Introduction
Neonatal diabetes mellitus is a rare condition with an incidence of approximately 1 in 200000 live births\(^1\). Approximately 50% of neonatal diabetes mellitus cases are caused by mutations in genes encoding the adenosine triphosphate-sensitive potassium (KATP) channel subunits\(^2\). Some patients with KATP channel mutations can exhibit developmental delay and epilepsy, a condition termed developmental delay, epilepsy, and neonatal diabetes mellitus (DEND) syndrome, while the less severe form without epilepsy is termed intermediate DEND (iDEND)\(^2\). However, the head magnetic resonance imaging (MRI) findings of DEND/iDEND syndrome remain unclear. Here, we describe the MRI findings of a case with iDEND syndrome.

Case Report
The patient was the first child of healthy, non-consanguineous Japanese parents. He was born at 39 weeks 6 days (birth weight 2740g) without postnatal problems. He could control his head at 3 months of age. Poor weight gain was noted at 5 months, although he was not examined further. At 8 months of age, he was admitted with fever. His body temperature was 39.1°C. Laboratory data

Head MRI in a Case with Intermediate DEND Syndrome

HIROTAKA TAKITA\(^1\), TARO SHIMONO\(^1\), TOMOYUKI KAWAMURA\(^2\), MASAKAZU HIROSE\(^2\), YONEO KASHIHARA\(^2\), and YUKIO MIKI\(^1\)

Departments of Diagnostic and Interventional Radiology\(^1\) and Pediatrics\(^2\), Osaka City University Graduate School of Medicine

Abstract
Developmental delay, epilepsy, and neonatal diabetes mellitus (DEND) syndrome is a rare condition of neonatal diabetes mellitus caused by dysfunction of adenosine triphosphate-sensitive potassium channels. There are limited magnetic resonance imaging studies of the head in DEND and intermediate DEND (iDEND) syndrome. Here we describe a iDEND syndrome patient with evidence of hyperintense signals on T2-weighted imaging and hyperintense on the apparent diffusion coefficient map in the symmetrical deep white matter around the bilateral anterior and posterior horns, and mild cerebral atrophy without cerebellar abnormalities. These imaging findings may be one of the possible features of DNED/iDEND syndrome.

Key Words: Developmental delay, epilepsy, and neonatal diabetes mellitus syndrome (DEND); Magnetic resonance imaging (MRI); White matter

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Case Report
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showed a blood sugar of 436 mg/dL, hemoglobin A1c (HbA1c) of 13.7%, and 3-hydroxybutyrate of 7900 μmol/L. Pancreatic autoantibodies were negative. He was diagnosed with type 1 diabetes mellitus and ketoacidosis. His glycemc control was improved after continuous insulin therapy, and he was discharged.

At 1 year and 8 months of age he was investigated for development delay, as he could not walk by himself and he spoke by babbling. Laboratory data showed a blood sugar of 62 mg/dL and HbA1c of 8.4%. Electroencephalogram examination was normal. MRI (Fig. 1) showed hyperintense

Figure 1. First brain MRI (magnetic resonance imaging) examination at 1 year and 8 months of age. T2-weighted imaging (T2WI) (A), T1WI (B), diffusion-weighted imaging (C), and apparent diffusion coefficient (ADC) map (D). Presence of symmetrical hyperintense signal lesions around the bilateral anterior and posterior horns, and mild dilatation of the bilateral lateral ventricle (arrows) (A). No abnormal signals (B and C). Presence of symmetrical hyperintense lesions around the bilateral anterior and posterior horns (arrows) (D).
signal on T2-weighted imaging (T2WI) and fluid attenuated inversion recovery (FLAIR) images, and hyperintense on apparent diffusion coefficient (ADC) map, in the symmetrical deep white matter around the bilateral anterior and posterior horns. T1WI, diffusion-weighted imaging, and susceptibility weight imaging showed no significant abnormalities. Mild dilatation of the bilateral lateral ventricles, suggesting mild cerebral atrophy, was also observed. A second MRI (Fig. 2) was performed at 2 years of age, with similar imaging findings except for slight progression of lateral ventricle dilatation.

iDEND syndrome was suspected from the clinical course. Genetic testing revealed an R50P KCNJ11 mutation (149G>C) and he was diagnosed with iDEND syndrome. After 3 months of oral glibenclamide therapy without insulin, he could walk by himself and speak 1-2 words. After 9 months his HbA1c was 5.5%.

Discussion
To our knowledge, only 14 DEND/iDEND (10 DEND, 4 iDEND) syndrome patients with head MRI have been reported2-12) (Table 1). Of the 10 DEND patients, six showed abnormal imaging findings including white matter lesions (four patients) and cerebral atrophy (two patients)5-7), while the remainder showed no significant abnormalities7-9). Of the four iDEND patients, one showed white matter lesions10, while the remainder showed no significant abnormalities7,11,12). In the present case, hyperintense signal on T2WI and hyperintense on the ADC map were observed in the symmetrical deep white matter around the bilateral anterior and posterior horns, as well as mild cerebral atrophy. Lesions around the anterior horns are uncommon in children over 1.5 years of age, while lesions around the posterior horns are more common, even in healthy children13).

In previous MRI studies, normal or subtle white matter lesions were observed in iDEND syndrome patients, while DEND syndrome patients showed more severe white matter injury, which

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Figure 2. Second brain MRI at 2 years of age (B) compared with first MRI at 1 year and 8 months of age (A). Imaging findings of the second MRI were similar to the first examination, except for a slight progression of lateral ventricle dilatation on T2WI.
likely reflect differences in disease severity between iDEND and DEND. We suggest that our iDEND case was more severe than normal. The abnormal white matter lesions observed in iDEND/DEND patients may relate to dysfunction of KATP channels, as follows. First, KATP channels are present in all brain regions and they play several important roles including regulation of the neurovascular unit and/or myelination. Thus, dysfunction of KATP channels may cause reduced blood flow and white matter abnormalities and/or delayed myelination in DEND/iDEND patients. Second, hyperglycemia can be excluded as a cause of abnormal imaging findings in our case, as the MRI was performed after his glycemic control was improved, and typical imaging findings of hyperglycemia are different from that in DEND/iDEND patients. Head MRI findings of type 2 diabetes mellitus patients in the hyperglycemic hyperosmolar state and with hyperglycemia-induced hemichorea hemiballismus have been reported. In the hyperglycemic hyperosmolar state, hypointense signals are seen in the bilateral subcortical white matter on FLAIR, while in hyperglycemia-induced hemichorea hemiballismus, hyperintense signals are seen in the unilateral basal ganglia on T1WI. Overall, these data may suggest that KATP channel dysfunction is a likely cause of abnormal brain MRI findings in our case.

Previous MRI studies have also reported no abnormal findings in DEND/iDEND patients, except for in the cerebrum. These negative findings are important, as several other diseases associated with neonatal diabetes mellitus can show structural brain abnormalities in regions other than the cerebrum. For example, cerebellar agenesis was reported in pancreas transcription factor 1 alpha-related neonatal diabetes mellitus, while cerebellar atrophy was reported in neurogenic differentiation 1-related neonatal diabetes mellitus. Thus, these negative findings may be one of the possible features of DEND/iDEND syndrome.

In conclusion, we describe the head MRI findings of a patient with iDEND syndrome, including symmetrical deep white matter lesions and mild cerebral atrophy without cerebellar abnormalities. These imaging findings may be one of the possible features of DNED/iDEND syndrome caused by dysfunction of KATP channels.

### Table 1. A summary of the MRI findings of DEND/iDEND syndrome in previous reports.

<table>
<thead>
<tr>
<th>Author</th>
<th>Disease</th>
<th>Age (years)</th>
<th>Sex</th>
<th>MRI Findings</th>
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<td>DEND</td>
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<tr>
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<td>Male</td>
<td>White matter lesions</td>
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</table>

MRI, magnetic resonance imaging; DEND, developmental delay, epilepsy, and neonatal diabetes mellitus; and iDEND, intermediate DEND.
Acknowledgements
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References