

EBV INFECTION WITH CONVULSIVE SYNDROME IN CHILDREN: FEATURES OF THE CLINIC AND DIAGNOSTICS

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ARTICLE INFO

Received 09 April 2018

Accepted 02 May 2018

Published 12 May 2018

KEYWORDS

Epstein-Barr virus,
EBV infection,
acute respiratory infections,
convulsive syndrome,
central nervous system

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ABSTRACT

Epstein-Barr virus infection is one of the most common human infectious diseases. Clinical manifestations of the disease caused by the Epstein-Barr virus are diverse and include infectious mononucleosis, damage of the liver, nervous system and other organs. Currently, the role of viruses in the occurrence of seizures in children is actively studied. According to modern ideas, persistent viruses can disrupt the mediator exchange in the brain. It is possible that the presence of an agent in the brain tissue can cause autoimmune reactions in relation to its own neurons. An in-depth study of the role of EBV in the development of convulsive syndrome in children has allowed us to confirm scientifically this assumption. In this article, the features of the clinical duration of ARI with convulsive syndrome caused by EBV are also presented.

Introduction. The convulsive syndrome in children under 3 years old is a reaction of the child functionally immature brain in response to the action of various adverse factors such as hyperthermia, hypoxia, toxins, tumors, etc [1]. Significant place in the structure of convulsive syndrome in children is occupied by febrile seizures - convulsive manifestations arising in childhood during febrile fever without apparent reasons or signs of infection of the central nervous system [4]. In 2-5 % of children under 3 years old there is at least 1 attack of febrile seizures [3, 5].

The attention of scientists from different countries is focused on studying the ability of persistent viruses to influence mediator disorders in the brain and to determine autoimmune responses to the own neurons of the body [2, 4, 6]. These abilities are inherent in herpesviruses, including the Epstein-Barr virus (EBV), which prompted us to in-depth study of the role of EBV in the development of convulsive syndrome in children.

Materials and methods. We examined 110 children aged from 4 months to 7 years with the diagnosis of acute respiratory infection (ARI), convulsive syndrome. All children were examined for the presence of respiratory viral antigens and the markers of herpesvirus infections (CMV, HSV 1/2, VEB, HHV-6). Specific antibodies (IgM, EA IgG, IgG) to herpesviruses were detected by the method of enzyme immunoassay (ELISA), DNA detection in the blood and CSF was performed by polymerase chain reaction (PCR). Determination of antigens of the respiratory group viruses (influenza, parainfluenza, adenovirus infection, RSV-infection) was made by the immunofluorescence method. Detection of early immunoglobulins IgM and EA IgG indicated the activity of herpesvirus infection. The diagnosis of herpesvirus infection was confirmed on the basis of at least two positive markers for the herpes virus. Of decisive importance was the detection of herpesvirus DNA in CSF, this confirmed the etiology of neurological disease.

Results and discussions. Our studies have revealed that a major contribution to the development of ARI with seizure syndrome belongs to EBV, markers of its active phase were found in 59 (53.6 %) of 110 patients. Of these 59 patients, the detection of only specific markers for EBV made it possible to diagnose a mono-EBV-infection and to regard it as the main disease in 34 (57.6 %) patients. The rest 25 (42.4 %) children had EBV association with respiratory viruses. Probably, infection with any other agents contributed to the reactivation of EBV, which was in a latent state, followed by irritation of the cerebral cortex and the appearance of convulsive contractions.

Perhaps, these patients' convulsive syndrome was caused by both the ability of VEB to cause disorders of the functioning of the central nervous system, and actually hyperthermia.

In patients with a lack of specific markers for EBV, respiratory viruses played a big role in the occurrence of seizures, which amounted to 40 (78.4 %) cases. Most often (33.3 % of patients)

convulsive syndrome complicated the course of adenovirus infection, slightly less (29.4 %) - influenza and parainfluenza. The appearance of the convulsive component in these children was caused by a significant hyperthermic reaction, and the diagnosis of "febrile seizures" was right. Adenovirus infection complicated by convulsions was most often seen as a major disease than in association with EBV. Influenza, parainfluenza, and RSV infection with an encephalic reaction were observed with equal frequency as mono-infections, and in association with EBV. In 11 (21.6 %) cases, the etiology of the disease was not established.

To study the features of the duration of herpesvirus infection with convulsive syndrome, the examined patients were divided into 2 groups: (1) with the presence of active phase markers of herpesviruses and (2) not infected with herpesviruses.

The dependance between the occurrence of ARI complicated by convulsive syndrome and the age of patients was revealed. Diseases of acute respiratory viral infection with encephalic reaction were observed mainly in children under 3 years old. Herpesvirus infection with seizure syndrome most often - 59 (78.7 %) patients - was observed in children aged from 1 to 3 years, suggesting the possibility of infection with herpesvirus in the postnatal period.

A main condition for the development of acute respiratory disease with convulsive syndrome was body temperature increase of various severity. The onset of seizures mainly occurred during the rise in body temperature to febrile values. However, there were some differences in the development of the temperature response in patients of both groups. In 43 (72.9 %) patients with EBV, there was an increase of body temperature to febrile values in the first 1-2 days of the disease, followed by a rapid decrease and retention of subfebrile values that alternated with normothermia. The long subfebrile temperature is probably associated with the constant presence of EBV in a patient's body and the immune response caused by it. Therefore, in the development of a convulsive component in patients with EBV infection, to ignore the role of hyperthermia is not advisable. So we can't neglect the properties of EBV to disrupt the work of the nervous system, after which a convulsive syndrome appears. Probably, significant hyperthermia is a provoking factor in the development of neurological complications caused by EBV.

In 14 (23.7 %) cases of EBV-infection, convulsive paroxysms were observed during subfebrile body temperature, in 2 (3.4 %) - with normothermia, although later there was an increase of body temperature to subfebrile values. The occurrence of seizures during subfebrile temperature was more typical for the course of the EBV infection than in the 2nd group. As a rule, these were children with manifestations of the EBV infection as the main disease. The occurrence of convulsive contractions in these patients is not caused by hyperthermia, but the properties of EBV to disrupt mediator exchange in the brain, and the diagnosis of "febrile seizures" in these patients is not appropriate.

The occurrence of seizures in cases with negative markers to EBV occurred during febrile fever. These patients had body temperature increase to febrile values on the first day of the disease, followed by a decrease to normal values, usually the next day. Therefore, clonicotonic convulsions in these patients were caused by real hyperthermia.

In the groups of patients where the EBV-infection markers were not detected, the clinical symptoms of adenovirus infection, influenza, parainfluenza, and RSV infection were quite typical with the convulsive syndrome. Such manifestations as fever, catarrhal phenomena, the presence of convulsive contractions were observed in patients of both groups. All in all there were some differences in the duration of clinical symptoms depending on the etiology of the disease (Table).

In patients with negative results of examination for EBV, the duration of hyperthermia and the main clinical manifestations were less, and the period of recovery was shorter, as indicated by $p < 0.05$. Catarrhal phenomena in patients of this group were significantly more expressed and longer than in patients with EBV infection. In 16 (31.4 %) children convulsion seizures were for the first time, in the rest 35 (68.6 %) had occurred earlier. Convulsive paroxysms were short-term, stopped themselves or after once used anticonvulsants at the prehospital stage.

Table 1. The duration of the main clinical symptoms (in days) in patients with ARI with convulsive syndrome depending on the infection of EBV

symptom	infection by EBV (n-59)	noninfection by EBV (n-51)	P
	days, (M±m)	days, (M±m)	
hyperthermia	8,5±1,1	2,0±0,2	<0,05
Rhinitis, cough	4,2±0,2	6,7±0,3	<0,05
lymphadenopathy	11,5±0,3	5,8±0,2	<0,05
nasal congestion	9,8±0,7	5,6±0,4	<0,05
Length of stay in hospital	13,5±0,4	7,3±0,7	<0,05

Repeating seizures were observed in 5 (9 %) cases, their multiplicity is equal to 1 or 2 times a day for the first 2 days. Violations in the neurological status and psychomotor development were not manifested. All children of this group were discharged in a satisfactory condition under the supervision of a neurologist.

Disease of the EBV infection with convulsive syndrome had a severe duration in comparison with patients with negative markers to EBV. A long period of hyperthermia (during 8.5 ± 1.1 days) was defined, patients were in the clinic in 1,8 times longer as compared to patients of the 2nd group (13.5 ± 0.4 and 7.3 ± 0.7 days respectively).

Catarrhal phenomena were mild or moderate (mostly mild mucous discharge from the nose and coughing as a manifestation of pharyngitis). The majority of patients experienced a prolonged difficulty in nasal breathing, which is due to the damage of the lymphoid tissue of the nasopharynx by EBV.

Convulsions were occurred in all patients with EBV infection. In 31 (52.5 %) cases convulsive paroxysms appeared for the first time in life, in the rest 28 (47.5 %) patients had occurred earlier. The duration of convulsive seizures in comparison with the patients of the 2nd group was expressive - from 2 minutes to 1 hour. Short-term convulsions, as a rule, stopped themselves, in other cases - with injection of sibazone.

Repeating convulsive seizures worried patients with EBV infection much more often than patients with negative markers to EBV, as evidenced by $p < 0.05$. Repeating seizures were observed in 13 (22.0 %) children, the frequency of their occurrence ranged from 1 time per day for 2 or 3 days to 10 episodes per day, which were repeating every 2 hour.

3 (5,1 %) patients with EBV-infection with convulsive syndrome were treated in the intensive care unit with the disturbance of consciousness to coma, which lasted from 1 to 3 days. 5 (8,5 %) children had a slight degree of impairment of consciousness - inhibition. 12 (20.2 %) patients were sleepy, emotionally depressed, 9 (15.2 %) - on the contrary: capricious, nervous, emotionally labile. In 6 (10.2 %) cases, tremors of the hands were determined. In 3 (5,1 %) patients visual hallucinations were observed on a background of body temperature increase. 2 (3.4 %) patients had speech disorders, which became slow, the patient had difficulty with the choice of the right word for a long time.

According our study it is clear that the disease of EBV infection with convulsive syndrome had a more severe and prolonged duration in comparison with patients of the 2nd group. However, all children were discharged from the hospital in a satisfactory condition at the dispensary supervision of a neurologist.

Conclusions.

1. The conducted researches allow to make conclusion, that one of the reasons of development of a convulsive syndrome in children of early age can be constant defeat of a CNS by EBV.

2. The diagnosis of EBV infection was confirmed on the basis of at least two positive markers for EBV. Detection of early immunoglobulins VCA IgM and EA IgG indicated the activity of herpesvirus infection. Of decisive importance was the detection of EBV DNA in CSF, this confirmed the etiology of neurological disease.

3. Diseases of EBV infection with convulsive syndrome have more severe and prolonged duration in comparison with patients without specific markers to EBV.

4. The convulsive syndrome in children, especially children under 3 years old, needs to be examined for herpesviruses, in particular for EBV, and in case of positive results, prescription of not only anticonvulsants, but also antiviral medicine in complex therapy is mandatory.

REFERENCES

1. Вашура Л. В. Судорожный синдром у детей: роль герпесвирусных инфекций / Л. В. Вашура, М. С. Савенкова, Н. Н. Заваденко / Детские инфекции. – 2014. – №2. – С. 48-52.
2. Крамарев С. А. Эпштейна-Барр вирусная инфекция у детей / С. А. Крамарев, О. В. Выговская // Актуальная инфектология. — 2013. — № 1. — С. 73-80.
3. Самсыгина Г. А. Герпес-вирусные инфекции у детей / Г. А. Самсыгина // Consilium Medicum. Педиатрия (Прил.). – 2016. - № 2. – С. 18–23.
4. Симованьян Э. Н. Эпштейна-Барр вирусная инфекция у детей: совершенствование программы диагностики и лечения. / Э. Н. Симованьян, В. Б. Денисенко, А. В. Григорян и др. // Детские инфекции. – 2016. - №1. – С. 15-23.
5. Millichap J. G. Epstein-Barr Virus Neurologic Complications / J. G. Millichap // Pediatric Neurology Briefs. - 2015. - № 29(11). - P.88
6. Tselis A. C. Epstein-Barr virus infections of the nervous system / A. C. Tselis // Handb. Clin. Neurol. — 2014. — Vol. 123. — P. 285-305.