

# The Reversible Corpus Callosum Splenium Lesion in A Neonate with Hypoglycemia and Seizure

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## Abstract-

**Purpose:** Reversible splenial lesion syndrome is a distinct clinicoradiological syndrome with diverse etiologies. Hypoglycemia induced reversible splenial lesion syndrome has been documented in adults and children, but rare in neonates. We demonstrate a neonate with hypoglycemia presenting with a typical reversible splenial syndrome.

**Case Report: Patient** A four-day-old male neonate had hypoglycemia and seizure, whose symptoms improved soon after glucose supplementation. Magnetic resonance imaging examination showed restricted diffusion of the splenium of the corpus callosum. Proton MR spectroscopy revealed a decreased N-acetylaspartate peak. The lesion resolved in subsequent MRI images. The patient is free from clinical symptoms and has normal development currently.

**Conclusion:** The patient presented typical clinical course and radiological features of reversible splenial lesion syndrome. Through timely and proper treatment, the outcome could be favorable.

**Key Words:** Reversible splenial lesion; Neonatal hypoglycemia; Diffusion-weighted imaging; MR spectroscopy

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## INTRODUCTION

Reversible splenial lesion syndrome (RESLES) is a distinct clinicoradiological syndrome with diverse etiologies such as mild encephalitis/encephalopathy<sup>(1)</sup>, metabolic disorders, and autoimmune disease. The exact mechanism is still uncertain. Hypoglycemic

encephalopathy in neonates often involves occipital and parietal cortex and subcortical white matter<sup>(2)</sup>, but less presents as reversible splenial lesions. We demonstrated a male neonate with hypoglycemia and seizure, whose magnetic resonance imaging (MRI) images revealed the reversible splenium of the corpus callosum (SCC) lesion. He was free from neurological developmental delay

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through prompt treatment.

## CASE REPORT

A male neonate had seizure on the 4th day of life. He was delivered via cesarean section at 38 1/7 weeks' gestation with birth weight 2750 gm at local obstetric clinic. The Apgar score was 8 and 9 at 1 and 5 minutes. The prenatal examination of the 36-year-old G1P1 mother was normal. She did not have history of diabetes mellitus. The neonate was found to have low blood glucose level (19 mg/dl) on the first day of birth. The follow-up blood glucose level after oral glucose solution supply returned to 62 mg/dl. No clinical symptoms of hypoglycemia developed at that time.

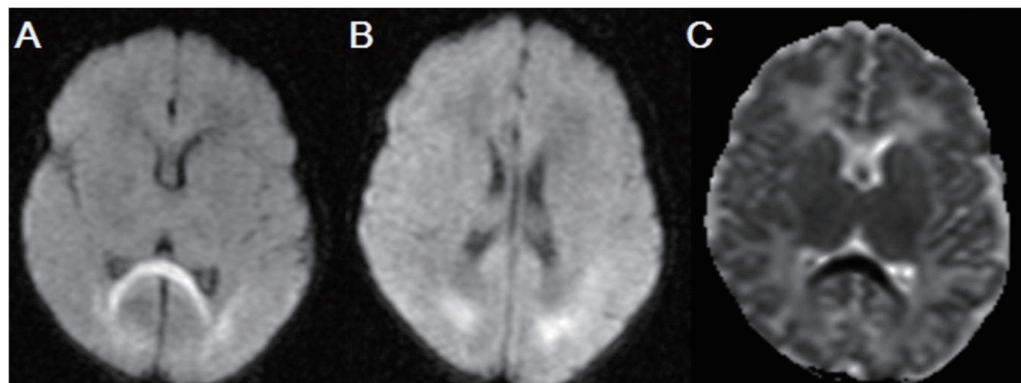
The neonate had blinking eyes, clonic movement of lower limbs and cyanosis at 4-day-old. Blood glucose level was 39 mg/dl. He was sent to local hospital soon. After emergent management with anticonvulsant (phenobarbital) injection and intravenous glucose supply, he was transferred to our hospital. On admission, blood glucose level was 86 mg/dl. We treated him with regular phenobarbital and seizure disappeared throughout the hospitalization period. Cranial sonography revealed mild brain edema with normal resistance index. The result of electroencephalography (EEG) showed epileptiform discharges over right frontal and central-posterior areas. All other tests for potential etiology of neonatal seizure,

including electrolytes, total serum IgM, cerebrospinal fluid analysis, lactate-to-pyruvate ratio, plasma amino acids profile and urinary organic acids analysis, were normal.

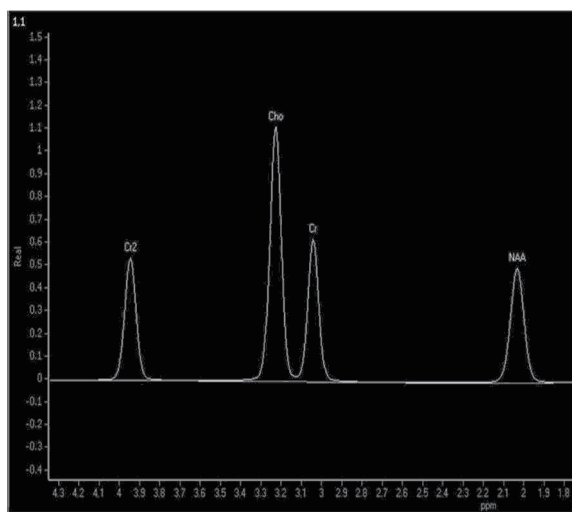
Shortness of breath was another problem on admission. Chest radiography revealed congenital pneumonia. Empiric antibiotics of ampicillin and cefotaxime were given and discontinued a week later. No pathogen was isolated from bacterial or viral culture. We weaned nasal ventilator from the patient on the 2nd day of hospitalization, and discontinued oxygen supply on the 7th day.

Brain MRI was then performed on the 8th day of hospitalization. Diffusion weighted imaging (DWI) demonstrated high signal intensity lesions in SCC, peritrigon white matter, and bilateral parietal deep white matter. (Fig. 1 A,B) The lesions seen on DWI were low signal intensity on apparent diffusion coefficient (ADC) map (Fig. 1 C), but not clearly revealed on conventional T1-weighted and T2-weighted images. Proton MR spectroscopy (MRS) obtained from the SCC revealed a decreased N-acetylaspartate (NAA) peak. (Fig. 2)

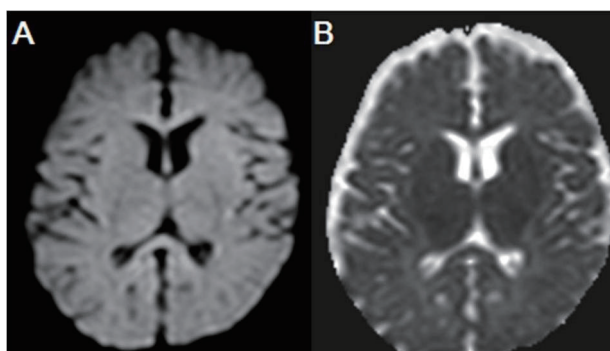
The patient was discharged on the 15th day of admission. At outpatient clinics, no further seizure was noted. EEG and MRI were repeated at 3-month-old. The result of follow-up EEG was normal. As for MRI, the signal intensity involving the SCC and peritrigon white matter on DWI and ADC became normal. (Fig. 3 A, B) His growth and development were within normal range.



**Figure 1.** (A) Diffusion weighted imaging (DWI) demonstrated high signal intensity lesions in splenium of corpus callosum, (B) peritrigon white matter, and bilateral parietal deep white matter, (C) The lesions were low signal intensity on apparent diffusion coefficient (ADC) map



**Figure 2.** Proton MR spectroscopy (MRS) obtained from the splenium of corpus callosum revealed a decreased N-acetylaspartate (NAA) peak



**Figure 3.** The follow-up (A) DWI and (B) ADC showed normal signal intensity involving the splenium of corpus callosum and peritrigon white matter

## DISCUSSION

Reversible lesions involving the SCC have been reported in many conditions such as clinically mild encephalitis/encephalopathy associated with Kawasaki disease, rotavirus, Japanese encephalitis virus, influenza, *Mycoplasma pneumoniae*, bacterial urinary tract infection, etc<sup>(1,3)</sup>. It is also observed in patients with epilepsy receiving antiepileptic drugs (especially phenytoin and carbamazepine), metabolic disorders (hypoglycemia or hyponatremia), and autoimmune disease<sup>(4,5)</sup>. The term

“reversible splenial lesion syndrome (RESLES)” refers to a distinct clinicoradiological syndrome generally with a benign course and good prognosis<sup>(6)</sup>.

Hypoglycemia induced RESLES has been demonstrated in several adult cases<sup>(7,8)</sup>, but was less reported in children<sup>(9)</sup>. It is even rarer in neonates, for brain injury in neonatal hypoglycemia mostly involves occipital and parietal cortex and subcortical white matter<sup>(5)</sup>. Two previous studies had identified neonates with hypoglycemia and SCC lesions, but the changes involving SCC were not really “reversible”<sup>(10,11)</sup>. One study reported 4 term neonates with hypoglycemia (12.6-27mg/dl)<sup>(10)</sup>. Three of them had seizure. Their MRI showed restricted diffusion in the corpus callosum, parieto-occipital white matter, and optic radiations. Follow-up MRI revealed generalized occipital lobe atrophy. Only one patient had visual impairment, microcephaly, and gross motor delay. The others had normal development and visual function. Another study reported 2 neonates, whose blood glucose levels were 5 and 11mg/dl, had abnormal MRI with restricted diffusion in the parieto-occipital gray and white matter and SCC.11 Follow-up MRI showed atrophic change in the initially affected areas including SCC. MRS obtained from affected areas demonstrated an increased lipid-lactate peak and a decreased NAA peak. These two patients both delayed in mental and motor development at their 10-month-old follow-up, and one of them had frequent episodes of seizures. Our patient, though had similar history and image abnormalities to the above studies, is consistent with the diagnosis of RESLES. Radiologically, all the restricted diffusion areas “reverted” to normal in follow-up images. Clinically, his condition improved soon after hypoglycemia corrected, without recurrent seizure or developmental delay.

The mechanism of pathogenesis of RESLES remains unclear, despite several theories including perturbed cellular fluid mechanism, intramyelinic edema, and inflammatory infiltrate have been proposed.<sup>8</sup> In our case, hypoglycemia itself can be an explanation. Areas of restricted water diffusion revealed high signal intensity on DWI with ADC reductions indicated of cytotoxic edema. This could be caused by hypoglycemia induced energy depletion and subsequent membrane ionic pump failure<sup>(12)</sup>. Further, a decreased NAA peak on MRS suggested neuronal damage, which possibly resulted from

hypoglycemia caused inflammatory reaction. Prompt management is crucial, for prolonged hypoglycemia can lead to irreversible brain injury and neurological deficit as mentioned in literature.

Though risk factors and associated conditions of RESLES have been reported, most data were collected from elder pediatric patients. Etiologies such as infectious encephalitis, Kawasaki disease, or urinary tract infection are usually found in children. In neonates, metabolic disorders are more common problems that physicians need to deal with. Besides hypoglycemia, electrolytes imbalance may also a potential risk factor. Further research is needed.

In conclusion, the abnormality in SCC in hypoglycemia is hardly reported in neonates and may be underestimated. Blood glucose level should be checked in a neonate who is small or large in gestational age, in whose mother has gestational diabetes mellitus, and in who presents symptoms of hypoglycemia. As for our patient, the definite cause of hypoglycemia was not known. Mild asphyxia resulted from congenital pneumonia may be a possible etiology. The transient change of SCC might not be detected on first MRI examination, because the lesion can revert as short as 12 hours in adult case report.<sup>8</sup> If the SCC lesion does show on images, physicians should be aware of the clinical implication: through timely and proper treatment, the outcome of RESLES could be favorable as which we reported in this case. Our patient has normal development currently at the age of 5 months. Long-term neurological outcome would be monitored by further follow-up.

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