

Factors of Damage to the Nervous System in Herpes Virus Diseases

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Abstract: Herpes is one of the most common uncontrolled human viral infections. Despite the fact that herpes has been known for more than 2000 years, only in the last decade has a real possibility of organizing effective herpes therapy appeared. Some infected individuals may have mild symptoms in the form of fever, adenopathy, or general infectious manifestations. Usually, HSV1 infection is not epidemic and occurs sporadically. In 20-40% of persons infected with HSV1, its spontaneous reactivation is observed in the form of rashes on the face.

Keywords: Hepatitis, chronic encephalitis, Schwann cells.

Etiology and epidemiology. The cause of the development of HE in adults and children older than 1 half a year of life is HSV1. The virus circulates widely in all age groups. Many laboratory animal species are susceptible to HSV1 infection. HSV1 is spread by respiratory or contact (through saliva) route. Primary infection is usually asymptomatic, sometimes observed in the form of a respiratory syndrome, pharyngitis, gingivostomatitis. Relapses of skin herpes in 5% of patients are observed with a frequency of about 1 time per month, in 60% - no more than 1 time per year. Various infectious diseases, emotional distress, and nonspecific factors can provoke rashes. In some patients, the appearance of rashes is associated with certain irritants. Reactivation of the virus in the central nervous system can occur without skin rashes. In 1-3% of healthy people, the virus is isolated from the nasopharynx at different times of life, which indicates a high frequency of asymptomatic carriage of the virus. More often this occurs in people with various non-specific diseases or in a state of stress, so the isolation of the virus from the nasopharynx does not serve as direct evidence of the connection of the disease with this pathogen. The ability of herpes simplex viruses type I and II (HSV1 and HSV2) to infect many organs and tissues of the human body causes a wide variety of manifestations of herpes infection (ophthalmo-herpes, stomatitis, hepatitis, interstitial pneumonia, proctitis, mono- and polyneuritis, neuralgia, meningitis and encephalitis, esophagitis, genital and skin herpes, Kaposi's eczema, herpes of newborns). Among the most formidable diseases caused by the herpes simplex virus, and accompanied by high mortality and disability of surviving patients, are acute and chronic encephalitis (HE) [1,3].

HE is the most common CNS infection in Europe, North America and Central Asia. Its share in the structure of viral encephalitis is about 20%, and the frequency is from 2 to 2.5 cases per 1 million population per year. From 1000 to 2000 cases of HE are registered annually in the United States, however, the epidemiology of chronic HE has not been studied enough to date, including in the Republic of Uzbekistan. Mortality in chronic HE in untreated cases reaches 80% or more, exceeding that in other viral encephalitis. A large number of severe complications from the neuropsychic sphere makes it necessary to pay even more serious attention to this form. The incidence of GE is usually uniform throughout the year. Some researchers note that the age distribution of the disease most often covers 2 groups: between 5 and 30 years and over 50 years. HSV1 is the cause of GE in 95% of cases.

In the vast majority of individuals, HSV can persist in the ganglia of the cranial nerves in a latent state indefinitely without clinical manifestations (activating in 20-40% of infected individuals in the form of relatively harmless recurrent herpes labialis). In a small proportion of patients, the latent infection is reactivated with transformation into acute or chronic HE. The reason for this outcome is unknown. The study of the state of the immune system in patients with HE did not reveal serious immune defects. The frequency of skin recurrent herpes in these individuals did not differ from the frequency and population. In some cases, GE may be the result of reinfection [1,2].

It is also known that primary infection with HSV can occur both during fetal development and at the time of birth, if the woman in labor has genital herpes. A patient with herpes of any localization can serve as a source of infection not only during the height of the disease or its remission, but also in the "prodromal" phase, when burning or itching appears, atypical rashes for herpes are still absent. Sero-epidemiological studies have shown that by the age of 13-14, 70-85% of children are already infected with the herpes simplex virus, and at the age of 50, more than 90% of the population is infected.

The pathogenetic mechanism of herpetic infection is based on the development of a latent infection in sensitive ganglia. The localization of latent herpes infection in the ganglia was predicted by Goodpasture in 1929 and experimentally confirmed 42 years later by Stevens and Cook (Klein, 1982) [5]. The main stages of herpes infection are: primary infection of the skin and mucous membranes, "colonization" and acute infection of the ganglia with the subsequent occurrence of latency in neurons. Latent HSV can periodically reactivate in the CNS and in some cases cause recurrent herpetic lesions of the brain. However, the details of this process are not well understood, and methods for early diagnosis of acute and chronic encephalitis need to be optimized. After infection, it may take a long time before the first signs of CNS damage appear.

Herpetic encephalitis often occurs when HSV1 spreads along the nerve pathways, but hematogenous drift can also occur. Migration of HSV1 along the nerve pathways is carried out by axoplasmic transport in ante- and retrograde directions. Such a virus spreads intraaxonally, perineurally, endoneurally, through Schwann cells. HSV1 replicates in neurons and glia. Viral particles penetrating the axon from the skin, epithelium and mucous membranes are sent to the ganglia, then the virus is transformed into the central nervous system. The impact on the body of various factors, such as trauma, surgery, radiotherapy, fever, hypothermia, insolation, increased flow of adrenaline into the blood, high doses of steroids or prostaglandin PGF₂, changes in immune reactivity, lead to the activation of a latent infection. The activating effect of these and a number of other factors is inextricably linked with the violation of the content of cAMP in the cell, the role of which in the implementation of various intracellular processes was established in subsequent years.

Electron microscopic studies revealed HSV in the temporal lobe of the brain in the region of the ammon's horn, in the basal frontal cortex - the most epileptogenic parts of the brain. The defeat of the temporal lobes is due to the fact that HSV from the nasal cavity along the olfactory nerves can penetrate into the brain. In the study of the brain of those who died from GE, using light and electron microscopy, severe lesions are detected in the temporal and parietal lobes, less often in the occipital region. Necrotic changes in neurons and lymphoid-histiocytic infiltration extending into the subarachnoid space are found in various parts of the nervous system. In the glia of the hippocampus, numerous inclusions are noted, in the nuclei - chromatin margination and a significant number of nucleocapsids, as well as empty capsids. In addition, profound changes in the structure of the membranes of these cells are observed, which is the cause of mesial temporal sclerosis, which causes symptomatic drug-resistant epilepsy. The early stages of the process are represented by spongy edema and necrosis, later - by multiple brain defects in the form of cysts. In some cases, pronounced hemorrhages are detected. With a long-term or recurrent process in the brain, simultaneously with gliofibrosis and formed cysts, which are the result of an already completed process, foci of spongy edema, necrosis and fresh foci of brain tissue decay are found, which, upon neuroimaging (MRI, CT), are diagnosed as dystrophic foci of demyelination, without accumulation of a contrast agent (gadolinium).

Cysts at the site of brain necrosis begin to form on average after 1-1.5 months. from the onset of the disease. A clearer manifestation of the boundaries of the focus during neuroimaging by this time suggests that the reduced density of its central part indicates the formation of a cyst. Regardless of the duration of the study, the foci usually have an irregular or oval shape, often with a clearly defined capsule, which is especially clearly visualized with contrast enhancement. In some patients, a mass effect can be determined in the form of deformation of the system of the ventricles and subarachnoid spaces on the side of the focus and displacement of the median structures in the opposite direction,

which can be erroneously interpreted as a volumetric process (tumor, abscess) or as an acute violation of cerebral circulation.

The clinic of primary herpetic infection is very diverse. The incubation period lasts from 2 to 12 days. Antibodies in the blood appear a few days after infection, their maximum accumulates by 2-3 weeks. In newborns, generalization of infection with a characteristic clinical picture is observed. HSV and maternal antibodies are passed to the fetus through the placenta. Maternal antibodies are transmitted to newborns through mother's milk. However, despite this, children are not always immune, even if women in labor have a high level of antibodies [3].

Clinical forms of damage to the central nervous system. The most common form of HE is acute meningoencephalitis with a predominant lesion of the anterior parts of the cerebral hemispheres. Encephalomyelitis, meningitis, myelitis, and other forms of damage to the nervous system caused by HSV1 have also been described. Some authors cited cases of HE with predominant stem localization of the process. HSV1 is also considered one of the causes of acute disseminated encephalomyelitis (ADEM) and encephalomyelorradiculitis. At present, the involvement of HSV1 in the genesis of neuritis of the facial nerve has been proven. Approximately 10-15% of patients may have deviations from the typical course in the form of an abortive, stroke-like or protracted nature of the disease [1,2].

The clinic of GE is very similar to the clinic of other viral encephalitis. Acute GE develops rapidly, the temperature rises, there is a sharp headache, repeated vomiting. Meningeal symptoms appear early. In the cerebrospinal fluid, pleocytosis is noted with a predominance of lymphocytes (from several tens to 1000 cells in 1 μ l or more), an increase in the amount of protein (up to 0.9 - 1.0 g / l). CSF pressure increased. His sanitation lags behind the clinical symptoms of meningoencephalitis, changes in the cerebrospinal fluid may persist for several weeks after recovery.

When describing the clinic and pathological anatomy of HE, many researchers point out that along with HE with necrosis of the temporal lobes of the brain, milder forms may occur. GE have an unfavorable course and are fatal in 50-90% of cases. Residual effects, often in the form of severe lesions of the central nervous system, remain in about 50% of those who have been ill [1, 5].

In a number of cases of HE, mental disorders are observed in the form of negativism, hallucinations (visual, olfactory, auditory), delirious syndrome, Korsakov's psychosis, schizophrenia-like conditions, etc. Focal brain disorders are characterized by damage to the frontotemporal and (less often) parietal lobes and manifest themselves in the form of memory disorders, aphasia, dyscalculia, dyspraxia, intellectual impairment, etc. Quite often, various depths of paresis, mainly of a spastic nature, are observed. The appearance of mental disorders at the onset of the disease can lead to the erroneous referral of such patients to psychiatric hospitals with diagnoses of acute psychosis, fibril schizophrenia, delirium tremens, etc. [2].

According to some authors, some of the patients with psychiatric diagnoses actually suffer from mild forms of subacute subclinical HE, and these undiagnosed forms of the disease are much more common than expected. In patients after the prodromal period, against the background of fever, excitement often appears, orientation in place and time is lost, gross thinking disorders in the form of fragmentation, incoherence join, fragmentary hallucinations, catatonic syndromes are noted. Since focal neurological symptoms may be absent or transient in the initial stages of HE, these patients are often diagnosed with psychiatric diagnoses, most often they are diagnosed with schizophrenia.

Difficulties in the differential diagnosis of HE are exacerbated by the fact that often emotional stress precedes the development of the disease. After the appointment of neuroleptics in patients, as a rule, catatonic stupor, mutism or epileptic seizures develop. In the midst of GE, the development of amentia is possible, often the disease is fatal. In most of the cases described, the assumption that the patient does not have schizophrenia, but an organic disease, occurs with doctors only after the patient has seizures.

There have also been cases of recurrent course of encephalitis. In the case described by M. L. Shearer, S. M. Finch [6], the boy had 17 episodes of organic psychosis over three years, which always occurred

against the background of relapses of herpes stomatitis. The duration of psychotic states was from seven to twelve days, they usually occurred a few days after the onset of herpetic eruptions.

The diagnosis of HE in psychiatric clinics was confirmed either by a significant increase in the concentration of anti-herpes antibodies during the course of the disease, or an accurate diagnosis was made after a brain biopsy and HSV obtained directly from the brain cells. In some cases, the diagnosis was based on a histopathological examination, sometimes the diagnosis was made post-mortem, based on the appearance in the brain cells of intranuclear inclusions characteristic of HE lesions. In the case of the death of patients, macroscopic examination of the brain showed signs of hyperemia and cerebral edema, pinpoint hemorrhages were found on the section of the brain.

Histopathological examination revealed foci of necrosis, signs of dystrophy and swelling of neurons, perivascular infiltration by lymphocytes and plasma cells. In typical cases, characteristic acidophilic intranuclear inclusions were found in astrocytes and neurons. It is obvious that psychopathological symptoms in viral lesions of the brain are largely determined by the localization and degree of damage to the brain structures.

Psychopathological symptoms are caused by subtle and partial changes in the temporal lobe of the brain, while the relative morphological preservation of brain tissues is required, the absence of gross organic destruction with a predominance of functional dynamic disorders.

The high susceptibility to pathological processes of the limbic structures of the brain, especially to HSV, is explained by the fact that the most intense metabolism occurs in the hippocampus region compared to other areas of the brain. In this part of the brain there is the most intensive protein synthesis. Viral DNA can be included in the cellular genome, which transmits information to the apparatus that reproduces the cellular protein. Chronic HSV infection in this region of the brain can lead to impaired protein synthesis and, as a consequence, to functional dynamic disorders in the limbic system of the brain. Cellular enzyme systems can be irreversibly damaged, while neurons remain alive and look completely normal on microscopic examination. At the same time, obviously, the violations of the molecular structure of proteins caused by HSV infection cannot be detected by standard morphologically oriented methods. A change in the molecular structure of the brain cell protein can cause the development of an autoimmune process, which may play a significant role in the pathogenesis of the disease [4].

Conclusion. Thus, HSV usually manifests itself as an acute infection, but the tendency of this virus to remain in the tissues for a long time in a latent state with periodic relapses makes this division of herpes infection into acute and chronic forms conditional. The transition of HSV neuroinfection to a chronic state is the main factor in the development of impaired functioning of the limbic region of the brain.

References

1. Artikova M. A., Djurayeva D. N. Clinical and anamnestic risk factors for the development of symptomatic epilepsy in infantile cerebral palsy //Web of Scientist: International Scientific Research Journal. – 2021. – T. 2. – №. 10. – C. 29-34.
2. Abdurahimovna N. N. Electroencephalography in the Diagnosis of Symptomatic Epilepsy in Patients with Infantile Cerebral Palsy //international journal of health systems and medical sciences. – 2022. – T. 1. – №. 5. – C. 176-179.
3. Isroilovich A. E. et al. The Role And Importance Of Gliah Neurotrophical Factors In Early Diagnosis Of Parkinson Disease //Texas Journal of Medical Science. – 2022. – T. 5. – C. 1-6.
4. Abdukodirov E. I. et al. Study of bioelectric activity of the brain in patients with neurosensorius deafness //Oriental Journal of Medicine and Pharmacology. – 2022. – T. 2. – №. 05. – C. 10-19.
5. Klein R.J. The pathogenesis of acute, latent and recurrent herpes simplex virus infections. - Arch. virol., 1982, 72, 3, 143-168.

6. Shearer M. L., French S. M. // *Engl. J. Med.* - 1964. - Vol. 27, №10. - P. 494-497.
7. Hikmatovna N. Z. Optimization of treatment of early neurological complications in cardioembolic stroke // *Middle European Scientific Bulletin.* – 2021. – Т. 8.
8. Артыкова М. А., НАБИЕВА Н. А. Нейровизуализационные Характеристики Структурных Изменений Головного Мозга При Детском Церебральном Пара-Личе И Эпилепсии // *Журнал неврологии и нейрохирургических исследований.* – 2020. – Т. 1. – №. 1.
9. Артыкова М. А., Набиева Н. А. Клинико-анамнестические факторы риска развития симптоматической эпилепсии при детском церебральном параличе // *журнал неврологии и нейрохирургических исследований.* – 2021. – №. SPECIAL 1.
10. Artikova M. A., Djurayeva D. N. Clinical and anamnestic risk factors for the development of symptomatic epilepsy in infantile cerebral palsy // *Web of Scientist: International Scientific Research Journal.* – 2021. – Т. 2. – №. 10. – С. 29-34.
11. Артыкова М. А. Клинико-Неврологические Особенности Больных, Перенесших Коронавирусную Инфекцию (Covid-19) // *Central asian journal of medical and natural sciences.* – 2021. – С. 338-342.
12. Abdurakhmanovna A. M., Abdurakhimovna N. N. Content and distribution of haptoglobin phenotypes in children with cerebral palsy complicated by symptomatic epilepsy. – 2021.
13. Artykova M. A., Nabieva N. A. Radiated semiotics of perfusion brain disorders in epilepsy in children cerebral paralysis. – 2020.
14. Artikova M. A., Nabyeva N. A. Complicated symptomatic epilepsy, content and distribution of haptoglobin phenotypes in children with cerebral palsy // *Turkish Journal of Physiotherapy and Rehabilitation.* – Т. 32. – С. 3.