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Case report

# Akathisia in association with herpes simplex encephalitis relapse and opercular syndrome in children

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**Abstract**

We report a 2-year-old boy with herpes simplex virus type 1 encephalitis (HSE) and opercular syndrome who presented with clinical relapse characterized by chorea-like involuntary movements that suggest akathisia. The patient initially presented with multiple focal seizures that cause epilepsia partialis continua, polymerase chain reaction (PCR) for herpes simplex virus type 1 was positive. He developed hypersalivation, speech and swallowing difficulties within 30 days. Based on these findings the patient was diagnosed as having opercular syndrome due to HSE. He developed akathisia on 44th day of admission as a relapse and he was successfully treated with propranolol.

Opercular syndrome might be seen HSE in children and it may cause neurological suquela. Akathisia might be seen after encephalitic process as a symptom of relapse, however diagnosis of akathisia is difficult in young children. It should be noted that because propranolol effective for these involuntary movements. It can be add additional choice of treatment in these patients.


*Keywords:* Akathisia; Relapsing herpes simplex encephalitis; Opercular syndrome; Propranolol

## 1. Introduction

HSE is the most common sporadic encephalitis in children. Its incidence is approximately 1:250,000–500,000 per year and it has a 70% of mortality rate when untreated. Therefore, it is important to diagnosis this disease and consider antiviral treatment as early as possible. Clinical manifestations of HSE are typically associated with fever, altered consciousness, behavioral disturbances, seizures and focal neurologic deficits [1]. However, nonspecific manifestations can be observed in younger ages.

Recently, it has been reported that acute opercular syndrome might occur as an initial manifestation of HSE in children. Opercular syndrome is characterized by disturbances of voluntary control of the facio-linguo-glosso-pharyngeal muscles that cause dysphagia, dysarthria, hypersalivation and pyramidal signs [2].

Although HSE mortality and morbidity have been significantly reduced by acyclovir treatment, neurologic relapses have been reported in 5–30% of HSE patients. The pathogenesis of HSE relapses is unclear. It has been suggested that symptoms might be delayed because of initial cerebral infection; that immuno-inflammatory disorders may play a role, or that relapses may be caused by the resurgence of viral replication [3].

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Involuntary movements, particularly choreoathetosis, can be observed with HSE in children who develop clinical relapse. Here, we report on a 2-year-old boy with HSE and opercular syndrome who presented with clinical relapse characterized by hyperkinetic movements, which are chorea-like involuntary movements that suggest akathisia; the child was successfully treated with propranolol.

## 2. Case report

A 2-year-old boy was admitted to our hospital with fever and multiple focal seizures involving his left arm and face; these secondary generalized symptoms continued for 4 days, and he was given repeated intravenous (IV) doses of benzodiazepine. He was born uneventful vaginal delivery and, there is no consanguinity between father and mother. In his family history there is no neurological disorders or specific viral infections. His neurodevelopmental history was normal. Physical examination revealed the followings: temperature 38 °C, pulse 142 beat/min, blood pressure 86/51 mmHg and respiratory rate 24 breaths/min. His head circumference was 44 cm (25th–50th percentile), his body weight was 13 kg (50th percentile) and his height was 125 cm (50th percentile). The initial neurologic examination revealed that the boy was lethargic, but there were no meningeal irritation findings. The cranial nerves were intact, and muscle tonus was normal. Deep tendon reflexes were normoactive, and there were no pathologic reflexes.

The laboratory findings at admission revealed the followings: WBC 10,700 cells/mm$^3$ (68% neutrofil), Hb 10.9 g/dl, and C-reactive protein 2.2 mg/dl (0–0.8 mg/dl). The erythrocyte sedimentation rate was 33 mm/h; the serum benzodiazepine level was 7375 mg/dl (50–500 mg/dl), and the serum electrolytes and urine analysis were normal. A cerebrospinal fluid analysis showed normal protein (41 mg/dl) and glucose (107 mg/dl) and 3 lymphocyte/mm$^3$; the PCR for HSV Type 1 was positive (>15,000 copy/ml).

An electroencephalogram (EEG) showed diffuse generalized delta and theta activity. Cerebral computerized tomography was initially normal. Cerebral magnetic resonance imaging (MRI) was performed on the 10th day and demonstrated increased signal intensity at the bilateral opercular cortex, predominantly on the right side, on T2 weighted images (Fig. 1).

Intravenous acyclovir (30 mg/kg/day) was given for 21 days. The seizures were stopped with intravenous diphenylhydantoin treatment. To decrease the high benzodiazepine level, flumazenil infusion (0.01 mg/kg/h) was given. After 3 days, the patient's serum benzodiazepine level and consciousness normalized. On the 10th day of hospitalization, a neurological examination revealed that his deep tendon reflexes were hyperactive. The Babinski sign was positive bilaterally; his muscle tonus was slightly decreased, and involuntary movements developed on his left side. He was unable to sit and to walk. There were partial recurrent seizures on his left arm, which were controlled with an IV midazolam infusion, oral levetiracetam and clobazam treatment. On the 21st day of admission, hypertension developed. A renal Doppler ultrasound and renal scintigraphy were normal. The hypertension was suggested to be a side effect of the acyclovir treatment. The controlled PCR result for HSV Type 1 was negative; therefore, acyclovir treatment was stopped. On the 31st day, the child had speech and swallowing difficulties and hypersalivation. Cerebral MRI performed on day 44 showed bilateral encephalomalacia at the right frontal opercular region (Fig. 2). In addition he manifested hyperkinetic behavior, hyperactivity, restlessness, sleeplessness with dyspnea, wyoclonic jerks, chorea-like involuntary movements, on the 44th day of admission. He was unable to remain motionless, even while eating. Haloperidol was given for the involuntary movement, but the symptoms continued. In laboratory, WBC 14,700 cells/mm$^3$ (62% neutrofil), sedimentation rate was 92 mm/h, serum HSV Type 1 immunoglobulin G was positive and immunoglobulin M was negative. We suggested that HSE relapse had occurred. Intravenous methylprednisolon (30 mg/kg/day) and intravenous immunogloblin (0.4 g/kg, 5 days) treatment failed. After being given 1 mg/kg/day propranolol treatment, the patient's involuntary movements dramatically improved. A 5-month follow-up neurologic examination was normal. The child could walk without support; however, swallowing, speech difficulties and hypersalivation continued.

## 3. Discussion

Herpes simplex encephalitis is generally characterized by fever, convulsions, focal neurological signs, altered level of consciousness and behavioral disturbances [4]. However, symptomatology at onset might be absent, and typical neurologic manifestations for HSE may appear during the following days. Nonspecific clinical presentations might be observed in children, particularly those under 2 years of age. Therefore, in children with suspected encephalitis, early treatment with acyclovir is important for the prognosis of HSE.

There are several reports describing opercular syndrome as an initial neurologic manifestation of HSE; these syndrome may also occur during the course of HSE in children. Herpes simplex encephalitis associated opercular syndrome has been rarely reported [5]. Bilateral opercular lesions cause the opercular syndrome and are characterized by paralysis of the masticatory, facial, pharyngeal, and tongue muscles. The clinical characteristics include difficulty chewing, bilateral facial weakness, incomplete closure of the mouth, drooling of