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Case report

Postinfectious immune-mediated encephalitis after pediatric herpes simplex encephalitis

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Abstract

We report a 3-year-old patient who presented a secondary acute neurological deterioration clinically characterized by a partial Kluver–Bucy syndrome, 1 month after the onset of herpes simplex encephalitis. This episode is unlikely due to continuation or resumption of cerebral viral replication but might be related to an immune-inflammatory process. In children, postinfectious immune-mediated encephalitis occuring after HSE are usually clinically characterized by choreoathetoid movements. This type of movement disorder was, however, not observed in this patient. On the basis of this case and a review of the literature, we hypothesize the existence of a spectrum of secondary immune-mediated process triggered by herpes simplex virus cerebral infection ranging from asymptomatic cases with diffuse white matter involvement to secondary acute neurological deteriorations with or without extrapyramidal features.

Keywords: Herpes simplex encephalitis; Relapse; Immune-mediated process; Postinfectious encephalopathy; Kluver–Bucy syndrome

1. Introduction

The evolution of herpes simplex encephalitis (HSE) in children may be characterized by the occurrence of postinfectious immune-mediated encephalitis [1]. These episodes are classically characterized by a secondary acute neurological deterioration with unilateral or bilateral choreoathetoid movements [1].

Kluver–Bucy syndrome (KBS) has been described in children after HSE with severe bilateral temporal lesions [2]. In the pediatric population, this syndrome is clinically characterized by altered emotional behavior, changes in dietary habits such as bulimia, hyperorality and hypersexuality, psychic blindness and hypermetamorphosis [2].

We report a young boy who presented an immune-mediated secondary acute neurological deterioration clinically characterized by a partial KBS. On the basis of this case and a review of the literature, we hypothesized the existence in children of a clinical spectrum of secondary immuno-inflammatory disorders induced by herpes simplex virus (HSV) cerebral infection.

2. Case report

A 3-year-old boy with normal previous medical and developmental history presented with a prolonged febrile left-side clonic seizure, which lasted 25 min and stopped after an intrarectal administration of diazepam (15 mg). During the 3 days preceding admission, he had fever (39 °C), headache and vomiting episodes. On admission,

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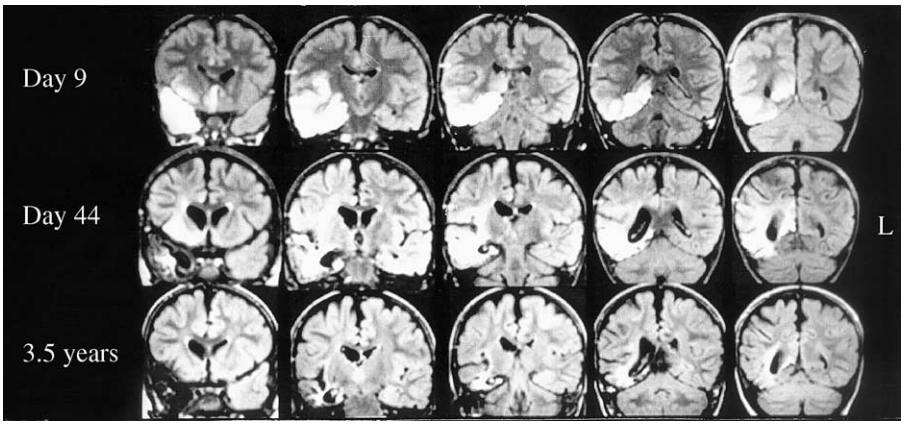

Fig. 1. Cerebral MRI performed at 1.5 T. Upper row: cerebral MRI performed on day 9 of the first HSE episode. Coronal fluid attenuated inversion recovery (FLAIR) MRI showing diffuse hyperintensity of the right temporal lobe, the insular cortex and the inferior frontal lobe together with focal cortical and subcortical hypointensity related to hemorrhage or cortical laminar necrosis (recovery time: 6000, echo time: 150, inversion time: 2000). Middle row: cerebral MRI performed on day 44, 12 days after the beginning of the secondary acute neurological deterioration. Coronal FLAIR MRI showing severe increased signal in the white matter of the right temporal lobe and the right subcortical region. Necrosis and atrophy of the cortical region involved in the initial episode can also be observed (recovery time: 5865, echo time: 140, inversion time: 2000). Lower row: cerebral MRI performed 3.5 years after the first episode of HSE. Coronal FLAIR MRI showing severe atrophy of the right temporal lobe and the right subcortical region (recovery time: 6500, echo time: 150, inversion time: 2100). An incomplete regression of the white matter lesions can be observed.

neurological examination was normal. Cerebrospinal fluid (CSF) analysis showed 80 leukocytes/mm^3 (69% lymphocytes), normal protein level and positive polymerase chain reaction (PCR) for HSV. The electroencephalogram (EEG) showed delta waves over the right hemisphere and no epileptic discharges. Cerebral computerized tomography was normal. Intravenous acyclovir was then started at a dosage of 60 mg/kg/day for 21 days and antiepileptic drugs were given in order to prevent seizure recurrence. Under these treatments, fever resolved after 36 h and seizure did not recur. Cerebral magnetic resonance imaging (MRI) performed on day 9 showed necrotic-hemorrhagic lesions involving the right temporal lobe, insula and orbito-frontal region (Fig. 1, upper row). The patient was discharged on day 25 with normal neurological examination.

He was readmitted on day 32 with increasing hyperactivity, aggressiveness, irritability, disinhibition, bulimia and sleep problems. Temperature was 37.7 °C. He was markedly overactive, had temper tantrums and palilalia. Interaction in general and visual contact in particular were poor and he seemed unable to recognize objects (psychic blindness), which he explored compulsively with his mouth (hyperorality). Neurological and general examination was otherwise normal. CSF analysis showed 13 leukocytes/mm^3 (94% lymphocytes), normal protein level and negative HSV PCR. EEG showed diffuse, symmetric slow activity. Acyclovir (60 mg/kg/day) was started for 10 days. Despite antiviral treatment, his neurological status progressively deteriorated. Four days (day 4) after this second admission, he stopped talking and eating. On day 8, his level of consciousness progressively deteriorated and seizures recurred. Cerebral MRI performed on day 12 showed severe white matter involvement in the right temporal lobe and subcortical regions (Fig. 1, middle row). At this time, corticosteroids (intravenous methylprednisolone 30 mg/kg/day) were given for 5 days and weaned over 6 weeks. Within 48 h on this treatment, the patient's state of consciousness and behavior improved. They normalized over the following 3 weeks. On day 18, CSF analysis showed an increased level of total immunoglobulin G (Ig G) (Ig G level: 6.1 mg/dl, normal Ig G level: 1.7–3.4 mg/dl) with a high CSF/serum ratio (ratio: 3.1). CSF isoelectric focussing demonstrated the presence of oligoclonal bands in the domain of alkali immunoglobulins. Oligoclonal bands were not evidenced in the serum. At the age of 6 years, the neurological examination has remained normal. Cerebral MRI performed 3.5 years after the onset of HSE showed severe atrophy of the right temporal lobe and the right subcortical region (Fig. 1, lower row).

3. Discussion

Postinfectious immune-mediated encephalitis occurring after HSE have been previously suspected in numerous children with secondary acute neurological deteriorations clinically characterized by choreoathetoid movements on the basis of absence of new necrotic-hemorrhagic lesion on cerebral imaging, absence of efficacy of antiviral treatment in preventing or improving the movement disorder, the existence of diffuse white matter involvement in some patients and the absence of virus isolation from brain biopsies when performed [1]. The secondary