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OUTCOMES OF PANENCEPHALITIS IN CHILDREN WITH DIFFERENT DISEASE DURATION

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Introduction: Panencephalitis is a serious disease characterized by inflammation of the brain. This condition can be caused by various causes, including infections, autoimmune processes, or neurodegenerative diseases. Depending on the etiology, panencephalitis can be classified as primary or secondary, as well as viral, microbial or toxic. One of the forms of panencephalitis is subacute sclerosing panencephalitis (SSP), which usually develops several years after measles and can lead to serious neurological consequences. Diagnosis of panencephalitis includes neuroimaging, cerebrospinal fluid analysis and serological tests. Treatment depends on the underlying cause and may include antiviral, anti-inflammatory, or immunomodulatory drugs. The importance of timely diagnosis and treatment cannot be overestimated, as early intervention can significantly improve the prognosis and quality of life of patients.

Keywords: Panencephalitis, inflammation of the brain, infections, autoimmune processes, neurodegenerative diseases, subacute sclerosing panencephalitis, analysis of cerebrospinal fluid, serological tests.

Subacute sclerosing panencephalitis (SSP) is a serious disease caused by the long–term effects of the measles virus on the central nervous system. The urgency of this problem is increasing due to the increase in the number of measles cases, especially among unvaccinated groups of the population. SSP is characterized by slow but steady progression, which leads to mental degradation, myoclonic convulsions and, ultimately, death [1]. The disease can develop many years after measles infection, and its diagnosis is difficult due to the variability of the clinical picture and the absence of changes in the early stages of magnetic resonance imaging [2]. The importance of measles vaccination cannot be overestimated, as it is the only reliable method of preventing SSP. Modern medicine has not yet developed an effective treatment for SSP, and the main focus is on supportive therapy to alleviate symptoms [3]. Given the potential increase in the number of cases as a result of recent outbreaks of measles, the relevance of the problem of SSP remains high, emphasizing the need to strengthen vaccine prevention measures at the global level.

The etiological agent responsible for the development of SSP, according to modern concepts, is the measles virus, which is an enveloped RNA virus belonging to the genus Morbillivirus of the Paramyxoviridae family. The pathogenesis of SSP includes factors of interaction between the measles virus and the host cell. The measles virus enters the central nervous system during primary infection. It is believed to reach the brain through infection of endothelial cells, possibly during acute exanthemic measles. Trans-synaptic transmission of the virus is also possible. The exact causes of the long-term persistence of the measles virus are unclear.

The morphological manifestations of SSP include inflammation, necrosis and regenerative processes. Brain biopsies taken in the early stages of the disease reveal moderate inflammation of the meninges

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and panencephalitis involving the cerebral cortex, basal nuclei and white matter. The death of neurons is detected only in the late stages, when demyelination processes occur. In the nuclei of neurons, astrocytes and oligodendrocytes, Caudary corpuscles of type A may be present – inclusions surrounded by a light halo. Electron microscopy shows that these inclusions contain tubular structures typical of paramyxovirus nucleocapsids. With the help of labeled antibodies, it was possible to prove that these inclusions contain antigens of the measles virus. The lesions are unevenly distributed in the brain, so a biopsy is not always diagnostically significant. During autopsy, necrosis and gliosis become the main histopathological findings. It is assumed that the cerebral cortex is initially affected, then the process spreads to the subcortical white matter and basal nuclei. Myoclonus occurs due to damage to the extrapyramidal system. An abnormal immune system response to the measles virus is a factor predisposing to the development of SSP.

Goal. To characterize the clinical and etiological, laboratory, radiation picture and outcomes of panencephalitis in children with different disease duration.

Materials and methods. In the children's multidisciplinary medical center of the Academy of Sciences of the Dijon region, 27 children with panencephalitis aged 3 months to 15 years were examined in the department of neurology. The inclusion criterion was a lesion of the white matter of the cerebral hemispheres, which has a diffuse hyperintensive signal on T2-VI during MRI. All children underwent MRI of the brain and spinal cord using pulse sequences (IP): SE, FSE, IR, FLAIR, DWI to obtain PD, T1 and T2-weighted images in three planes. With DWI, the measured diffusion coefficient (MDC) was calculated using a standard method. Omniscan or magnevist in a dose of 0.2 mg was used to contrast enhance the foci/kg IV, contrast-free MR angiography was performed once, as well as venography to exclude vascular abnormalities. Etiological diagnosis included examination of blood and other biological media (saliva, urine, feces) for a group of infections (herpes viruses type 1-6, rubella, measles, tick-borne encephalitis, influenza, enteroviruses, parvovirus B19, adenovirus, borrelia burgdorferi, mycoplasma, chlamydia by PCR methods. Immunocytochemistry, immunoblot, and RSC were used for a number of infections and the IgG avidity coefficient was determined. Oligoclonal IgGs were studied in blood and cerebrospinal fluid by isoelectrofocusing. In cerebrospinal fluid, cytosis, total protein, and the content of the main protein myelin (MPM) are determined. The catamnesis was 5-10 years old. All patients underwent etiopathogenetic therapy aimed at eradication infections, remyelination and cytoprotection, and in case of chronic course – repeated courses of anti-relapse treatment.

Results and discussion. It was found that in 84.4% of cases, panencephalitis develops in children of the first 3 years of life and the average age of their manifestation is 1.6 ± 0.8 years. In 71.9%, the development of panencephalitis is associated with congenital infections, the etiology is dominated by viruses of the Herpesviridae family types 1-6 in 62.5% of cases in the form of mono- and combined infections, and the most common pathogens are cytomegalovirus (37.8%) and herpes type 6 (21.9%). Rubella etiology of panencephalitis was observed in 2 cases (6.2%), and measles. She was absent. The study revealed that in 68.7% of cases, panencephalitis has a chronic course with a gradual development of symptoms and is manifested by a delay in the formation of motor and speech/pre-speech skills, followed by the addition of pyramidal, cerebellar and other focal symptoms. Epilepsy and extrapyramidal disorders are significantly more common in children under 1 year of age, and cerebellar and sensory disorders are more common in older age. Common infectious extracerebral syndromes precede (weeks or months in advance) or accompany neurological symptoms in 90.6% of cases. The severity and variety of neurological symptoms increases with the duration of the disease.

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Panencephalitis is manifested on MRI by diffuse foci in the white matter of the brain of both hemispheres in 93.8%, and in 6.2% of one hemisphere, in ½ of cases they have periventricular localization, accompanied by foci in the trunk (28.1%), cerebellum (31.3%), spinal cord (21.9%), as well as in subcortical ganglia (34.4%). Focal changes on MRI have different morphostructural characteristics (mass effect, contrast) related to the duration and "activity" of the neuroinfection process. With a duration of symptoms up to 3 months (n=22), panencephalitis is characterized by inflammatory–demyelinating changes, which is manifested by a moderate mass effect of 45.5%, contrasting foci ~1/3 of the time. With a disease duration of more than 3 months (n = 10), degenerative sclerosing changes develop, which is manifested by the lack of mass effect and contrasting foci, in the hearths. Inflammatory changes in cerebrospinal fluid also depend on the duration of the disease. Thus, in the group of children with a duration of panencephalitis up to 3 months, an increase in the basic protein myelin is observed in the cerebrospinal fluid on average 4.2 ± 0.8 pg/ml, and the cytosis index is 38 ± 17 cells per ml. With a duration of panencephalitis of more than 3 months, cytosis remains within the normal range in 60% of children, the average value of the main protein myelin in the cerebrospinal fluid does not exceed normal values (0.56 ± 0.1 pg/ml) and in 90% of cases (versus 63.2% in the first group) oligoclonal bands are detected in the cerebrospinal fluid. The outcomes of panencephalitis are determined by the duration of the disease and the severity of degenerative-sclerosing changes in the central nervous system at the time of initiation of therapy. The stages of processes in the central nervous system are described in the literature for measles of panencephalitis, where as. As the disease progresses, axon and neuron death develops, astroglia activation occurs with the formation of gliosis zones. This process was observed in a group of patients with panencephalitis with a disease duration of more than 3 months.

The results obtained allow us to conclude that the development of infection during the formation of the immune and nervous systems, especially in utero, is crucial in the appearance of diffuse forms of damage to the white matter of the central nervous system. In this case, the disease is often characterized by low symptoms in the early stages of development. Thus, panencephalitis in children in almost 2/3 of cases is associated with congenital infections, in modern conditions it is most often caused by cytomegaloviruses and human herpes virus Type 6, accompanied by extensive foci of demyelination followed by the formation of gliosis zones in the dynamics of the disease. Clinical and laboratory, MRI parameters and outcomes of panencephalitis depend on the timing of the onset of etio-pathogenetic therapy, with the appointment of which positive dynamics occurs in 75% of cases.

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