Abstract. Herpes simplex encephalitis (HSE) is a severe viral infection of the central nervous system and it’s one of the most common causes of life-threatening fulminate necrotizing viral encephalitis. Most frequently the patients’ presentation is a non-specific one, consisting of fever, headaches, vomiting, focal neurological signs, and seizures in association with an altered consciousness. The management of HSE has been improved in the last years through the availability of intravenous acyclovir therapy and PCR - based diagnostic assays, reducing mortality and morbidity rates and decreasing rates of neurological sequelae. The objective was to expose clinical data, laboratory test sequencing and management courses in HSE among children - a clinical case report. We present the case of a 15 month-old boy, admitted in the ICU of National Institute for Infectious diseases “Prof. Dr. Matei Bals” for fever, vomiting, diarrhoea, focal and generalized seizures, drowsiness, bulging anterior fontanel and altered mental status. The diagnosis of HSE was established corroborating data from the clinical findings with the neurological exam, and confirmed by detecting the HSV type I DNA in CSF using PCR; Brain MRI was highly suggestive for HSE. The patient was treated with i.v Acyclovir; anticonvulsant drugs, anti cerebral-edema therapy and i.v human immunoglobulin. The child was discharged after 25 days with a good clinical and neurological condition.

Keywords: herpes simplex type 1 encephalitis, polymerase chain reaction (PCR), cerebrospinal fluid, antiviral therapy

Introduction

Herpes simplex encephalitis (HSE) is a severe viral infection of the central nervous system and is the most common cause of life-threatening necrotizing viral encephalitis. Herpes simplex virus spreads to the brain by means of direct neuronal transmission from a peripheral site to the brain via the olfactory or trigeminal nerve. The exact pathogenesis and the precipitating factors or the predisposing underlying conditions are still unclear. [5]

The clinical presentation is non-specific consisting of fever, headaches, vomiting, focal neurological signs, seizures and altered level of consciousness. The etiologic diagnosis is established using rapid polymerase chain reaction (PCR) on cerebrospinal fluid (CSF) samples, although the combination of the clinical findings, CSF demonstrating pleocytosis with normal or elevated protein levels, specific brain MRI changes and diffuse abnormal electroencephalogram pattern with focal epileptic discharges. [2] It is known that herpes simplex virus has a high affinity for limbic system, insular cortex, medial temporal lobes, and inferolateral frontal lobes, affecting these areas bilaterally but presenting with asymmetrical involvement. [3]

HSE management has been improved in the last years through the availability of i.v. acyclovir therapy and PCR - based diagnostic assays, reducing mortality from 80% to 20%, significantly decreasing morbidity rates and subsequent neurologic sequelae. [6] Untreated HSE is a progressive and fatal condition in 70% of the cases in 7-14 days from onset.
Clinical case

We present the case of a 15 month-old boy, admitted in ICU of National Institute for Infectious diseases “Prof. Dr. Matei Bals” for fever, vomiting, diarrhoea, focal and generalized seizures, drowsiness, bulging fontanel and altered mental status. The symptoms’ onset occurred 7 days before the patient admission with high fever (40 ºC), diarrhoea and vomiting. The child was initially admitted in a regional paediatric facility where he received empiric antibiotic therapy, i.v. fluids and antipyretics with initial unfavourable clinical evolution. Latter on he experienced repeated vomiting, irritability and drowsiness, high fever, axial hypotonia and focal seizures and he was consequently transferred to our clinic, The National Institute for Infectious diseases “Prof. Dr. Matei Bals”.

On admission the clinical examination revealed: a 15 month old boy, well nourished, with mediocre general condition, running a fever of 39,7 ºC; presenting with pale skin; no abnormal respiratory sounds were noted over the lungs area, cardiac rhythm was regular, no extra-beats or murmurs were identified during the initial evaluation; heart rate - 120-130 beats/min, blood pressure - 95/52 mmHg; no cyanosis was noted; oxygen saturation measured by pulse oximetry was 98% in room atmosphere, the abdominal exam found a symmetric, soft and non tender abdomen, no hepatosplenomegaly was discovered; physiological diuresis was present, the neurological examination describes a normotensive fontanel, drowsiness, axial hypotonia, no focal neurological signs. In the first hours after admission the child experienced recurrent focal seizures with rapid neurological deterioration, bulging fontanel and decreased level of consciousness (GCS 5/15).

The initial brain MRI studies revealed diffuse enhancement of hippocampus and parahippocampal gyrus, anterior inferior temporal lobe, insular cortices, internal occipital lobe and parieto-occipital lobe in left brain hemisphere and parahippocampal gyrus and intern occipital lobe in right brain hemisphere; small foci of signal loss representing hemosiderin deposition in affected areas (Fig 1, 2, 3).

The electroencephalogram (EEG) showed abnormal brain electrical activity: diffuse high amplitude slow-wave background activity without definite epileptiform discharges.

Serological tests using enzyme-linked immunosorbent assay (ELISA) came back positive for Herpes simplex Virus for the acute (Ig M) antibody subclass. Lumbar puncture was performed and revealed clear CSF, hypertensive, pleocytosis with predominance of lymphocytes and elevated protein; PCR assay for HSV type 1 was positive in CSF.

He was treated with i.v. Acyclovir for 24 day, anticonvulsant drugs in order to control seizures (Phenytoin and Levetiracetam), anti cerebral-oedema measures were implied - consisting of intravenous 20% mannitol and pulse steroid therapy with Methylprednisolone was initiate and was followed by a Dexamethasone regimen in a tapering down doses protocol, i.v human non-specific immunoglobulin were administered.

The clinical and neurological evolution was good with the rapid recovery of consciousness and complete seizure control during the first 48 hours after admission, with progressive improvement in the ability to perform fine/ gross motor skills and without sensory
impairment. The child was discharged after 25 days in good condition even though subsequent brain MRI re-evaluation showed cystic encephalomalacia in affected areas (Fig 4,5).

It was hard to predict whether the over crossed life-threatening condition would affect his cognitive and language development. In these cases careful and long term follow-up is required in order to identify the late effects on the patient’s cognitive or affective development and consequently guide the speech and the occupational therapies.

**Discussions**

Herpes simplex encephalitis (HSE) remains one of the most devastating infections of the central nervous system with severe sequelae and long term consequences, despite available antiviral therapy. It is highly recommended to initiate optimal antiviral therapy in front of a suspected HSE in a paediatric patient, pending confirmation of the diagnosis since acyclovir, the drug of choice, is relatively nontoxic and because the prognosis of untreated herpetic encephalitis is poor.[5]

The diagnosis should be established as soon as possible after the symptoms’ onset in order to obtain good clinical progressions, with reduced mortality and morbidity. Even with early administration of therapy after the onset of disease, nearly 60-70 % of survivors will have significant neurological deficits.[1, 4]

Pulse steroid therapy with Methylprednisolone may be beneficial in HSE, particularly in reducing the consciousness disturbance and in improving the neurological deficits. High doses of Methylprednisolone i.v. may improve the cerebral oedema and regulate the host immune response. The combination therapy using both acyclovir and pulse corticosteroids therapy can achieve a better outcome in patients with HSE.

**Conclusions**

- Herpes simplex encephalitis is the most common cause of sporadic fatal encephalitis worldwide and it is a medical emergency that requires urgent etiological treatment.
- PCR for detecting HSV DNA from CSF remains the gold standard in the diagnosis of HSE.
- Early initiation of antiviral therapy with i.v. Acyclovir improves the clinical and neurological outcomes.
- Pulse steroid therapy in conjunction with antiviral therapy could achieve a better prognosis for children with HSE.
- Mortality ranges dramatically depending on how early treatment is implied.

**References**


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