Postictal Focal Cortical High Signal Intensity Changes on MRI in Nonketotic Hyperglycemic Seizures

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ABSTRACT

Case report: A 48-year old male with diabetes mellitus was taking oral hypoglycemic agents for the previous three years, but had stopped medication for the last three months. On the day before admission, MRI of the head revealed no significant abnormalities. Blood glucose was elevated (23.7 mmol/L), hemoglobin A1c concentration was 12.6%, and serum osmolarity was 285.3 mOsm/L on the day 1 admission. The first several days after admission, the patient with recurrent NKH seizures and loss of consciousness were obtained. On hospital day 5, T2-weighted MRI demonstrated gray matter hyperintensity in the left temporal cortex. When hyperglycemia and seizures was controlled by insulin, he was discharged and prescribed insulin subcutaneous. On follow-up two months later, the hyperintensity had subsided in the left temporal cortex.

Conclusions: Our observations demonstrated that the postictal focal hyperintensity cortex signal should be attributed to the cell edema with laminar necrosis provoked by NKH focal seizures, but are reversible when hyperglycemia and seizures are well controlled by insulin. This information may be important in patient with diabetes enduring treatment.

Keywords: Magnetic resonance imaging, Seizures, Focal neuronal lesion, Nonketotic hyperglycemia.

INTRODUCTION

Nonketotic hyperglycemia (NKH) often causes focal lesions in the brain that can result in epileptic seizures. These NKH seizures can be suppressed by rapidly reducing blood glucose concentrations and controlled by maintaining stable blood glucose. Postictal magnetic resonance images (MRI) revealed lesions in the subcortex and putamen were described in cases of NKH seizures1,2, and focal T2 high signals changes in the left occipital lobe from one NKH seizure case was also reported3. The focal seizures refers to seizures that arise from a particular focal region of the brain such as subcortex or cortex. Although the hyperintensity cortical signals in patients with focal seizures from others brain disease have been reported4,5, the hyperintensity in the cortex after NKH with focal seizures has not been reported to date and represent a rare event. Here, we report an unusual NKH focal seizure case who presented with focal cortical edema and laminar necrosis, and we describe its clinical course and postictal MRI changes in the left temporal cortex.

CASE REPORT

(Because the case report involved only a review of records obtained as a part of routine medical care, without patient consent was required)

A 48-year old male with diabetes mellitus was taking oral hypoglycemic agents for the previous three years, but had stopped medication for the last three months. The patient reported headaches and a respiratory infection, characterized by fever and sore throat, but without previous history of childhood epilepsy and meningitis, also no previous history of head trauma and the family history of epilepsy.

On the day before admission, MRI of the brain was normal. On initial observation, body temperature was 37.9 °C, pulse was 78 beats/min, respiration was 19 times/min, and blood pressure was 140/100 mm Hg. On neurologic examination, the patient was fully alert and aware. His speech was fluent, but he demonstrated subnormal cognitive faculties. Cranial-nerve functions were intact. He reported no neck pain on touching his chin to his chest or on the extension of the legs at the knees. Blood glucose was elevated (23.7 mmol/L) an admission.

The day, night after admission, the patient had two generalized tonic–clonic seizures followed by unconsciousness. Each episode lasted for two minutes. Treatment with insulin and diazepam was initiated. On the second day after admission, blood glucose was 20.3 mmol/L, the hemoglobin A1c concentration was 12.6%, white cell count was 8300/mm3, neutrophils were 80.1%, and hematocrit was 41.0 %. Serum sodium was 132.8 mmol/L, serum potassium was 3.9 mmol/L, and serum osmolarity was 285.3 mOsm/L. There were no ketonuria or systemic acidosis. Tests of liver and renal function were all within normal ranges. An electrocardiogram showed no abnormalities and a chest radiograph revealed that the heart and lungs were normal. A lumbar puncture yielded clear, colorless cerebro-spinal fluid with six white cells/mm3, glucose level of 10.2 mmol/L, and a total protein level of 0.35 g/L. Staining for acid-fast bacilli and a test for cryptococcal antigen were both negative. During the three postictal days, the patient had no seizures, and the electro- encephalogram was normal.

On the forth days after admission, he experienced a focal paroxysmal events with lost of consciousness, rightward deviation of the eyeballs, leftward head turning, and stiffness–twitching in the right face, arm, and leg. Seizure frequency was 8-10/h for several hours, and each seizure lasted about 1 min, and unconsciousness in duration. Aggressive glucose control
was again implemented. After blood glucose had been controlled (8.2 mmol/L), he had no additional seizures. On hospital day 5, T2-weighted MRI demonstrated gyral hyperintensity (Fig. A) in the left temporal cortex.

The patient was diagnosed with nonketotic hyperglycemia epileptic seizures, but he remained asymptomatic for the rest of his hospital stay. Several days later, he was discharged and prescribed a rapid-acting insulin analog before early meals and a long-acting analog (subcutaneous) before dinner, and he did not use any anti-epileptic drugs. On follow-up MRI two months later, the focal left temporal lobe hyperintensity on T2-weighted MR images were less intense than observed in the postictal period (Fig. B).

**DISCUSSION**

Focal seizures are usually due to structural lesions of the brain, but occasionally are caused by systemic metabolic disturbances like NKH associated with diabetes mellitus. On the day before admission, our patient showed no abnormalities MR signals in brain, but he began to experience episodic seizures several hours after admission. Except for diabetes mellitus and discontinuation of hypoglycemic treatment for the past three months, he did not report any prior neurologic illnesses or history of seizures. Neurological examination showed no focal deficits. Further tests revealed the biochemical result of negative urine ketone bodies, elevated blood glucose and hemoglobin A1c, and the cerebro-spinal fluid was normal. Therefore, the epileptic seizures were likely caused by nonketotic hyperglycemia due to remit with hypoglycemic agents. Upper respiratory tract infection may be the precipitating factors of nonketotic hyperglycemia.

In general, hyperglycemia-induced oxidative injury to the vascular endothelium, either by interruption of focal cerebral blood flow or by focal breach of the blood-brain barrier, induces serious diabetic complications in the brain. High glucose was shown to activate several proteins involved in apoptotic cell death, including anti-apoptotic and pro-apoptotic Bcl-2 family members and caspases. Therefore, neuronal protein's activity is one possible cause of neuronal damage induced by severe hyperglycemia, but the molecular mechanisms are unclear. Other studies suggested that insulin deficiency played a compounding role to that of hyperglycemia in neuronal damage underlying primary diabetic encephalopathy.

Acute hyperglycemia can initiate seizures. Hyperglycemia increases GABA metabolism and thereby reduces the seizure threshold, while dysfunctional glutamate transport leads directly to ictogenesis. Studies have suggested that these perturbations in the excitatory-inhibitory balance act on a previously silent cortical lesion (focus) to render it epileptogenic. Recently, many studies have been demonstrated that areas of neuronal hyperactivity during the perictal phase have their microstructural changes. In addition, in rats, described increased signal intensity in diffusion -weighted images (DWI) one hour after kainite-induced seizures but before the development of measurable changes on T-weighted images. Although the preictal T2-weighted MR images in patient reported no abnormalities signals, our imaging studies revealed an intense signal on MR images several days after the onset of epileptic seizures, suggesting neuronal proteins abnormally activity may be negative on conventional MRI.

The study of postictal MRI in brain lesions from hyperglycemia confirmed that the subcortical high signal represents a cell edema, whereas the study of postictal MRI in non NKH seizures confirmed that the cortical high signal is a cell edema compatible with laminar necrosis. In our patient, the focal increases in T2-weighted signal intensity was also observed several days after NKH with focal seizures, hence, likely reflecting the cell edema compatible with laminar necrosis.

In conclusion, our Imaging showed that a normal preictal MRI evolved into a focal high signal intensity lesion should be attributed to NKH-induced focal seizures. Fortunately, when hyperglycemia and focal seizures were controlled by insulin, the hyperintensity had subsided in the left temporal cortex. The implication from these findings is that the potential NKH-induced focal brain injury, such as the cell edema and laminar necrosis is reversible if NKH seizures is controlled by insulin.

**Disclosure**

No conflict of interest.

**Funding sources**

None.

**Competing interests**

None declared.

**Novelty statement**

We identified cortical T2 hyperintensity as a rare change after NKH seizures. This information may be important in prospectively determining severity of NKH seizures and in patient with diabetes enduring treatment.

**REFERENCE**


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**Figure 1.** A, Results of the T2-weighted MR image performed on the day 5 after seizures shows hyperintensities in the left temporal cortex. B, on follow-up MRI two months later, the focal left temporal lobe hyperintensity on T2-weighted MR images was less intense.