

Progression of enteroviral encephalitis in children

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ABSTRACT

The article presents analysis of the results of a dynamic follow-up of 35 children with enteroviral encephalitis. The average age of these children suffering enteroviral encephalitis was 6.04 ± 0.84 years old. Maximal morbidity rate of enteroviral encephalitis was observed in August and September and corresponded to the common morbidity rate of all enteroviral infections.

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Болаларда энтеровирусли энцефалитнинг ривожланиши

АННОТАЦИЯ

Мақолада энтеровирусли энцефалит билан касалланган 35 нафар болани динамик мониторинг натижалари таҳлил қилинган. Энтеровирус энцефалити бўлган боланинг ўртача ёши $6,04 \pm 0,84$ ёшни ташкил этади. Энтеровирус энцефалитининг максимал тарқалиши август–сентябр ойларида кузатилади ва умумий энтеровирус инфекциясининг кўпайиши билан мос келади.

Калит сўзлар:

Энтеровирусли энцефалит
Диагностика
Клиника
Даволаш
Болалар

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Прогрессирование энтеровирусного энцефалита у детей

АННОТАЦИЯ

Ключевые слова:

Энтеровирусные
энцефалиты
Диагностика
Клиника
Лечение
Дети

В статье проведен анализ результатов динамического наблюдения за 35 детьми с энтеровирусными энцефалитами. Средний возраст детей, больных энтеровирусными энцефалитами, составил $6,04 \pm 0,84$ года. Максимальная заболеваемость энтеровирусными энцефалитами наблюдается в августе-сентябре и совпадает с ростом общей заболеваемости энтеровирусными инфекциями.

Enteroviral infection is characterized by a wide clinical polymorphism, lesion of central nerve system, gastrointestinal tract, skin and muscles. Compatibility of enteroviruses to nerve tissue provides often involvement of brain tissue and meanings into the pathological process, a great range of clinical variants, long term and severity of the disease. 65-70% of all encephalitis in children are the forms with isolated cerebral lesions [1, 4].

According to some authors the average age of the children with encephalitis varies between 4.2 ± 1.5 and 5.5 years old [2; 3]. The basic clinical manifestations of encephalitis are consciousness impairments (86.5%) and epileptic seizures (76.9%). Together with etiological factor, vital functions, expression of common cerebral and focal symptoms these serve to be the factors determining the outcome of the disease [4-6]. The part of viruses in the etiological structure of encephalitis reaches 80-89% of all etiological factors causing the pathology [1]. Among the viral reasons of encephalitis there are enterovirus (12%), Herpes Simplex virus (5%), and cytomegalovirus (2%) [3; 6].

THE OBJECTIVE

To study characteristics of epidemiology, clinical progression of encephalitis with enteroviral etiology in children at the time of therapy.

RESEARCH METHODS AND DATA

The research was based on the data of 35 children with viral encephalitis. The average age of the children with enteroviral encephalitis was 6.04 ± 0.84 years old. 65.7% of all these patients were boys.

Analysis of the age characteristics of enteroviral encephalitis revealed its prevalence among boys of 11-14 years old (37.5%), 6-7 years old (25%), 3-5 years old (18.8%). Among the girls there was prevalence in the following ages: 3-5 years old (41.7%) and 7-9 years old (25%).

All the children were checked in compliance with the diagnostic and therapeutic standards approved by the Ministry of Health of the RUz.

RESULTS OF THE STUDY AND ITS DISCUSSION

Analysis of enteroviral encephalitis morbidity rate confirmed its higher prevalence in summer and autumn seasons (74.23% of the patients), with maximal rate in August-September (54.3%). According to the observation results intra-annual dynamics of enteroviral encephalitis was as follows: December -February (11.42%), April (8.57%), May (5.71%), June (5.71%), July (8.57%), August (34.3%), September (20%), and October

(5.71%). In March and November there were no registered patients with enteroviral encephalitis.

In few cases we revealed participation of water transmission factor (5.71%) and contact with people suffering ARVD (17.1%) in the development of the disease.

In our studies there was a prevalence of isolated damage of brain. Encephalomyelopolyradiculoneuritis took only 5.7% in the structure of enteroviral encephalitis. Other manifestations of enteroviral infection in these patients were hepatitis, gastroenteritis, herpetic tonsillitis, pancreatitis, exanthema the prevalence rate of which varied from 2.86 to 11.4%.

Enteroviral encephalitis is characterized by acute start of the disease. At the debut encephalitis 88.6% of the patients had registered rise of temperature up to sub-febrile (38.7%) and febrile values (54.8%). Pyretic fever was observed in 6.45% of the cases.

Prostration and weakness were mentioned by 60% of the patients. Neurological symptoms in the patients with enteroviral encephalitis had debut manifestation both in hyper excitability (motor dysfunctions, seizures, ICH) and symptoms of CNS suppression. Common cerebral symptoms such as variable intensity headache, dizziness (37.1%), intensive and not very intensive vomiting (34.3%), impairments of consciousness (sopor, amentia)(8.57%). Convulsive syndrome was noted in two patients (3 and 13 years old). Intracranial hypertension syndrome was registered only in the patients under 1 year old. Development of focal symptoms was observed at the 2-8th days of the disease. In the debut of enteroviral encephalitis focal cerebral damage syndrome was manifested by cerebellar ataxia, disorders of standing and walking (42.9% of the patients), less often there were oculomotor disorders (diplopia, ptosis, strabismus) (20%), and vary rare speech disorders such as aphasia (2.86%). In the debut of the pathology 57.1% of the patients had a combination of two neurological syndromes, while 42.9% had mono syndrome.

In the dynamics of enteroviral encephalitis we determined the prevalence of combination of several neurological syndromes with the growth of the frequency of their registration. The rise of temperature (sub-febrile, febrile, pyretic fever) within the acute period was registered in 77.1% of the patients with enteroviral encephalitis. Average duration of the fever was 4.95 days out of which febrile and pyretic ones were 2.61 days, while sub-febrile one was 2.91 days. Maximal duration of temperature reaction was observed in the patients with concomitant somatic pathology (cardiac vascular system, gastrointestinal tract) and super ARV infection.

Development of intracranial hypertension (71.5% patients) with incomplete complex of meningeal symptoms was characteristic for 17 patients (48.57%) with enteroviral encephalitis. We registered Kernig's symptom, upper Brudzinski symptom (28.6%), "heavy head" symptom (31.4%), and occipital muscles rigidity (25.7%). These symptoms were predominant in the patients above 4 years old (average age was 8.54 years old) expression of the symptoms varied from + to +++.

Average term of hypertension was 6.71 days, which did not exceed the term of hypertension in patients with enteroviral meningitis (6.7 ± 0.42 days). The longest preserved symptom was "heavy head" (5.45 days), while the soonest eliminated ones were Kernig and upper Brudzinski's symptoms (2.8 days).

Various degrees of impairments of consciousness (spoor, coma, stunning) were registered during the follow up only in 7 patients (20%). The impact of impairments of consciousness in debut or dynamics of enteroviral encephalitis on the outcome of the

disease was not reliable. Lethal outcome was registered in one patient with progressing disorders in consciousness up to deep coma.

Two out of 6 patients with sopor and blackout of consciousness in the acute period had recovery without complications. Four patients with impairments of consciousness in acute period recovered with formation of neurological deficit or complications (cerebral asthenic syndrome).

Short-term convulsive syndrome within the acute period of enteroviral encephalitis was observed in three patients (8.57%) (general and partial seizures). The outcome of the disease in the patients with convulsive syndrome in acute period was recovery with lasting intracranial hypertension and asthenic syndrome and formation of neurological deficit (spastic tetraparesis).

Pyramidal and extra pyramidal symptom in the patients with enteroviral encephalitis was tremor of limbs which was registered less often than convulsive syndrome (5.71%), and was not combined with seizures. For the patients with tremor in limbs in acute period recovery with further asthenic syndrome was characteristic.

In the cases of enteroviral encephalitis we registered stem, cerebellar, hemispheric and combined variations of enteroviral encephalitis (cerebellar+stem 3.13%). The basic manifestations of the cerebellum involvement into the pathologic process were dynamic and static ataxia, nystagmus, muscular hypotension at the side of focal damage, ataxic walk, shift to the side of the damaged hemisphere during walking, intention tremor, and falling at standing. Stem forms were characterized by the development of alternating syndromes (development of hemiparesis, hemianesthesia, hemiataxia at the side opposite to the damaged one). Stem form, the basic clinical manifestations of which was deep coma in a patients with ptosis, strabismus, nystagmus, damage of facial nerve, bulbar and common cerebral symptoms, finished by lethal outcome.

Results of the study of cerebrospinal liquor in the cases of enteroviral encephalitis in 56.7% revealed pleocytosis. In six patients amount of cells in the liquor was above $100 \times 10^6/L$. In the rest of the cases the average cytolysis rate was equal to $18.8 \times 10^6/L$. Pleocytosis had lymphocytic and mostly lymphocytic (lymphocytes were more than 70% of the cells) character. Only in three cases the level of protein in CSL did not exceed the values normal for certain age. In all other groups the amount of protein was increased, and in some cases up to 1.1-1.9 g/L. Average protein level in CSL in the cases of enteroviral encephalitis was equal to 0.67 g/L. According to Skripchenko N.V. [2], rate of detection of the agent in the cases of encephalitis can reach 90% at the time of diagnostic within early terms and in a well-equipped laboratory. For etiological diagnostics of enteroviral encephalitis we used isolation of enterovirus in CSL and feces by means of PCR method. The agents of the disease were detected in PCR in 77.1% of the cases.

Therapy of encephalitis with enteroviral etiology corresponded to modern requirements to therapeutic-safety routine, etiotropic, pathogenetical, and symptomatic therapy. The aim of the performed therapy was correction of liquor hypertension, disorders in liquor dynamics, and metabolic disorders. Complex therapy included application of parenteral osmодиuretics, tablet carbohydrase inhibitors, agents improving cerebral circulation and metabolism, modern antihypoxants, and nootropic agentes. For the performance of etiotropic therapy we applied recombinant interferon alpha 2 (viferone) suppositories, and cycloferon for injections. Frequency of the aforesaid agents application varied from 34% among the children above 12 to 81% among the children

under 7 years old. The term of etiotropic therapy depended on the age of a child, severity of associated pathology, and dynamics of clinical symptoms.

All patients with enteroviral encephalitis with impairments of consciousness, expressed neurological impairments and encephalomyelopolyradiculoneuritis received dehydration therapy (osmodiuretic mannitol, diacarb), hormonal therapy (dexamethasone 1 mg/kg/day). The term of parenteral dehydration varied from 6 to 11 days and depended on the age of a child, presence of associated neurological symptoms.

The agents improving microcirculation in CNS by means of vasodilatation (cavinton, vinpocetin) were applied parenterally with further change for enteral way for children above 7. For the improvement of nucleic acids exchange and stimulation of exchange processes in nerve tissue within acute period nootropic agents parenteral injection was prescribed to all patients. Change for enteral injection was performed with background positive clinical dynamics and improvement of patients' condition. With neurotrophic and reparative purpose we applied actovegin in the doses corresponding to patient's age parenterally with further change for tablets (actovegin dragge for 1-2 months).

Antihypoxants and antioxidants increasing the activity of antioxidative enzymes and improving cerebral circulation (mexidol, cytoflavin) were administered by 100% of the patients in acute period of enteroviral encephalitis. Patients with polyneuropathy administered agents improving myelination of nerve fibers and impulse transmission to the CNS such as glyatilin and neuromidin additionally to the aforementioned ones. Systemic enzyme therapy (vobenzim) was used for the improvement of rheological properties of blood and increase of the efficacy of antiviral agents. Taking into account that the agent is produced in a tablet form it was prescribed to children above 7.

Majority of the patients had acute progression of the disease with positive dynamics of the basic syndromes. Undulating progression was observed in two patients. Average term of the therapy for patients with enteroviral encephalitis in a specialized unit was 23.9 days. Undulating progression was registered in patients with residual organic damage of CNS (22.9% patients with syndrome of vegetative-visceral disorders, emotional labile impairments, hydrocephalic syndrome, atrophic alterations in frontal lobes, brain, cystic arachnoiditis) and chronic somatic pathology.

The cases of enteroviral encephalitis in children were characterized by the following early outcomes of the disease: clinical recovery at the moment of discharge from the hospital (28.57%); clinical recovery with the preservation of asthenic vegetative manifestations, moderate or little expressed intracranial hypertension (37.1%); formation of neurological deficit (focal neurological symptoms with various expression, ataxic syndrome, spastic tetraparesis) requiring performance of the therapy in specialized psycho neurological unit (31.4%).

Lethal outcome was observed in one case. Clinical recovery was registered in patients with moderate or severe forms of neuro infection with mild neurological manifestations, absence of explicit alterations in MRI or CT images of brain. Correspondingly, lethal outcome and formation of neurological deficit was more typical for the patients with severe form of the pathology with explicit and/or long-term neurological manifestations, rough alterations revealed by means of instrumental tests. Analysis of long-term outcomes of enteroviral encephalitis and meningoencephalitis was not performed.

CONCLUSION.

Thus, maximal morbidity rate of enteroviral encephalitis was observed in August and September and corresponded to the growth of the common morbidity rate of enteroviral infections. Patients with enteroviral encephalitis had less expressed intoxication syndrome, common cerebral symptoms, intracranial hypertension syndrome compared to those with enteroviral meningitis. Enteroviral encephalitis is characterized by lower pleocytosis rate than that observed in cases of enteroviral meningitis. The agents of the disease were isolated by means of PCR method in 77.1% of the cases. Acute progression of the disease with final recovery in the majority of cases was conditioned by the performance of complex therapy (parenteral osmодиuretics, carbonic anhydrase inhibitor tablets, agents improving cerebral circulation and metabolism, modern antihypoxants, and nootropic agents).

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