福岡大医紀（*Med. Bull. Fukuoka Univ.*）：37(4), 181–185, 2010

A Case of West Syndrome Associated with Neonatal Hypoglycemic Brain Injury

Sawa Yasumoto*, Noriko Nakamura, Yuko Tomonoh, Takako Fujita, Yukiko Ihara, Shinya Ninomiya, Hiroshi Ideguchi, Takahito Inoue and Shinichi Hirose

Departments of Pediatrics, Faculty of Medicine, Fukuoka University

Abstract：We herein report a 9–month–old male with West syndrome associated with neonatal hypoglycemic brain injury. We describe his MRI and EEG findings since the neonatal period. The clinical features show that the patient was born from a mother with toxemia at term. One day after birth, he suffered from neonatal seizures and intractable hypoglycemia（<10 mg/dl), caused by hyperinsulinemia. It took more than 12 hours to normalize his blood glucose level. From birth to the age of 9 months, he developed psychomotor retardation with visual disturbances. After that, he suffered from tonic spasms which appeared daily in a series. When the patient was two weeks old, MRI showed white matter T2 prolongation of the bilateral parieto–occipital lobes. An EEG showed hypsarrhythmia with occipital paroxysms. Clonazepam combined with Zonisamide was effective for the tonic spasms and improved his psychomotor development. However epileptic seizures increased after reaching one year of age and his EEG findings worsened. His family did not want ACTH therapy, so we added Gabapentin to his previous medication. At two years of age, the patient has left severe psychomotor retardation, though his clinical seizures have decreased. This study indicates that severe neonatal hypoglycemia can cause symptomatic West syndrome.

Key words：**Hypoglycemia, Neonate, West syndrome, Parieto–occipital lesion**

Introduction

It is well known that severe neonatal hypoglycemia causes neuronal damage to the central nervous system. The neurological sequelae of severe neonatal hypoglycemic brain damage include developmental delays, visual impairment and epilepsy.[1)-4)] Caraballo et al. reported that neonatal hypoglycemia causes symptomatic epilepsy, most frequently occipital lobe epilepsy, usually with a good prognosis, and occasionally epileptic encephalopathy with refractory seizures.[5)] Burns et al. reported that 12 of 35 infants with neonatal hypoglycemialater developed later seizures.[6)] However, there have so far only been a few reports on the association between neonatal hypoglycemia and West syndrome.[6)7)] This study reports the clinical features, and EEG and MRI findings of a case of West syndrome associated with severe neonatal hypoglycemia–induced brain injury.

Patients

The patient was born at term from a mother with toxemia. One day after birth, he suffered from neonatal seizures and intractable hypoglycemia（<10 mg/dl), caused by hyperinsulinemia (15.8 μU/ml). It took more than 12 hours to normalizehis blood glucose (Fig. 1). Laboratory data at NICU admissionis shown in Table 1. From birth to the age of 9 months, the patient developed psychomotor retardation with visual disturbances.

Correspondence to：Sawa Yasumoto, MD, PhD
Department of Pediatrics, School of Medicine, Fukuoka University, 45–1, 7–chome Nanakuma, Jonan–ku, Fukuoka 814–0180, Japan
E–mail：yasumosw@fukuoka–u.ac.jp

After that, he suffered from tonic spasms, which appeared daily in a series. EEG showed hypsarrhythmia with occipital paroxysms (Fig. 2). Clonazepam combined with Zonisamide was effective for tonic spasms and improved his psychomotor development. At the age of 10 months, the hypsarrhythmia had disappeared and therewere frequent spikes and waves in the occipital area (Fig. 3).

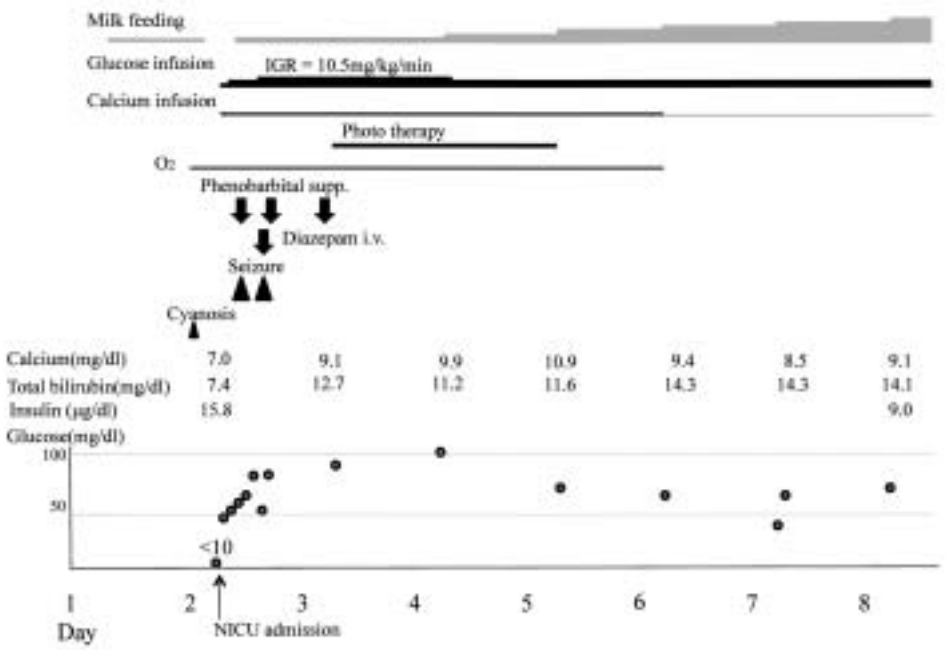


Fig. 1 Clinical features on admission.

Table 1 laboratory data

At NICU admission

RBC	4860000 /μl
Hb	19.4 g/dl
Ht	56.2 %
WBC	13600 /μl
Plt	135000 /μl
TP	5.5 g/dl
Alb	2.9 g/dl
T.Bil	7.4 mg/dl
AST	58 IU/l
ALT	23 IU/l
LDH	700 IU/l
CK	1137 IU/l
BUN	7 mg/dl
Cr	0.9 mg/dl
Glu	10 > mg/dl
Na	142 mEq/l
K	4.9 mEq/l
Cl	108 mEq/l
Ca	7.0 mg/dl
Mg	2.3 mg/dl
CRP	0.3 mg/dl
lactate	22 mg/dl

Hormonal workup

insulin	15.8 μU/ml
TSH	3.063 μIU/ml
Free-T4	1.67 ng/dl
cortisol	8.6 μg/dl
GH	10.4 ng/ml

Arterial blood gases

pH	7.387
O_2	111.0 mmHg
CO_2	36.1 mmHg
HCO_3	21.2 nmol/l
BE	- 2.6 nmol/l

Urine dipstick screening

White cells	(-)
Bilirubin	(-)
Glucose	(-)
ketones	(-)
Hemoglobin	(-)

Metabolic workup

Carnitine level
Urine organic acids
Plasma amino acids levels
} Normal

At the age of 9 months

Hormonal workup

insulin	10.5 μU/ml (intial check)
	2.1 μU/ml (2 weeks later)
ACTH	25.4 pg/ml
IGF-1	29 mg/dl
cortisol	8.6 μg/dl
GH	1.93 ng/ml

Metabolic workup was within normal limits

However, epileptic seizures increased after he was 1 −year−old, and his EEG findings worsened. His family did not want ACTH therapy, so we added Gabapentin to the previous medication. At two years of age, the patient has left severe psychomotor retardation, although the clinical seizures have decreased. Fig. 4 shows the brain MRI findings of the patient over the course of treatment. At 17 daysof age, MRI showed T2 prolongation of the white matter and a part of the cortex in bilateral parieto −occipital lobes.

Discussion

In the study by Burns et al., the risk factors for symptomatic neonatal hypoglycemia were pregnancy−induced hypertension, a family history of seizures or neurologic disease, emergency cesarean section, and the need for resuscitation. Some infants who suffered from prolonged/recurrent hypoglycemia showed intrauterine growth restriction (IUGR), or received an underlying metabolic or en-

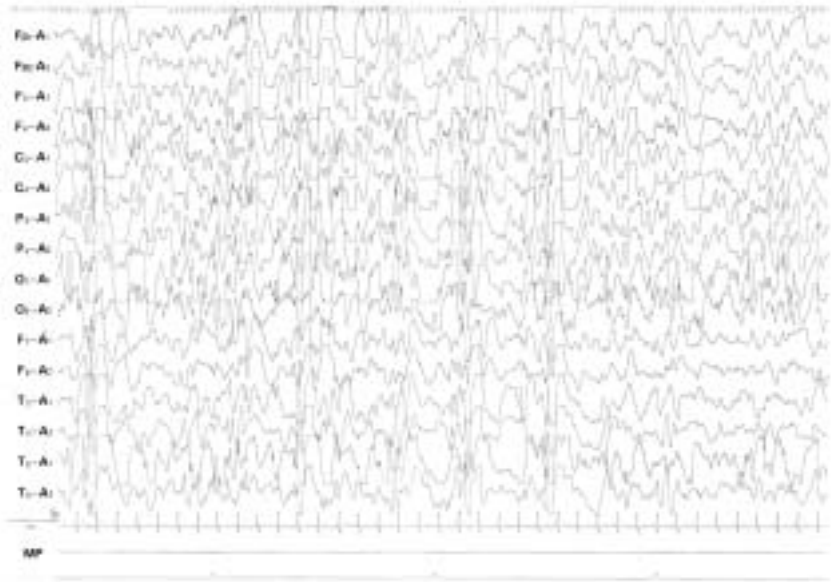


Fig. 2 EEG at 9 months of age. The EEG showed hypsarrhythmia with occipital spikes.

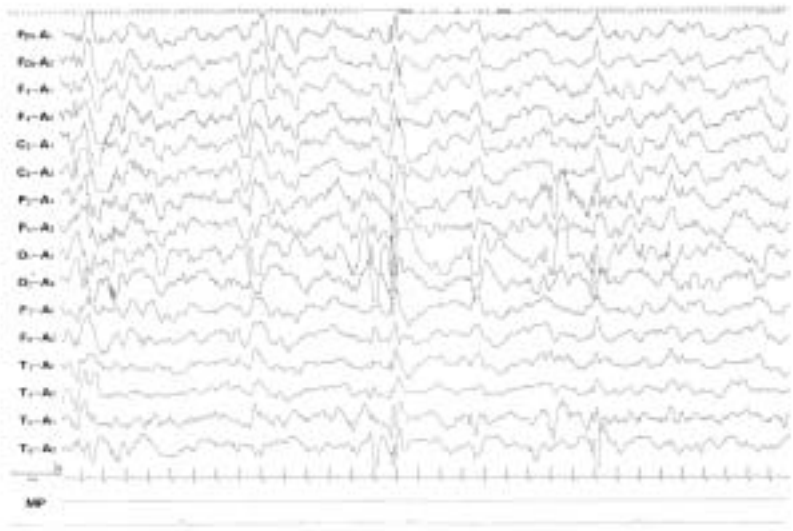
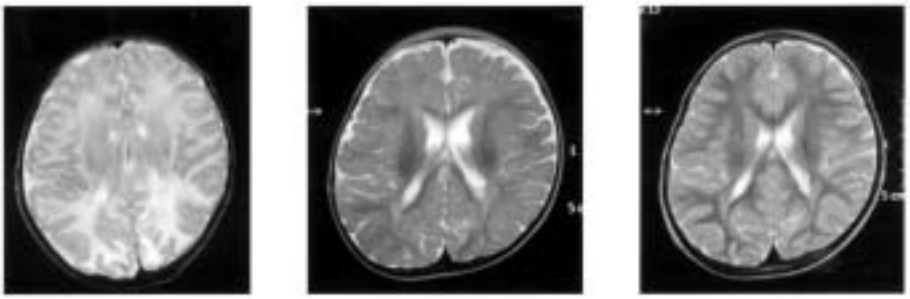


Fig. 3 EEG at 10 months of age. The hypsarrhythmia had disappeared, and there were frequent spike and waves in the occipital area.



17-days-old　　9-month-old　　3-year-old

Fig. 4 Brain MRI. At the age of 17 days, the patient's white matter and a part of cortex showed T2 prolongation in bilateral parieto-occipital lobes. At the age of 9 months, white matter and a part of the cortex T2 prolongation was localized and scarred. Trigone was dilatated, and the peripheral lesion T2 was prolonged. At the age of 3 years, white matter and a part of the cortex T2 prolongation was more localized than before, and the terminal zone T2 was prolongation. The ventricles were dilatated.

docrine diagnosis.[6] Montassi et al. reported that hypoxia, neonatal seizure and pathological jaundice exacerbate hypoglycemic brain injuries.[8] Our patient was born from a mother with toxemia, had neonatal seizures and pathological jaundice. Although transient hyperinsulinemia occurred, on laboratory testing, his illness was not diagnosed as metabolic or endocrine disease.

The early MRI findings were instructive for predicting the neurodevelopmental outcomes.[9][10] The main neurodevelopmental outcomes were cerebral palsy, mental retardation, developmental delays, seizure, and visual impairment. The severity of white matter injury was a good predictor of the outcome : 80% of infants with moderate or severe outcomes had severe white matter injury.[6] All infants showing severe white matter changes with normal/mildly abnormal outcomes had either unilateral or asymmetric injuries. In our case, bilateral parieto-occipital white matter and some cortical damage showed on early MRI, which is similar to the observation of previous reports.

Caraballo et al. reported that neonatal hypoglycemia causes symptomatic epilepsy, most frequently occipital lobe epilepsy, usually with a good prognosis, and occasionally epileptic encephalopathy with refractory seizures.[5] Burns et al. reported that 12 of 35 infants with neonatal hypoglycemia later developed seizures.[6] Three had infantile spasms, 2 had generalized seizures, 1 had focal seizures, and 2 had unknown-type seizures. All seizures developed before the age of 2 years. Montassir et al. reported the long-term clinical course of 6 patients with symptomatic occipital lobe epilepsy secondary to neonatal hypoglycemia. EEGs showed parieto-occipital spikes in all patients. One patient had spasms in clusters at the age of 10 months, and a series of EEGs revealed hypsarrhythmia.[7] Our patient developed a series of tonic spasms and was diagnosed with West syndrome based on EEG findings of hypsarrhythmia with occipital paroxysms. Drug treatment was effective for tonic spasms, but the abnormal EEG findings continued.

Severe neonatal symptomatic hypoglycemia with cerebral lesions is therefore considered to be a risk factor for West syndrome, and follow-up EEG examinations are thus important for infants whodemonstrate had neonatal hypoglycemiain order to rule out neurological damage.

References

1) Koivisto M, Blanco-Sequeiros M. Krause U. Neonatal symptomatic and asymptomatic hypoglycaemia : a follow-up study of 151 children. Dev Med Child Neurol 14 : 603-614, 1972.
2) Menni F, Lonlay P, Sevin C, Touarti, Peigné C, Barbi V, Fékété N, Saudubray JM, Robert JJ. Neurologic outcomes of 90 neonates and infants with persistent hyperinsulinemic hypoglycemia. Pediatrics 107 : 476-479, 2010.
3) Baker L, Stanley CA. Neonatal hypoglycemia. Curr Ther Endocrinol Metab 5: 376-380, 1994.

4) Dalgic N, Ergenekon E, Soysal S, Koc E, Atalay Y, Gucuyener K. Transient neonatal hypoglycemia—long-term effects on neurodevelopmental outcome. J Pediatr Endocrinol Metab 15 : 319–324, 2002.
5) Caraballo RH, Sakr D, Mozzi M, Guerrero A, Adi JN, Cersosimo RO, et al. Symptomatic occipital lobe epilepsy following neonatal hypoglycemia. Pediatr Neurol 31 : 24–29, 2004.
6) Burns CM, Rutherford MA, Boardman JP, Cowan FM. Patterns of cerebral injury and neurodevelopmental outcomes after symptomatic neonatal hypoglycemia. Pediatrics 122 : 65–74, 2008.
7) Montassir H, Maegaki Y, Ohno K, Ogura K. Long term prognosis of symptomatic occipital lobe epilepsy secondary to neonatal hypoglycemia. Epilepsy Res 88 : 93–99, 2010.
8) Montassir H, Maegaki Y, Ogura K, Kurozawa Y, Nagata I, Kanzaki S, et al. Associated factors in neonatal hypoglycemic brain injury. Brain Dev 31 : 649–656, 2009.
9) Yalnizoglu D, Haliloglu G, Turanli G, Cila A, Topcu M. Neurologic outcome in patients with MRI pattern of damage typical for neonatal hypoglycemia. Brain Dev 29 : 285–292, 2007.
10) Filam PM, Inder TE, Cameron FJ, Kean MJ, Hunt RW. Neonatal hypoglycemia and occipital cerebral injury. J Pediatr 148 : 552–555, 2006.

(Received on April 13, 2010,
Accepted on September 10, 2010)