

NONCONVULSIVE STATUS EPILEPTICUS CAUSED BY VIRAL ENCEPHALITIS: CASE REPORT

Rodica Cozac^{1,2}, Lilia Rotaru³

¹„N. Testemitsu“ University of Medicine and Pharmacy Chisinau, Republic of Moldova

²Institute of Emergency Medicine, Chisinau, Republic of Moldova

ABSTRACT

In pediatric patients Epstein-Barr virus (EBV) infection may have miscellaneous neurological manifestations. Children with acute viral encephalopathy may present prolonged electrographic seizure activity consistent with non-convulsive status epilepticus (NCSE). NCSE condition is difficult to diagnose due to absence of motor seizures, presenting only changes in behavior and consciousness. In this report we present a clinical case of EBV infection in 3.5-year-old girl. On admission she suffered of confusional state and irritability after an episode of motor partial complex seizure being in good health. The condition evolved twenty five days after an episode of respiratory infection diagnosed as bacterial tonsillitis by the family physician and treated with antibacterials. Laboratory blood evaluation as well as chest radiography, urinalysis, bleeding time, fibrinogen were within the normal range. Magnetic resonance imaging of the brain and spinal cord revealed a subcortical increased signal in the left occipital lobe on T2-weighted image. Electroencephalography (EEG) pattern revealed nonconvulsive status epilepticus (NCSE). EBV infection was revealed by serum antibody test. The present case emphasizes the importance to evaluate the role of EBV in acute neurological syndromes in pediatric patients, in particular, in presence of behavioral changes with EEG evidence of seizures. NCSE in children denotes electrographic seizures without convulsive activity and often manifests as altered mental status. It may be difficult to diagnose in pediatric patients in whom changes of behavior and consciousness may not be as easily recognized as in adults.

Keywords: epstein-Barr virus, nonconvulsive status epilepticus, pediatric neurology

INTRODUCTION

In pediatric patients Epstein-Barr virus (EBV) infection may have miscellaneous neurological manifestations, including encephalitis, meningitis, acute disseminated encephalomyelitis, as well as acute inflammatory polyneuropathy. In this report we present a clinical case of EBV infection in 3.5-year-old girl. The patient suffered of confusional state on admission. Electroencephalography (EEG) pattern revealed nonconvulsive status epilepticus (NCSE). EBV infection was revealed by serum antibody test.

CASE PRESENTATION

The family history of the patient was unremarkable. The patient was the first female child born at 40 weeks gestation by normal delivery to non-sanguineous parents. Birth weight was 3.5 kg, length 50 cm, head circumference 34 cm. The psychomotor development was within physiological index of patient's age.

At the age of 3 years and 4 months, the patient developed fever (39.5 C°) and sore throat which lasted for 3 days. After assessment by family physi-

Author for correspondence:

Rodica Cozac, Department of Neurology, Neurosurgery and Medical Genetics, Institute of Emergency Medicine, 1 Toma Ciorba Street, Chisinau, Republic of Moldova

E-mail: cozac.rodica@yahoo.com

cian a diagnosis of bacterial tonsillitis was made. Peroral treatment with cephalosporin was started. After 25 days from the end of the antibacterial treatment the patient exhibited a motor partial complex seizure being in good health. The seizure involved right arm and right leg and lasted for less than 3 minutes. The seizure was followed by an acute confusional state that lasted for 2 hours.

On admission her weight was 13.5 kg (10th percentile), height 95 cm (10th percentile), and head circumference 49 cm (50th percentile). Clinical examination revealed absence of fever and mild cervico-mandibular lymphadenopathy. Blood pressure was normal, liver and spleen were within normal limits. Significant irritability was observed in arousal. There were no signs of meningeal irritation, and cranial nerves examination was normal. Muscle trophism, perception of touch, body temperature was normal. Deep tendon reflexes were all normal.

Laboratory blood evaluation revealed normal cell and platelet counts and C-reactive protein level. Radiography of the thorax, urine analysis, biochemical laboratory serum values, coagulation pa-

rameters were within the normal ranges. Brain and spine magnetic resonance T2-weighted imaging revealed an increased signal in the left occipital subcortical region. EEG assessment showed disorganization and presence of a chaotic background activity, with low-voltage spikes, and primary generalization (see Fig. 1). Diagnosis of NCSE as per Neurocritical Care Society 2012 Guidelines, Kaplan *et al.* 2007 (1).

Treatment with sodium valproate with a daily dose of 20 mg per kilogram was started. Improvement of EEG patterns, was observed after three days (organization of background activity).

CSF examination showed mild pleocytosis with normal glucose and protein concentrations. Antibody test to *Toxoplasma gondii*, *Human Immune-deficit Virus* and *Cytomegalovirus* was negative. IgM antibody titers against EBV were 4,18 UI/mL (0–0.9) and IgG antibody titers were 5.1 UI/mL (0.7–35), and IgG antibody titers against EBV early antigen were also positive at 1:160 suggesting acute EBV infection. Therefore, acyclovir was initiated at a dose of 10 mg/kg/day intravenously. After about three days of admission, the patient



FIGURE 1. EEG showed a generalized slow activity with high amplitude. Spikes and spikes-slow waves complex appear singly or in group and are unilateral or bilateral.

showed a progressive improvement of general conditions and of behavioral changes.

One month after treatment, she presented a full clinical recovery and neurological examination was normal. EEG showed normal activity with a good *alpha* organization in the occipital area.

DISCUSSION

The diagnosis of EBV-associated encephalitis in this reported case was made on the clinical and laboratory findings, EEG, CSF and MRI features and antibody serum detection. Encephalitis is defined as inflammation of the brain parenchyma. It can be caused by antiviral infective process: HSV-1, VZV, EBV, mumps virus, measles virus, and enteroviruses (2). Various central nervous system manifestations of EBV infections have been reported, such as optic neuritis, facial and hypoglossal palsy, transverse myelitis, Guillain-Barré syndrome, aseptic encephalitis and meningitis (3). In the pediatric age patients the symptoms of EBV encephalitis are heterogeneous and may manifest with seizures, altered consciousness, focal neurological signs and meningism.

The pathogenesis of EBV encephalitis is considered by many researchers to be caused by an immune-mediated mechanism rather than a direct invasion of the brainparenchyme (4). The brain areas that are reported as being most frequently involved in the pathological process are cerebral hemispheres, cerebellum, basal ganglia, thalamus, brain stem and limbic system.

Clinical onset with seizures and behavioral changes was another interesting aspect in this case. NCSE is very often underestimated in children. NCSE is defined as a cognitive or behavioral change that lasts for at least 30 min, with evidence of seizures on EEG (5). In pediatric patients it includes a variety of different conditions, which can be classified into the following groups (6): acute neurological injuries (trauma, metabolic syndromes, encephalitis, stroke); epileptic syndromes (myoclonic astatic syndrome, Lennox-Gastaut or Dravet syndrome); and nonprogressive encephalopathy (Landau-Kleffner or Angelman).

As reported by various researchers, NCSE in group with acute neurological injuries associated with a high incidence of coma or stupor and poor outcome (7). However, it may occur in the absence of any acute disorder, thus making it difficult to perform a correct diagnosis.

NCSE is a highly heterogeneous clinical condition which is less studied in children and adoles-

cents. It is characterized by critical activity as evidenced by EEG, but without obvious convulsive activity (5). Frequently this condition manifests as alternated mental status or coma. One of the first detailed descriptions of NCSE (or “*automatisme ambulatoire*”) was presented by Charcot in 1888. He described a patient who came into conflict with the law dueto boarding a train without ticket (Charcot, 1888) (8). Another famous specialist, Lennox described in 1949 an 11-year-old boy who suffered of periods of confusion. He described these periods as “days when he was able to eat, but does not communicate with others”. Lennox called these phenomena status of “*petit mal*”, he successfully treated the condition with Tridion (8).

In a recent study conducted by our team in the Paediatric Department of the Institute of Mother and Child (Calcii *et al.* 2014 (9)) 39 pediatric cases with status epilepticus (SE) were examined, 27 cases with convulsive SE and 12 with NCSE. The age of the patients varied between 3 months and 2,5 years. We compared laboratory tests, ophthalmoscopy, EEG, computed and magnetic resonance tomography of each patient. NCSE was established in 30.79% of children with SE. The following characteristics of NCSE were identified: the major part (41%) of the patients were under age of one year; with a slight prevalence of boys (58%). Background pathology were distributed as follows: hypoxic-ischemic cerebral pathology (58,3%), acute infections (25%), intracranial hemorrhage (8,3%), refractory epilepsy (8,3%). The majority (83,3%) had pathologic changes on computed and magnetic resonance tomography. All patients presented on EEG critical changes without typical clinical manifestation.

CONCLUSION

The present case emphasizes the importance to evaluate the role of EBV in acute neurological syndromes in pediatric patients, in particular, in presence of behavioral changes with EEG evidence of seizures. NCSE in children denotes electrographic seizures without convulsive activity and often manifests as altered mental status. It may be difficult to diagnose in pediatric patients in whom changes of behavior and consciousness may not be as easily recognized as in adults. EEG examination plays a crucial role in the evaluation of a patient with NCSE. Continuous observation as well as long-term research is needed to improve both management and outcome of such patients.

REFERENCES

1. **Kaplan P.W.** EEG criteria for nonconvulsive status epilepticus. *Epilepsia*. 2007; 48(8):39–41.
2. **Koskiniemi M., Rantalaiho T., Piiparinen H. et al.** Infections of the central nervous system of suspected viral origin: a collaborative study from Finland. *Journal of NeuroVirology*. 2001;7, (5):400–408.
3. **Kleines M., Schiefer J., Stienen A., Blaum M., Ritter K., Häusler M.** Expanding the spectrum of neurological disease associated with Epstein-Barr virus activity. *European Journal of Clinical Microbiology & Infectious Diseases*. 2011; 30(12):1561–1569.
4. **E. Bathoorn, B.J. Vlamincx, S. Schoondermark-Stolk, R. Donders, M. van der Meulen, and S.F.T. Thijsen.** Primary Epstein-Barr virus infection with neurological complications. *Scandinavian Journal of Infectious Diseases*. 2011; 43(2):136–144.
5. **Gretchen M.B., Bell R., Claassen J. et al.** Guidelines for the Evaluation and Management of Status Epilepticus. *Neurocritical Care*. 2012, 17(1):3-23
6. **Greco F., Cocuzza M.D., Smilari P., Sorge G., Pavone L.** Nonconvulsive Status Epilepticus Complicating Epstein-Barr Virus Encephalitis in a Child. *Case Reports in Pediatrics*. 2014; 2014:547396. doi: 10.1155/2014/547396. Epub 2014 Mar 12.
7. **Tay S.K., Hirsch L.J., Leary L., Jette N., Wittman J., Akman C.I.** Nonconvulsive status epilepticus in children: clinical and EEG characteristics. *Epilepsia*. 2006;47(9):1504–1509.
8. **Lennox W.** The petit mal epilepsies: their treatment with tridione. *JAMA*. 1945; 129:1069–1073.
9. **Calcii C., Trofim R., Cozac V.** Non convulsive status epilepticus in children. Annual scientific conference of collaborators and students, „Nicolae Testemitanu” University of Medicine and Pharmacy. Collection of scientific abstracts. Chisinau. 2014; 179.