiological parameters, patients with symptomatic epilepsy of posttraumatic etiology were included in the comparison group (see Table 1).

Table 1 Distribution of selected patients by groups

Group features	Characteristics of groups	n=210
1 group	Patients with mild GVE SE	31
2 group	Patients with moderate transient GVE SE	13
3 group	Patients with severe GVE SE	56
4 group	Comparison Group (TG)	20
5 group	Main Group (AG)	59
6 group	Control group (NG)	41

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Therefore, we divided these patients into 2 more groups: in addition to increased doses of KBZ to anticonvulsant therapy optimized for AG, the second Zonisamide [6, 46-51; 89, 18-58] drug up to 300-400 mg per day in two doses, and in NG, we studied patients who received anticonvulsant therapy only with optimized doses of KBZ increased to the middle therapeutic level - 800-1200 mg per day in two doses. The average age of patients is 37.3±1.0 years, in men - 37.6±1.5, in women - 37.1±1.3. Table 2 shows the mean age of male and female patients in the groups, and the age of these male and female patients increased from mild to moderate to severe. Also, table 2.2 shows the age composition of the treated group - AG and NG, in this table the average age of the groups is compared with each other (see table 2).

Table 2 Groups of patients selected for the study average age, M±m

Groups	Classification of groups	men M±m	Women M±m	Both genders M±m
1 group	Patients with mild GVE SE	39,5±2,1	33,8±1,6	35,6±1,4
2 group	Patients with moderate transient GVE SE	33,8±4,5	37,0±2,6	34,8±2,9
3 group	Patients with severe GVE SE	41,1±2,0	41,2±2,1	41,1±1,5
4 group	Comparison Group (TG)	29,0±4,2	31,8±3,8	30,7±2,8
5 group	Main Group (AG)	40,1±1,9	38,9±1,9	39,5±1,3
6 group	Control group (NG)	36,9±2,6	37,7±2,1	37,4±1,6
	All patients	37,6±1,5	37,1±1,3	37,3±1,0

A study of seizure frequency in patients with symptomatic epilepsy following herpesvirus encephalitis revealed a wide variation in seizure frequency from newly diagnosed seizures to 2-3 seizures per day.

Thus, 3 (3%) patients had seizures for the first time, 28 (28%) - from 1 time in 2-3 months to 1-3 times a month, 13 (13%) - 4-5 times a month, 49 (49%) - 5-7 times a month, 7 (7%) – from 1 time in 2-3 days to 2-3 times a day. When determining the frequency of seizures in TG, the first seizure occurred in 10 (50%) patients, 7 (35%) once every six months, and 3 (15%) once every 2-3 months. When seizures were examined by sleep-wake cycle, it was found that the majority (88%) had seizures while awake. Aura was not observed in most of the patients we examined. Patients reported that aura was detected in 34% of GVE SE patients and 25% of

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TG patients. In addition, with the severity of epilepsy, the frequency of aura in patients increased.

EEG studies of patients

All GVE with subsequent SE and TG patients underwent EEG during the interictal period. The localization of interictal epileptiform activity (IIEF) was determined and evaluated in the analysis of EEG during the interictal period. We understood this term as sharp waves, spikes, as well as "sharp-slow" wave and "spike-slow" wave complexes, which correspond to the generally accepted frequency and amplitude characteristics. (Zenkov L.R., 2010). EEG studies were performed in all patients with symptomatic epilepsy. GVE was detected as sharp-wave activity in EEG in patients with subsequent SE. Spikes were observed in 38 (38%) patients, acute slow-wave activity was observed in 43 (43%) patients, and spike-slow-wave activity was observed in 19 (19%) patients.

Our patients had mono-, di- and multifocal epileptiform foci in the brain. The distribution of these foci in patients with GVE post-SE depending on the severity of epilepsy is clearly shown in Figure 1, where it can be seen that the tendency of epileptogenic foci to increase with the severity of the disease in patients was determined, which indicated the appearance of many demyelination foci in the brain and an increase in EEG indicators (see Figure 1).

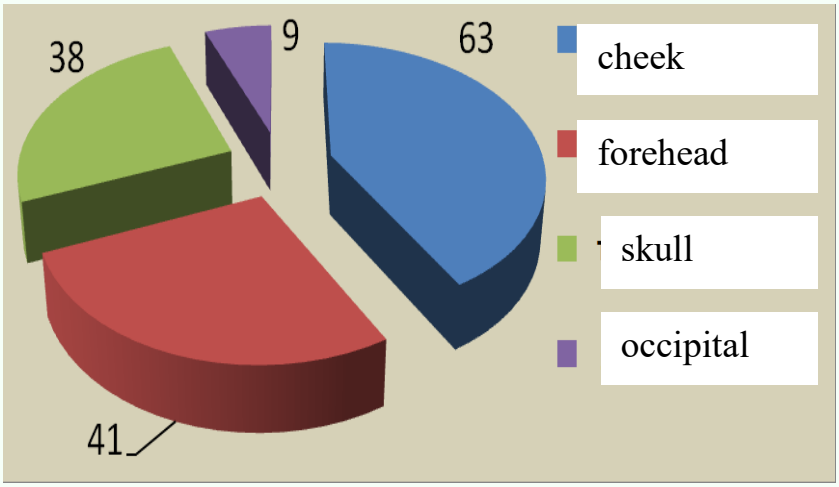

Figure 1. Localization of epileptic foci in patients along the brain

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Foci of pathological activity were noted in different areas of the brain, multifocal foci were noted in some patients. When GVE analyzed the distribution of epileptic foci across the brain in EEG patients with subsequent SE, its main localization was shown in the temporal (63 foci) and forehead (41 foci) and to a lesser extent in the top (38 foci) and nape (9 foci) areas (Fig. 3.2). In 20 patients of TG, EO' was mainly localized in the forehead - 10, temple - 6, crown - 2 and nape - 2. Thus, during the study of EEG in the interictal period, in patients with SE after GVE, mono- and difocal foci in the form of spikes and sharp-slow wave complexes were more pronounced in the temporal and forehead areas, and a tendency for these indicators to worsen in patients with a severe degree of SE was revealed.

Summary

Neurological symptoms of symptomatic epilepsy after herpesvirus encephalitis, in addition to various forms of epileptic seizure attacks, the presence of scattered microsymptomatics and mild changes in the brain, in the form of cognitive changes (95%), vegetative dysfunction (52%), mild movement disorders (20%), sensation (15%)) and cerebral (15%) are characterized by disorders.

During neuroimaging of patients, epileptic foci were often detected in the temporal-forehead areas, demyelination areas (forehead and temporal areas, subcortical-amygdala body, hippocampus, hypothalamic nuclei, thalamus) and slight expansion of the external and internal cerebrospinal fluid spaces were detected.

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