Case Report

The Case of Migrating Partial Seizures in Infancy Associated with Hypoplasia of Corpus Callosum and Cytomegalovirus Infection

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Abstract

The report describes the author’s clinical observation of the case of migrating partial seizures in infancy associated with callosal hypoplasia and cytomegalovirus infection including a detailed description of the anamnestic, clinicodiagnostic and laboratory data, as well as the applied therapeutic approach. The present clinical case has been reviewed on the basis of available literary data and own reasoning’s.

Key Words: Migrating Partial Seizures in Infancy; Epilepsy; Epileptic Encephalopathy; Cytomegalovirus Infection

In 1995, G. Coppola et al. published an article on a rare epileptic syndrome in early childhood, clinical and instrumental characteristics of which had some distinctive features as compared to epileptic encephalopathies known up to this time [1]. The following characteristics for the described syndrome named migrating partial seizures in infancy (MPSI) were identified: manifestation of idiopathic multifocal seizures with high frequency before the age of 6 months, normal psychomotor development before the onset of the disease and its subsequent pronounced delay, resistance to therapy with standard antiepileptic drugs [2,3]. Over the last decade, observations of this epileptic syndrome have been supplemented by descriptions of similar cases in Japan (Okuda et al 2000), Europe (Wilmshurst et al 2000; Veneselli et al 2001), Israel (Gross-Tsur et al 2004), USA (Marsh et al 2005), Russia (Mukhin et al. 2014) [4,5].

We present the case of migratory partial seizures in infancy associated with parencephalia (callosal hypoplasia) and cytomegalovirus infection. The significance of cytomegalovirus infection (CMV) infection is that in a number of cases it causes distant neurological consequences in the form of sensorineural hearing loss, cognitive and behavioral disorders, arrested motor development and cerebral palsy, convulsions, visual impairment.

Patient O.I., born July, 2015. Entered the department for children with nervous system pathology at the age of 3 months with complaints of daily convulsive seizures on top of constant intake of antiepileptic therapy and impaired motor and psycho emotional development.

As is known from medical history the child was born from the 1st pregnancy at the gestational age of 40 weeks by means of emergency caesarean section. The cause of emergency caesarean section was toxemia of pregnancy and the developing fetal hypoxia. Pregnancy proceeded with complications (the mother was diagnosed with ureaplasmosis and chronic bilateraladnexitis; she was treated with antibacterial therapy as part of prophylaxis measures.

On the third day after birth tonic spasms appeared in child’s extremities. On top of phenobarbital intake at a dose of 2.1 mg/kg/day the attacks were stopped and then resumed at the age of 22 days in the form of clonic jerks of the right arm and "nods" of the head. The treatment was supplemented with valproate sodium which also led to temporary relief of seizures. Several attempts to reduce the dose of phenobarbital led to resumption of seizures. While receiving phenobarbital at a dose of 2.1 mg/kg/day and valproate sodium at 30 mg/kg/day the attacks resumed again at the age of 2.5 months for which reason topiramate was assigned to the patient.

At the time of primary hospitalization to the neurological department of regional hospital at the age of 2 months the following was determined in a child’s neurological status: the child is conscious, fixes his eyes, has pursuit eye movements, smiles, raises his head in face-down position. Does not group. No support on the feet. The anterior fontanelle does not bulge.

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No pathology detected on the part of cranial nerves. No abnormalities in muscle tone. Tendon-periosteal reflexes are brisk and without side differences. No pathologic plantar reflexes and meningealsigns manifest. The following character of seizures is observed:

- Rolling eyeballs up and to the sides (more often to the left), accompanied by a tonic tension of the right or left hand with a clonic twitching of the head (or without it) secondary to unconscious state;
- Cyanosis of the nasolabial triangle followed by acrocyanosis and respiratory arrest within a few seconds;
- Clonic twitching of the hand of right or left arm alongside with retained consciousness lasting from several minutes to several hours.

Values of blood and urine analysis did not reveal any pathology. The activity of liver enzymes, electrolyte status, glucose levels were within normal limits.

Electroencephalography (EEG) at the age of two months: the main activity is represented by a low-amplitude rhythm. No paroxysmal and local epileptiform activity registered.

In addition to the antiepileptic therapy received by the patient (phenobarbital 2.1 mg/kg/day, valproate sodium 28 mg/kg/day, topiramate 2.6 mg/kg/day), a course of dexamethasone was administered at a dose of 1 mg/kg per day for 10 days with the subsequent transition to oral administration of prednisolone in 2 mg/kg for two months. Subsequently, the dose of phenobarbital was increased to 3.6 mg/kg per day. In the course of the treatment there was certain positive dynamics in seizures: their number decreased to 1-3 per day (some seizures persisted: rolling the eyeballs to the right in the unconscious state lasting up to 1.5 minutes).

At the time of this admission neurological status showed decrease of mental alertness. No fixation behavior on examination. The pupils were equal. The patient did not track a moving object. An innate interest and mental alertness. No fixation behavior on examination. The pupils were equal. The patient did not pull the head and periosteal reflexes were symmetric D=S. Landau reflex was not retained consciousness lasting from several minutes to several hours.

The following changes were noted on the EEG at the time of admission: in the episode of recording - the appearance of ictal epileptiform activity in the form of a set of sharp waves in the left parieto-posttemporal region (Figure 1) with transition to delta deceleration, subsequent appearance of new ictal patterns in the form of sharp waves in the right centrotemporal region and after a short period - in the left centrotemporal region (Figure 2), thereafter - another ictal event with sharp waves in the posttemporal-parieto-occipital region to the left and fronto-temporal region to the right (Figure 3,4).

The results of enzyme-linked immunosorbent assay (ELISA) for cytomegalovirus infection (CMV) and the Epstein-Barr virus (EBV): IgM CMV negative, IgG EBV 74.9 mg/ml.

The dose of valproate sodium was increased to 35 mg/kg/day, and the dose of topiramate was reduced to 1.8 mg/kg per day.

The above-described seizures were then accompanied by myoclonic and clonic seizures in left extremities (first in the arm, then in the leg), hemiconvulsive seizures in the right half of the body, myoclonias in the form of a “nod” of the head and clonic contractions of the eyeball and perioral muscles, as well as breath-holding seizures.

EEG at the age of 4 months: diffuse EEG changes, accentuation of slow theta and delta waves, diffuse multistage waves with periodic predominance now on the right then on the left.

Neurosonography (NSH) at the age of 4 months: enlargement of lateral ventricles in the region of anterior horns and bodies. One can’t exclude the dysgenesis of the corpus callosum. Given these data a computed tomography (CT) was performed which revealed a slight ventriculomegaly and changes on the part of corpus callosum of the following character: corpus callosum is fairly well visualized in the anterior and posterior regions and partly - in the middle regions.

The patient was titrated against diazepam at a dose of 2.5-5 mg per day for 4 days and carbamazepine was added at a dose of 8 mg/kg. After adding carbamazepine there was a significant deterioration in the form of dramatic increase in the number of seizures and, therefore, this drug was canceled. Due to inefficiency, valproate sodium and phenobarbital were also canceled and clonazepam was administered in the dose of 0.08 mg/kg per day. However, this did not lead to a significant change in the number of seizures.

At the fifth month of life CMV DNA was detected in blood and urine by the polymerase chain reaction (PCR):

- Saliva for CMV (PCR) - CMV DNA detected in the quantity of 6,57 \times 10^5;
- Blood for CMV (PCR) - DNA detected in amounts of 128 copies/ml;
- Urine for CMV (PCR) - CMV DNA detected in the quantity of 8,98 \times 10^5;

At this stage antiepileptic therapy was represented by clonazepam 0.1 mg/kg/day and topiramate 7 mg/kg/day.

From this point on, for the purpose of antiviral therapy of CMV infection, the child was prescribed ganciclovir at a dose of 40 mg x 2 b.i.d. intravenously for 20 days.

After a course of ganciclovir, the tests for the presence of CMV infection in the body were continued. On the 21st day since the beginning of antiviral therapy:

- Urine for CMV (PCR) - CMV DNA detected in the amount of less
than 100 IU in ml;

• Saliva for CMV (PCR) - CMV DNA detected in the amount of less than 100 IU in ml;
• Blood for CMV (PCR) - DNA not detected;
• Blood for CMV - IgM negative.

Alongside with antiviral therapy, the correction of antiepileptic treatment was made for the child: valproate sodium was assigned once again (up to 40 mg/kg per day), clonazepam and topiramate were canceled.

After the course of ganciclovir, the patient’s condition improved with respect to seizures: the secondary generalized seizures completely disappeared, the number of focal seizures decreased considerably. EEG during this period showed epileptiform activity with a predominance of slow wave activity in the right brain hemisphere.

At discharge, the child’s condition was satisfactory, however, some short-term seizures with alteration of consciousness continued in the form of turning the head to the right and nystagmus, fibrillation of the tongue, twitching of the lips with a background of general hypotension. Reactions of auditory and visual concentration were reduced, contact was difficult. Patient had negative reaction on general surveying: Fixed his eyes briefly, traced fragmentarily. Did not turn over, did not reach for toys, did not hold the head. Landau reflex was not formed. No support and tendency to decussation.

Discussion

Based on the clinical data (polymorhic partial seizures of multifocal nature involving eyeballs, hyper salivation, apnea, periodic development of secondarily generalized seizures; regress of psychomotor development; undulating course of seizures with deterioration and some improvement), the presence of migrating foci of epiactivity on EEG, no change in the data of laboratory tests (clinical blood test, biochemical blood test, CSF), absence of confirmed genetic studies on metabolic disorders the following diagnosis was set: severe infantile epilepsy with migrating partial seizures, drug-resistant and status progress. Significant psychomotor developmental disorder. By way of conducting NSG and CT, the patient was diagnosed with congenital malformation of the brain (callosal hypoplasia), which can clinically manifest itself by various neurologic disorders, including epileptic seizures. Detection of CMV infection in a patient at the age of 5 months and conducted etiotropic therapy with ganciclovir resulted in a significant improvement in clinical and laboratory indicators in respect of epileptic process. According to literature data, primary CMV infection can be associated with neurological pathologies only if it is congenital; however, the detection of CMV DNA is clinically significant only in the first month of the patient’s life, in the future it is impossible to differentiate the congenital CMV infection from postnatal. Nevertheless, we believe that the presence of clinical and instrumental indicators of the improvement of described patient’s condition after performing etiotropic therapy may indirectly indicate a certain contribution of CMV infection to the development of epileptic syndrome.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Figure 1: The appearance of high-amplitude sharp waves in the left hemisphere (mainly P3-O1, O1-T3)

Figure 2: The development of focal slowing in the left leads P3-O1, O1-T3 and F3-O1.
Figure 3: The appearance of high-amplitude sharp waves in the right leads \( \text{F}_{4}-\text{T}_{4} \), \( \text{C}_{4}-\text{F}_{4} \), and then in the left \( \text{F}_{3}-\text{T}_{3} \) and \( \text{C}_{3}-\text{F}_{3} \) without generalization of the process.

Figure 4: The development of multifocal sharp-wave activity on the left (mainly in \( \text{P}_{3}-\text{O}_{1}, \text{O}_{1}-\text{T}_{3} \)) and on the right (\( \text{F}_{4}-\text{T}_{4} \)).

References


