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Epilepsy with Pyrexial Remissions in Children

Leanid Shalkevich[1]*, Olga Lvova[2]

[1]Child Neurology Department Belarusian Medical Academy of Postgraduate Education, 220013, Republic of Belarus, Minsk, Brovki, 3/3
[2]Child Neurology and Neonatology Department Ural State Medical University, 620219, Russia, Yekaterinburg, Repina str., 3

* Corresponding author
Dr. Leanid Shalkevich
Associate professor, Head of Child Neurology Department Belarusian Medical Academy of Postgraduate Education
e-mail: shalkevich_@tut.by
Fax: +375 17 233 55 84
Telephone: +375 29 754 09 54

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Abstract

Problems: In the investigation of epilepsy the most attention pays to seizure as a result of increasing of body temperature. Epileptic conditions in which seizures are reduced during the febrile term are not studied.

Experimental approach: We examined 5 children with epilepsy with atypical response to the increase of body temperature as a reduction in the number and severity of seizures.

Findings: The common features were in all of these children onset in early childhood; intractable seizures of different types; epileptiformic changes on EEG; marked organic neurological disturbances; atrophic changes of the brain.

Conclusion: These fits allow separate the epilepsy with hyperthermic remissions in a unique epileptic syndrome.

Key words: febrile seizures, epilepsy, pyrexial remissions, children.

Introduction

While studying epilepsy in children and the effect of the body temperature on the character and course

of the paroxysmal syndrome, primary consideration is given to seizures due to pyrexia. Febrile seizures have been studied well enough. These are feverish attacks caused by extracerebral diseases [1, **Error! Reference source not found.**6, 7, 8, 11]. A "Generalized epilepsy with febrile seizures plus" syndrome as well as Dravet syndrome have been described and continues to be studied at present. This is a combination of non-febrile seizures and febrile convulsions [2, 0, 5, 9, 10]. At the same time, epileptologists often neglect the situations when an increase in the body temperature leads to a decreased number of seizures or their disappearance in a patient with epilepsy during the whole feverish period.

Materials and Methods

We observed five children (three boys and two girls) with severe daily seizures, which were difficult to arrest, the degree of manifestation and frequency of occurrence being dependent on the body temperature. When the temperature rose to 37.5^{o} C and higher, frequency of seizures decreased up followed by their full disappearance in one child. Such remissions lasted during all feverish period and some days after the temperature had normalized. After that, the seizures recurred with former severity and frequency. An increase in the body temperature was mainly caused by various infections, more rarely by the inflamed catheterized vein and dental eruption. Periods of "pyrexial" remissions occurred independent of taking antispasmodic preparations.

All children underwent general clinical and neurological examination, electroencephalography and one of neurovisualizing investigations (computed tomography or magnetic resonance imaging). Laboratory indices of total and biochemical blood count, urinalysis and cerebrospinal fluid were also studied. Polymerase blood chain reaction (PCR) for the presence of cytomegalovirus infection, toxoplasmosis and simple herpes virus I and II was performed in three of them.

Results and Discussions

The age of the onset of seizures ranged from the second day to three years of life. By the time of the onset of the paroxysmal syndrome, four children had neurological disorders of this or that degree of manifestation: from moderately arrested motor development to hemiparetic cerebral palsy (CP) in one of them. The only one child was normal before the onset of seizures.

All children developed convulsions suddenly, without any apparent cause, seizures being persistent and resistant to therapy. The interval between the first and the second seizure was relatively small: from several hours to several days. All convulsions were of a polymorphous character and included the following semiotic types of seizures:

- generalized tonico-clonic (in all 5 children);
- myoclonic (in 3 children);
- alternating hemiconvulsive seizures (in 3 children);
- infantile (epileptic) spasms (in 4 children);
- seizures with turning the head to the left, bending the left leg and tonic tension of both the hands (in one child);
- tonic seizures with apnea and impaired cardiac function in the form of marked bradycardia (in one child).

It should be noted that among various types of seizures, different combinations of seizures were observed in all the children, a combination of both generalized and partial spastic paroxysms being common for all of them.

It is also of interest that the most severe seizures (with the development of apnea and impaired cardiac function) observed in the child with CP, disappeared completely during the period of pyrexia, while others, less severe by their manifestations, did not disappear completely but occurred considerably rare and sometimes could be seen as a single seizure during the feverish period.

After beginning of seizures all children had organic neurological symptoms: ataxia, arrest of psychomotor development aggravating with the disease progression. One children had spastic hemiparesis additionally.

The results of electroencephalography showed evident general slow-wave changes in bioelectrical activity of the brain in theta- and delta-range with pointed waves by all the leads. Besides, isolated "spike-slow wave" complexes were recorded in the child with CP over the left hemisphere in parietotemporal leads.

Computed tomography performed for two children and MRI investigation for one children revealed mild and moderate brain changes of atrophic character with the formation of normotensive external and internal hydrocephalus. MRI investigation performed in one child was normal and the child with CP demonstrated subatrophic changed in the left hemisphere. The analysis of cerebrospinal fluid in all children had no deviations from the norm. PCR for the presence of herpetic, cytomegaloviral and toxoplasmotic infection performed for three children was negative.

The results of total blood count and urinalysis taken in seizure–free periods did not differ from the norm, being of non-specific inflammatory character in the period of infectious processes. Blood biochemistry showed a slight decrease in ionizing calcium only in one child.

All mothers had a threat for interrupted pregnancy at various terms (mainly, at 20-21 and 30-32 weeks),

with infectious diseases (acute respiratory infection, bronchitis) occurring during the first weeks and months of pregnancy.

Two mothers had unremarkable delivery, and one child had asphyxia combined with birth trauma, which led to further development of hemiparetic form of cerebral palsy.

Epileptic heredity was not aggravated in all the five cases. All children received practically the whole spectrum of anticonvulsive therapy available at the time treatment. Such preparations as sodium valproates, benzodiazepines (clonazepam, diazepam), barbiturates (phenobarbital, benzonal), carbamezepine, lamotrigine, acetazolamide were used in age-specific doses with an attempt to increase the doses if well tolerated. While taking anticonvulsants, a short-term amelioration of the condition was noted at the beginning of therapy with loss of efficacy on the second or third week of mean therapeutic dose administration. Further increase in doses had no effect. Relatively beneficial effect from taking synthetic adrenocorticotropic hormone (sinacten-depot) was observed in one child which resulted in the disappearance of serial seizures, their decreased duration and frequency of occurrence.

At present, all children are receiving more than one antiepileptic drug. Four of them take two medicines and one of them takes three antiepileptic agents. They are sodium valproate, phenobarbital, lamotrigine, topiramate and acetazolamide.

All children, irrespective of their receiving anticonvulsive therapy, had more rare seizures or no seizures at all during the time of rising the body temperature from 37.5^{o} C and higher.

To sum it up, epilepsy with pyrexial remissions was characterized by the following features:

- onset in early childhood;
- polymorphous character of seizures with combination of generalized and partial manifestations;
- slow-wave EEG with diffuse pointed waves discharge;
- reduced frequency and manifestation of seizures (up to their complete disappearance) during subfebrile and febrile pyrexia;
- seizures resistant to the administered of antiepileptic drugs;
- marked organic disturbances in the neurological status manifested by central paresis, arrested motor, psychic and speech development from moderate to severe forms of mental retardation progressing in the course of the disease;
- atrophic changes of the brain as seen on the CT (MRI) with external and internal hydrocephalus.

The brain is a unique organ not only due to peculiarities of its cellular structure, the presence of specific

proteins, neurotransmitters or ionic channels, but also because of its ability to create and maintain the systems of interneuronal links, both vertically and horizontally, which contributes to transmission and transformation of information streams. At the same time, this linking ability can lead to the formation of the epileptogenic brain. Interexciting compounds normally used for binding functionally common but anatomically different neurons, can lead to their abnormal hypersynchronization and distribution of epileptic activity discharges along the cortex. The focus of the epileptogenic activity can be located on the level of subcortical and stem formation (thalamus, hypothalamus, etc.), the cortex and interneuronal communications between them. There are close anatomical and functional links between the cortex and hypothalamus. Activation of hypothalamic pyrexial centers leads to the transformation of neuronal information streams from hypothalamus and reticular formation to the cortex changing its excitability. In this case, pyrexia can lead to both increased and decreased cortical epileptogenity. This effect is most pronounced in the childhood, before the functional maturity of the hypothalamus heat center has occurred. Maturation of central heat mechanisms normally occurs in children by 1.5-2 months of life. Hypoxia (intrauterine including), the nervous system impairment of infectious, traumatic or ischemic genesis in the perinatal period can lead to increased neurons' excitability with concomitant pyrexial effects on epileptogenesis, most common in the form of febrile convulsions, more rarely in the form of reverse phenomenon – hyperpyrexial remission. Genetic predisposition to the effect of pyrexia on cortical excitability cannot be excluded too.

Conclusion

Positive effect of pyrexia on suppression of spasms is likely to lie in the potentiated detoxicative function of the organism, increased energy supply for oxygenative and regenerative processes, and activation of stress reaction. There may exist genetically determined defense reaction of the organism when decreased paroxysmal activity of the brain is a non-specific phenomenon of pyrexia.

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Authors Column

Leanid Shalkevich, MD, PhD, Associate professor, Head of Child Neurology Department Belarusian Medical Academy of Postgraduate Education.

He was graduated from the Belarussian Medical University in 1996 and now he is a specialist in pediatric neurology. The field of his interests is epilepsy in children, neurological disorders in newborns and infants, different methods of rehabilitation in children suffered from CP. He is experienced in EEG and clinical neurophysiology.

Dr. Shalkevich a Leader child neurologist of Belarusian Ministry of public health, the 1st Vice-president of Belarusian League Against Epilepsy, member of ICNA and Belarusian Society of Neurology and Neurosurgery.