Brain & Development 31 (2009) 240–243

BRAIN & DEVELOPMENT
Official Journal of the Japanese Society of Child Neurology

www.elsevier.com/locate/braindev

Case report

Different neuroradiological findings during two stroke-like episodes in a patient with a congenital disorder of glycosylation type Ia

Nobutsune Ishikawa [a,*], Go Tajima [a], Hiroaki Ono [b], Masao Kobayashi [a]

[a] *Department of Pediatrics, Hiroshima University Graduate School of Biomedical Sciences, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan*
[b] *Department of Pediatrics, Hiroshima Prefecture Hospital, Hiroshima, Japan*

Received 22 December 2007; received in revised form 24 March 2008; accepted 30 March 2008

Abstract

Congenital disorders of glycosylation type Ia (CDG-Ia) are the most common type of CDG and are characterized by liver dysfunction, coagulation disorders, mental retardation, hypotonia, cerebellar dysfunction, polyneuropathy, seizures, and stroke-like episodes. Stroke-like episodes occur in 40–55% of cases, but their etiology is not fully understood. Although it has been stated that an epileptic process may cause the stroke-like episodes, there is no clear evidence of ischemic stroke. Here, we describe two stroke-like episodes in a patient with CDG. We performed radiological studies during each episode and obtained two distinct magnetic resonance imaging (MRI) findings: one revealed an ischemic stroke, and the other demonstrated marked edema followed by focal necrosis. This is the first direct evidence of ischemic stroke, and we report that another process may affect the etiology in the same patient.

Keywords: Congenital disorder of glycosylation; Stroke-like episode; MRI; Ischemic stroke; Epilepsy

1. Introduction

Congenital disorders of glycosylation (CDG) type Ia is characterized by decreased activity of the enzyme phosphomutase owing to mutations in the *PMM2* gene [1,2]. The clinical features include liver dysfunction, coagulation disorders, mental retardation, hypotonia, cerebellar dysfunction, polyneuropathy, seizures, and stroke-like episodes. The stroke-like episodes occur in 40–55% of cases [3,4]. Despite much speculation [3,5–7], the mechanism of these stroke-like episodes is not fully understood.

We evaluated a boy with genetically confirmed CDG-Ia, who experienced repeated stroke-like episodes. The magnetic resonance imaging (MRI) findings during these two stroke-like episodes suggest that different etiologies caused these stroke-like episodes.

* Corresponding author. Tel.: +81 82 257 5212; fax: +81 82 257 5214.
E-mail address: ishikan@hiroshima-u.ac.jp (N. Ishikawa).

0387-7604/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.braindev.2008.03.012

2. Case report

An 11-month-old boy was referred to our hospital due to abnormal liver function and coagulation activities. At that time, he already showed developmental delay with hypotonia and ataxia, which gradually became more severe. MRI performed at 11 months of age demonstrated atrophy of the cerebellar hemispheres and vermis. We made a diagnosis of CDG-Ia based on the isoelectric focusing of serum transferrin and *PMM2* gene analysis (P113L/R194X) [8].

He experienced hemiplegia of the right extremities with vomiting and conjugate eye deviation to the left, with a high fever at the age of 5.2 years. Subsequently, intermittent clonic-convulsions of the right extremities occurred, which were stopped with a continuous midazolam infusion. He was not fully responsive at the first occurrence, which lasted for 1 h. An electroencephalogram (EEG) during the episode of hemiplegia showed a right hemispheric high-voltage slow wave superimposed on an inter-

mittent low-voltage fast wave, and a moderately low voltage pattern in the left hemisphere. After he had recovered consciousness, he remained quite irritable for several days. This was the first stroke-like episode. On the first day, head computed tomography (CT) showed a hypodense lesion in the left temporo-parietal watershed area (Fig. 1D). His laboratory data showed disorders of both coagulation and anticoagulation: prothrombin test (PT) 39% (normal 70–130), anti-partial thrombin test (APTT) 65.6 s (normal 23.0–35.0), fibrinogen 270.9 (normal 150–400), fibrin digested product (FDP) 22.53 μg/ml (normal 0–5.0), ATIII 28%, protein C 6%, and D-dimer 15.7 μg/ml (normal <1.0). The platelet count was $37.4 \times 10^4/mm^3$. The next day, the platelet count and fibrinogen decreased to $13.9 \times 10^4/mm^3$ and 114.9, respectively, while the FDP increased to 454.6 μg/ml. D-dimer also increased markedly (101.0 μg/ml). These data suggested that disseminated intravascular coagulopathy (DIC) was developing. After commencing anti-DIC therapy, the laboratory data gradually returned to the original levels. On day 3, the EEG showed a high-voltage slow wave in the right hemisphere and a low-voltage pattern in the left hemisphere. Four days after the onset of this episode, head CT revealed a subdural hematoma on the right side (Fig. 1D). Serial MRI also revealed these lesions (Fig. 1A and B). Acute-phase diffusion-weighted imaging (DWI) revealed a hyperintensity lesion in the left temporo-occipital area. Magnetic resonance angiography (MRA) demonstrated occlusion of the distal middle cerebral artery (MCA) and left posterior cerebral artery (PCA) (Fig. 1C). Follow-up MRI showed left cerebral atrophy. These findings suggested that this episode was an ischemic stroke, complicated by a subdural hematoma. His hemiplegia persisted for several months, and subsequently improved gradually. Since this episode, he has suffered several episodes of hemiplegia that resolved completely within 12 h. The radiological studies performed during the subsequent episodes of hemiplegia found no evidence of ischemia or infarction. These episodes could be distinguished from the first episode. He has also experienced seizures without subsequent hemiparesis.

At the age of 6.8 years, a second stroke-like episode occurred. He experienced a hemi-clonic-convulsion and subsequently developed hemiplegia of the left extremi-

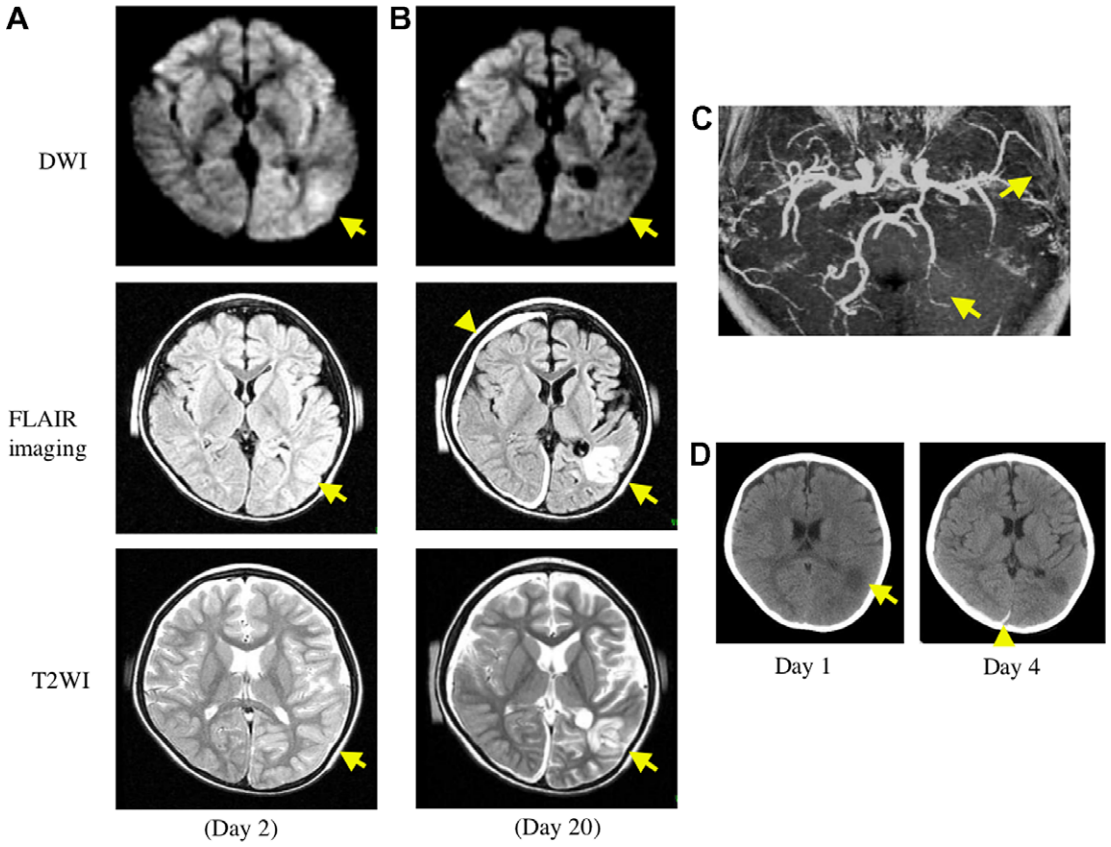

Fig. 1. Serial MRI, CT, and MRA findings during the first stroke-like episode. MRI was obtained on days 2 (A) and 20 (B). Diffusion-weighted imaging (DWI), fluid-attenuation inversion recovery (FLAIR) imaging, and T2-weighted imaging (T2WI) showed mildly high signal intensity in the left temporo-occipital watershed area (arrows) on day 2 (A). On day 20, although the DWI showed reduced intensity in the corresponding lesion, FLAIR imaging and T2WI documented hyperintensity in the subcortical white matter involving the gray matter. In addition, a right-sided subdural hematoma (arrowhead) was seen on FLAIR imaging and T2WI. MRA showed occlusion of the distal middle cerebral artery (MCA) and left posterior cerebral artery (PCA) (C). CT on day 1 revealed a low-density lesion in the left temporo-parietal watershed area (arrow) (D, left) and on day 4 the right-side subdural hematoma (arrowhead) was seen (D, right).