

Chronic subdural hematoma, as an initial manifestation of glutaric aciduria type-1

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A 10-month-old male with glutaric aciduria type-1 (GA-1) is reported. This patient showed frequent partial motor seizures, irritability, and involuntary movements, including oral dyskinesia at the age of 3 months. On admission, magnetic resonance (MR) scanning revealed a chronic subdural hematoma and widening of the bilateral insular cisterns. Urine organic acid analysis showed marked excretion of glutaric acid, 3-hydroxy glutaric acid and glutaconic acid, suggesting GA-1. Removal of the subdural hematoma was effective for the irritability but not for the extrapyramidal signs. This is the first report of a subdural hematoma as an initial symptom in a patient with GA-1. However, the complication of subdural fluid collection in GA-1 is not rare. To our knowledge, of 29 patients with GA-1 who underwent computed tomographic or MR scans, 5 had subdural fluid collection. Disproportional hypoplasia of the temporal lobes may be a suggestive etiology of subdural fluid collection/chronic subdural hematoma.

Key words: Glutaric aciduria type-1; Chronic subdural hematoma; Subdural fluid collection

INTRODUCTION

Glutaric aciduria type-1 (GA-1) is an autosomal recessive metabolic disorder caused by a defect of the enzyme, glutaryl coenzyme A dehydrogenase. About 40 cases were reported previously, and the clinical manifestations are mainly extrapyramidal; dystonia, oral dyskinesia and choreoathetosis. In addition to the extrapyramidal signs, subdural fluid collection in GA-1 is not rare. Computed tomography (CT) scanning or magnetic resonance (MR) imaging has been reported in 29 GA-1 patients, of whom 5 had subdural fluid collection [1–3].

We present herein an infant with GA-1 who showed a chronic subdural hematoma as an initial manifestation.

CASE REPORT

This 10-month-old boy was born uneventfully at full term to unrelated Japanese parents. His birth weight was 3,550 g. A 2-year-old male sibling was healthy. He

smiled at 1 month and gained head control at 3.5 months. He developed normally until 5 months when he was admitted to a hospital with an upper respiratory tract infection followed by focal motor seizures. Although the seizures were controlled by the administration of phenobarbital, he gradually developed irritability and involuntary movements. He was transferred to our hospital for further evaluation at 6-months old.

His body weight was 7,405 g (−0.8 S.D.), length 68.2 cm (+0.1 S.D.), and head circumference 43.5 cm (+0.1 S.D.). He was lethargic and irritable. He was hypotonic and could not support his head. The muscle stretch reflex was normal and the plantar responses were flexor. He exhibited oral dyskinesia and a dystonic posture, which were exacerbated by crying. Serum creatine kinase was elevated, being 1,460 mU/ml (46–188 mU/ml). The serum free and acyl carnitine values were 19.0 mmol/l (30–50 mmol/l) and 8.0 mmol/l (<10 mmol/l), respectively. CT scanning on admission showed marked widening of the bilateral insular cisterns (Fig 1). MR scanning revealed abnormal subdural spaces, which appeared as high intensity areas in both T₁ (TE/TR = 440/15.0) and T₂ (TE/TR = 2,500/100) weighted images (Fig 2). A chronic subdural hematoma was suspected. Bilateral craniotomy was performed and xanthochro-

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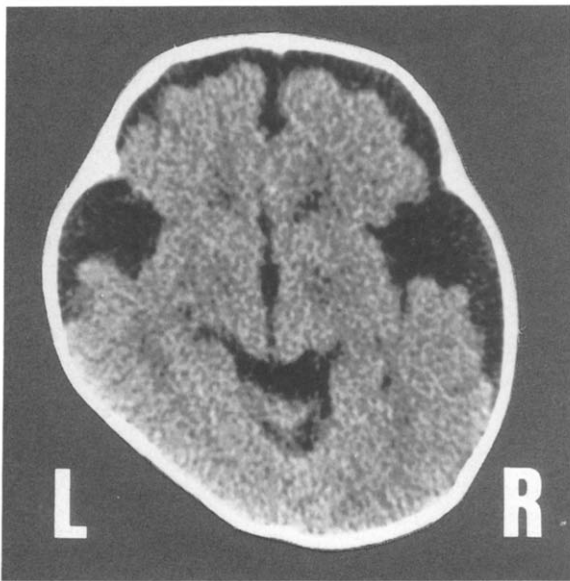


Fig 1. CT scan at the age of 6 months. Widening of the frontal subdural spaces and the insular cisterns can be seen.

mic fluid was removed. The drowsiness and irritability disappeared after the operation, but the extrapyramidal signs persisted. In a MR scan, the subdural space was observed to be slightly decreased.

Urine organic acid analysis revealed marked increases in glutaric acid, 3-hydroxy-glutaric acid and glutaconic acid. Glutaryl-CoA dehydrogenase activity was not detected in cultured fibroblasts obtained from biopsied skin. Thus, the diagnosis of GA-1 was made.

He was placed on a low lysine, low tryptophan diet

involving S-30 milk (Snow Brand Milk Product Co.). Excretion of glutaric acid, 3-hydroxy-glutaric acid and glutaconic acid in the urine decreased, but the extrapyramidal signs and muscle hypotonia did not improve. Baclofen (GABA neuron activator) at a dose of 2 mg/kg was effective for the athetosis and oral dyskinesia. However, it was discontinued because of two apneic episodes. Now he is receiving a protein restriction diet and L-carnitine (50 mg/kg/day). He can fully follow objects and smiles spontaneously, but cannot support his head at 10 months old.

DISCUSSION

To our knowledge, around 40 patients with GA-1 have been presented since the first report of Goodman et al. in 1975 [4]. The neuroradiological features on CT scanning or MR imaging have been reported in 29 GA-1 patients. They are characterized by the following three points: (i) widening of the insular cisterns (17/29) [1,3,5,6], (ii) enlargement of the frontal horns with loss of caudate nuclei (13/29) [1,3,5,7,8], and (iii) diffuse attenuation of the cerebral white matter (8/29) [1,3,8-10]. The first character is the most prominent feature in this disease. It was also seen in our patient and thus was a clue for the diagnosis.

There have been no other reports of a patient with both GA-1 and a chronic subdural hematoma, but we found 5 cases of subdural fluid collection in the literature. The latter cases and ours had no episodes of trauma. The high incidence of GA-1 accompanied by sub-

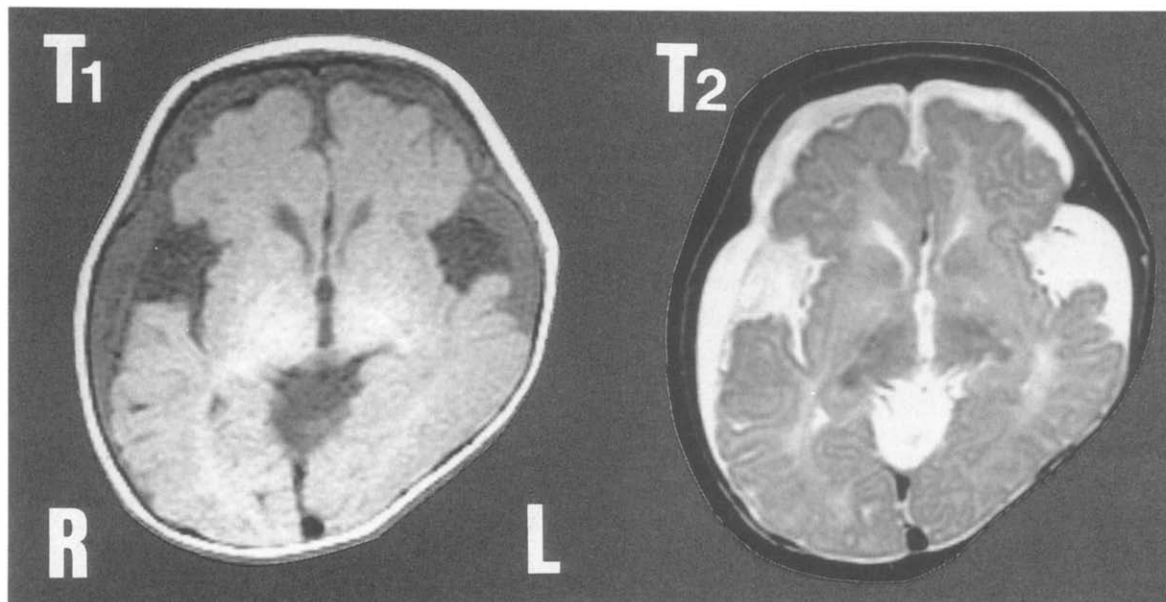


Fig 2. MR imaging at the age of 6 months shows a diffuse bilateral subdural hematoma accompanied by frontotemporal lobe hypoplasia. The hematoma shows high intensity in both T₁- and T₂-weighted images.

dural effusion (5/39) does not seem to be coincidental. One theory for subdural fluid collection is that rupturing of the arachnoid membrane causes cerebrospinal fluid to enter the subdural space [11]. There is a possibility that disproportional temporal lobe hypoplasia or atrophy of GA-1 is prone to tearing the arachnoidal membrane. We could not find any relationship between subdural collection or a hematoma and other metabolic diseases in the literature.

It has been proven in many cases that subdural effusion subsequently develop into a subdural hematoma through hemorrhaging from the outer membrane of the fluid collection [11], and it is sometimes difficult to distinguish a hematoma from effusion. We propose that both subdural effusion and a hematoma are probable complications of GA-1.

Little attention has been paid to these two diseases accompanying GA-1. However, we have shown that they are not rare complications of GA-1. To prevent secondary neuronal damage, we must be aware of subdural effusion and hematomas in GA-1 patients.

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