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Clinical Observations

Postictal Subcortical Restricted Diffusion in a Child With Focal Symptomatic Epilepsy



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ABSTRACT

BACKGROUND: Diffusion abnormalities on MRI are well described after prolonged seizures. However, isolated, focal, subcortical restricted diffusion is uncommon. **PATIENT:** A girl of Kurdish descent experienced focal-onset epilepsy secondary to a left thalamic infarction at age 3 years. At age 6 years, she developed status epilepticus in the context of a febrile illness. **RESULTS:** Four days after the seizure, she had neurological deterioration including involuntary posturing movements and irritability. A brain MRI revealed left hemisphere subcortical restricted diffusion, predominantly in the frontal and occipital regions. She experienced persistent right hemiparesis for 2 months after the initial seizure. **CONCLUSIONS:** This presentation is reminiscent of acute encephalopathy with biphasic seizures and late reduced diffusion, a syndrome thus far reported almost exclusively in Japan. This represents one of the few documented examples of acute encephalopathy with biphasic seizures and late reduced diffusion in an individual not of east Asian descent.

Keywords: magnetic resonance imaging, epilepsy, acute encephalopathy with biphasic seizures and late reduced diffusion, hemiparesis, status epilepticus

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Introduction

Diffusion abnormalities on magnetic resonance imaging (MRI) are well described after a prolonged seizure.^{1,2} However, isolated, focal, subcortical restricted diffusion is uncommon.³ For reasons that are not clear, this radiologic pattern is primarily observed in pediatric patients with seizures occurring in the context of febrile illness.⁴ We present a child with focal status epilepticus who subsequently developed persistent neurological deficits and subcortical restricted diffusion on MRI.

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Patient description

At age 3 years, this girl suffered a left thalamic infarction secondary to cerebral venous sinus thrombosis, possibly related to severe anemia. She subsequently developed focal epilepsy with seizures characterized by clonic movements of the right face and arm. Her seizures were generally well controlled on levetiracetam; however, she continued to have infrequent episodes of focal status epilepticus associated with postictal weakness. One episode required intensive care unit admission and intubation.

She had previously exhibited left hand preference and moderate global developmental delay. Her physical examination was significant for bilateral microphthalmia and congenital cataracts. Her parents were first cousins, both from the region of Kurdistan. The family history was significant for a brother who also had microphthalmia and cataracts, as well as two brothers with congenital ichthyosis, and multiple individuals with carnitine transport deficiency. Although there was a high index of suspicion that the patient had an underlying genetic or metabolic disorder, thorough testing did not yield a diagnosis.

At age 6 years, she presented with generalized tonic-clonic status epilepticus during a febrile illness. She was intubated upon arrival at the hospital and required multiple antiepileptic medications including lorazepam, fosphenytoin, and a midazolam infusion. The total duration of

seizure activity was estimated at 90 minutes. Computed tomography scan performed 4 hours after seizure onset revealed no acute change. Evaluation for infection later revealed an enterovirus and/or rhinovirus upper respiratory tract infection, enterococcus urinary tract infection, and a suspected atypical pneumonia. An electroencephalography approximately 10 hours after the seizure revealed diffuse nonspecific slowing.

She was extubated after <12 hours and appeared to return to her baseline level of consciousness within 2 days. She did, however, have persistent right hemiparesis. Four days after the seizure, she was still remained hemiparetic and developed involuntary posturing movements of her right arm and leg. She also had an episode of headache with irritability that parents felt was very abnormal. With these new features, a repeated electroencephalography was performed and revealed frequent bifrontal epileptiform discharges, with a background still slightly slow for age.

MRI of the brain under general anesthetic was performed on day 4 after the seizure and revealed T2 hyperintensity in the left hemisphere, primarily in the occipital and frontal regions. These same areas were associated with restricted diffusion in the subcortical white matter including U fibers, with sparing of the cortex (Fig 1). Vascular imaging was normal and no abnormal enhancement was observed with gadolinium. A repeat MRI 2 months later revealed resolution of these changes with interval atrophy of the left cerebral hemisphere (Fig 2). The patient continued to have gradual improvement of the right hemiparesis, but still had persistent weakness at 2-month follow-up.

Discussion

We present a child with epilepsy who presented with status epilepticus in the context of a febrile illness. After a relatively lucid interval, her neurological function deteriorated and an MRI demonstrating subcortical cytotoxic edema. A similar clinical pattern has been described as acute encephalopathy with biphasic seizures and late reduced diffusion (AESD), a syndrome thus far recognized almost exclusively in Japan.⁵

The classic AESD clinical phenotype involves a prolonged seizure in the context of a febrile illness.⁵ Immediately after the seizure, patients have a normal MRI and a lucid interval of several days before again developing seizures and encephalopathy. MRI at this time reveals subcortical restricted diffusion. Follow-up MRI reveals resolution of the diffusion abnormalities but often demonstrates cerebral atrophy. Patients with the same radiologic findings, without the

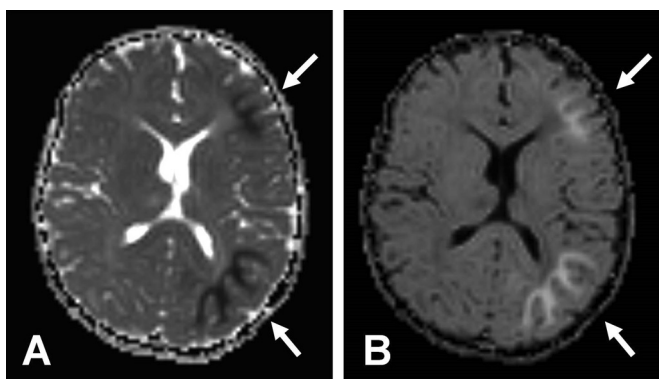


FIGURE 1. Axial apparent diffusion coefficient (A) and diffusion weighted imaging (B) images from a study 4 days after the initial seizure. Subcortical cytotoxic edema is observed in the left hemisphere, primarily in the frontal and occipital regions (arrows).

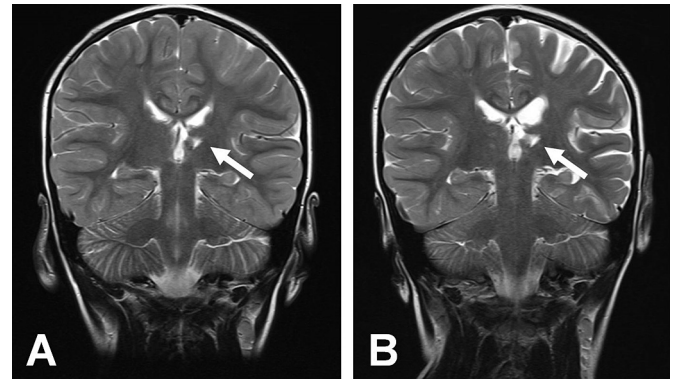


FIGURE 2.

Coronal T2-weighted images taken 4 days after the initial seizure (A) and at follow-up 2 months later (B), illustrating interval atrophy of the left cerebral hemisphere. Both images also demonstrate the left thalamic encephalomalacia secondary to the remote venous sinus thrombosis infarction (arrow).

biphasic course, are considered to have acute encephalopathy with subcortical restricted diffusion.⁵

This girl's clinical presentation fits within the spectrum of acute encephalopathy with subcortical restricted diffusion, with some features that have not been previously described. She had prolonged hemiplegia, well beyond what is considered normal for a simple postictal paresis, and clinical deterioration 4 days after the initial seizure. The precise mechanism for her late deterioration is not clear; however, late seizures could explain the brief periods of irritability and involuntary right arm movements. Her initial computed tomography scan did not reveal white matter abnormalities, suggesting that the cytotoxic edema may have appeared after some delay. Our patient illustrates that the acute encephalopathy with subcortical restricted diffusion pattern can be observed in patients with symptomatic epilepsy. Additionally, if this child's presentation can be accepted as within the sphere of AESD this would be only the second reported patient outside of Asia and one of the few in a non-Japanese individual.^{5,6}

The pathophysiology of postictal subcortical restricted diffusion remains poorly understood. Biomarker studies have demonstrated differences in cerebrospinal fluid between AESD and febrile status, specifically that levels of visinin-like protein-1, tau protein, and S100B are elevated in AESD.⁷⁻⁹ The precise significance of these differences is unclear; however, the pattern suggests increased neuronal damage, which could explain why patients with AESD develop atrophy and persistent neurological impairment.

Given the seemingly high prevalence of AESD in Japanese individuals, an underlying genetic or metabolic disorder is likely a contributing factor in cases of postictal subcortical restricted diffusion. This hypothesis is further supported by the reports of similar postictal radiologic patterns in a number of genetic and/or metabolic diseases including non-ketotic hyperglycemia,^{10,11} incontinentia pigmenti,¹² and Dravet syndrome.¹³ Our patient's suspected underlying genetic and/or metabolic disorder likely played a role in her presentation; however, the exact contribution is difficult to determine given the lack of a precise diagnosis.

References

1. Goyal MK, Sinha S, Ravishankar S, Shivshankar JJ. Peri-ictal signal changes in seven patients with status epilepticus: interesting MRI observations. *Neuroradiology*. 2009;51:151-161.
2. Gujjar A, Jacob PC, Al-Asmi A, Ramachandiran N, Obaidi A, Jain R. Reversible MRI changes in prolonged status epilepticus: a case report. *Int J Neurosci*. 2011;121:341-345.
3. Cianfoni A, Caulo M, Cerase A, et al. Seizure-induced brain lesions: a wide spectrum of variably reversible MRI abnormalities. *Eur J Radiol*. 2013;82:1964-1972.
4. Takanashi J, Oba H, Barkovich AJ, et al. Diffusion MRI abnormalities after prolonged febrile seizures with encephalopathy. *Neurology*. 2006;66:1304-1309. discussion 1291.
5. Hayashi N, Okumura A, Kubota T, et al. Prognostic factors in acute encephalopathy with reduced subcortical diffusion. *Brain Dev*. 2012;34:632-639.
6. Yadav SS, Lawande MA, Kulkarni SD, Patkar DA. Acute encephalopathy with biphasic seizures and late reduced diffusion. *J Pediatr Neurosci*. 2013;8:64-66.
7. Shiihara T, Miyake T, Izumi S, et al. Serum and cerebrospinal fluid S100B, neuron-specific enolase, and total tau protein in acute encephalopathy with biphasic seizures and late reduced diffusion: a diagnostic validity. *Pediatr Int*. 2012;54:52-55.
8. Hasegawa S, Matsushige T, Inoue H, et al. Serum and cerebrospinal fluid levels of visinin-like protein-1 in acute encephalopathy with biphasic seizures and late reduced diffusion. *Brain Dev*; 2013.
9. Tanuma N, Miyata R, Kumada S, et al. The axonal damage marker tau protein in the cerebrospinal fluid is increased in patients with acute encephalopathy with biphasic seizures and late reduced diffusion. *Brain Dev*. 2010;32:435-439.
10. Chen CC, Chai JW, Wu CH, Chen WS, Hung HC, Lee SK. Neuroimaging in seizure patients associated with nonketotic hyperglycemia. *Neuroradiol J*. 2011;24:215-220.
11. Raghavendra S, Ashalatha R, Thomas SV, Kesavadas C. Focal neuronal loss, reversible subcortical focal T2 hypointensity in seizures with a nonketotic hyperglycemic hyperosmolar state. *Neuroradiology*. 2007;49:299-305.
12. Abe S, Okumura A, Hamano S, et al. Early infantile manifestations of incontinentia pigmenti mimicking acute encephalopathy. *Brain Dev*. 2011;33:28-34.
13. Abe S, Okumura A, Uematsu M, Imataka G, et al. Acute encephalopathy in children with Dravet syndrome. *Epilepsia*. 2012;53:79-86.

We can never really be prepared for that which is wholly new. We have to adjust ourselves, and every radical adjustment is a crisis in self-esteem: we undergo a test, we have to prove ourselves. It needs inordinate self-confidence to face drastic change without inner trembling.

Eric Hoffer