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Restricted Diffusion in the Bilateral Subcortical Motor Areas Associated with Status Epilepticus in an Infant with Kawasaki Disease

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ABSTRACT

Status epilepticus (SE) often causes neuronal death in the cerebrum and consequent long-term sequelae. Acute encephalopathy with biphasic seizures and late reduced diffusion is clinically characterized by SE associated with fever and seizure clusters that occur 3–9 days after symptom onset. MRI reveals reduced diffusion in the frontal or frontoparietal subcortical white matter, with sparing of the perirolandic region following seizure clusters. Kawasaki disease (KD) is an acute self-limited vasculitis secondary to activation of the immune system; KD is rarely complicated by acute encephalopathy. We report the case of a male infant who developed SE associated with KD and showed late reduced diffusion in the subcortical white matter beneath the bilateral motor cortices (primary motor, premotor and supplementary motor areas) and the right frontal cortex. The patient had characteristic neurological sequelae in the chronic phase, including clumsiness of fingers and forearms, impaired discrimination of tactile sensation and position sense on digits in his hands and feet, corresponding to the lesions with reduced diffusion at the acute phase.

Key words acute encephalopathy with biphasic seizures and late reduced diffusion; Kawasaki disease; perirolandic region; status epilepticus; subcortical white matter

Status epilepticus (SE) results from failure of the mechanisms underlying seizure termination or triggering of mechanisms that contribute to abnormally prolonged seizures. Depending on the type and duration of seizures, SE results in long-term complications, including neuronal injury or death and alterations in neuronal networks.[1] Acute encephalopathy with biphasic seizures and late reduced diffusion (AESD), a disorder caused by viral infection, develops following high fever and is clinically characterized by SE within 24 hours of fever onset. Seizure clusters occur 4–6 days after SE. Increased subcortical glutamate levels associated with SE induce excitotoxic neuronal injury.[2–5] Magnetic resonance imaging (MRI) is usually unremarkable over the first 2 days and reveals reduced diffusion in the frontal or frontoparietal subcortical white matter, with sparing of the perirolandic region after seizure clustering.[2]

Central nervous system (CNS) involvement in Kawasaki disease (KD), such as aseptic meningitis, cerebral infarction, encephalitis, and acute encephalopathy is rare.[6] Regarding acute encephalopathy/encephalitis, posterior reversible encephalopathy syndrome (PRES) and clinically mild encephalitis or encephalopathy with a reversible splenial lesion are reported.[7, 8] Only two previous case reports have described AESD that presented with frontoparietal or fronto-occipital subcortical white matter involvement and perirolandic region sparing.[9, 10]

We report the case of an infant who developed SE associated with KD and showed late reduced diffusion in the subcortical white matter beneath the bilateral motor cortices. The patient showed neurological sequelae associated with the primary motor, premotor and supplementary motor areas.

PATIENT REPORT

A nine-month-old male infant without a history of neurological disorder was admitted to a hospital for evaluation of asthma and a 2-day history of fever. He also showed conjunctival injection, erythema of the lips, rash, and a reddish scar of the Bacillus Calmette-Guerin vaccine and was diagnosed with incomplete KD.

The patient was transferred to the hospital via ambulance owing to the status of generalized clonic seizures (day 1). Seizures persisted for 45 min and ceased after he received a midazolam injection. Cranial MRI revealed slightly high signal intensity in the left posterior central gyrus on diffusion-weighted imaging (DWI). Cerebrospinal fluid analysis showed pleocytosis

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Abbreviations: AESD, acute encephalopathy with biphasic seizures and late reduced diffusion; CNS, central nervous system; DWI, diffusion-weighted imaging; KD, Kawasaki disease; HIE, hypoxic-sichemic encephalopathy; MRI, magnetic resonance imaging; ODS, osmotic demyelination syndrome; PRES, posterior reversible encephalopathy syndrome; SE, status epilepticus

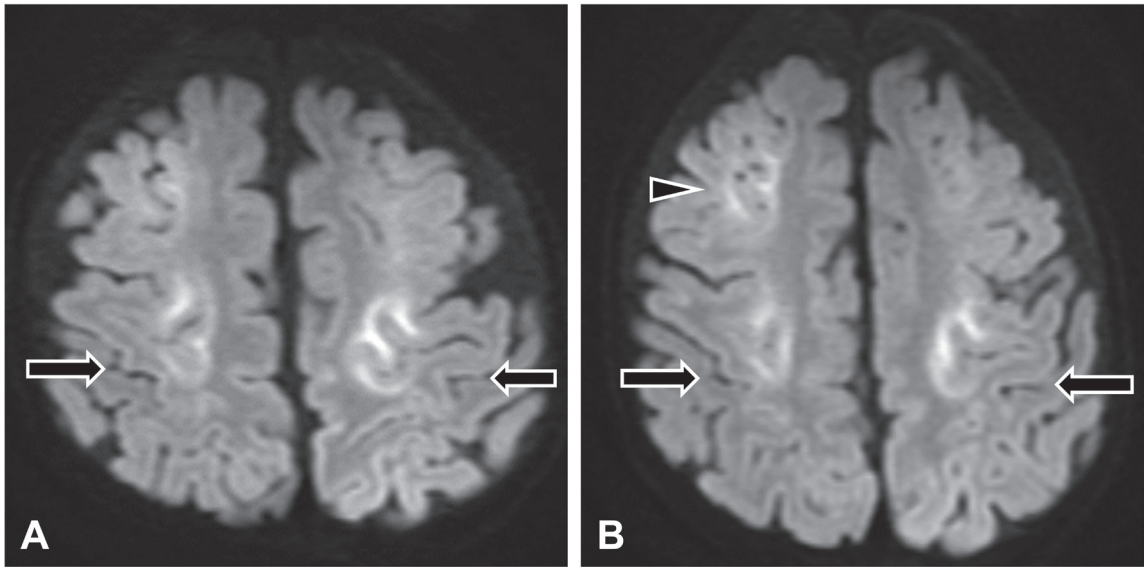

Fig. 1. Cranial diffusion-weighted MRI scan obtained on day 4 after status epilepticus onset. High signal intensities are observed in the subcortical white matter beneath the bilateral motor cortices (**A** and **B**, arrows) and the right frontal cortex (**B**, arrowhead). Arrows show central sulcus.

and negative results for bacterial culture and herpes simplex virus. The patient was treated with continuous intravenous midazolam infusion for the seizure, high-dose immunoglobulin (2 g/kg) for KD, and mannitol, edaravone, and acyclovir for probable onset of encephalitis. His consciousness continued to deteriorate.

On day 4, the patient developed motor seizure clusters and was treated with phenobarbital. Cranial MRI-DWI performed on day 5 revealed high signal intensities in the subcortical white matter beneath the bilateral motor cortices and the right frontal cortex (Fig. 1). Immunoglobulin (1 g/kg) and methylprednisolone pulse therapy (30 mg/kg/day for 3 days) were administered for management of acute encephalitis. The signal changes observed on DWI resolved after day 10.

The patient remained drowsy until one month after symptom onset and was discharged on day 77. As a sequelae he showed trunk muscle weakness, right upper extremity spasticity, flaccid paralysis of the left lower extremity, mild intellectual disability, focal dystonia, ataxia, and dysarthria.

His neurological status was re-evaluated at 11years of age, the patient's full-scale intelligence quotient was 67 based on the Wechsler Intelligence Scale for Children-Fourth Edition. Although he did not show pyramidal, cerebellar, or dorsal cord signs, we observed clumsiness during finger exercises and forearm rotation. Discrimination of tactile sensation was impaired in the second and third digits in his right hand and foot and in the second and fourth digits in his left hand and foot. Position sense was also impaired in these digits. Cranial MRI and electroencephalography revealed no abnormalities.

DISCUSSION

We present the case of an infant who showed late reduced diffusion in the subcortical white matter beneath the bilateral motor cortices after febrile SE associated with KD, together with characteristic motor and sensory impairments during the chronic phase.

Our patient showed diffusion abnormalities in the motor area after SE. This distribution differs from that associated with frontal or frontoparietal lesions in cases of AESD. As similar cases, pericentral gyrus injury is observed in neonatal hypoxic-ischemic encephalopathy (HIE), PRES, and osmotic demyelination syndrome (ODS).[11–13] Our patient's clinical course did not correspond with the features of neonatal HIE and ODS. Vasogenic edema is the pathophysiological mechanism underlying PRES[14] and it may occur in KD.[7] In addition PRES shows watershed pattern,[14] which contains perirolandic area. Although the CNS symptoms are rare in KD, 30% of the patients with KD subclinically shows reduced cerebral blood flow, which is also seen in the condition of vasogenic edema.[15] Although our patient did not present with apparent lesions on the initial MRI, increased vascular permeability associated with vasculitis in KD (which was mild and undetectable on imaging) may have generated motor cortices and caused SE.

In AESD, initial SE causes glutamate-induced excitotoxic cortical injury, which manifests with subcortical lesions 3–9 days later, with concomitant seizure clusters.[2, 3] Our patient developed SE on the third day of fever, which was late to meet the diagnostic criteria of AESD.[4] However, the course of SE onset without MRI-documented lesions, followed by restricted diffusion in the subcortical white matter accompanied by seizure clusters observed in our patient resembles that of AESD. SE that showed foci in the bilateral motor cortices may have been associated with vascular permeability commonly observed in KD, which led to excitotoxic neuronal injury and restricted diffusion in the same areas, the characteristic findings in this patient.

Although no clear brain atrophy was observed during the chronic phase, focal dystonia, ataxia, tactile and deep sensory disturbances, and dysarthria persisted in our patient. Disruption of the circuit between the basal ganglia, cerebellum, supplementary motor area and prefrontal cortex induce to the focal dystonia,[16] which cause sensorimotor integration associated with specific sensory dysfunctions in kinaesthesia and spatial-temporal discrimination.[17] Ataxia is sequelae reported in case of infraction of precentral gyrus.[18] Dysarthria is attributable to bilateral frontal motor cortex injury.[13] The sequelae observed in our patient may be attributed to chronic injury to the motor cortices based on DWI lesions observed during the acute phase.

The authors declare no conflict of interest.

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