

Two cases of citrullinaemia presenting with stroke

J. H. Choi · H. Kim · H. W. Yoo

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Summary Urea cycle disorders are known to be unusual causes of stroke. We report two infant cases of citrullinaemia that both initially presented with a stroke and suggest that urea cycle disorders should be included in the differential diagnosis of unexplained stroke during infancy and childhood.

Introduction

Urea cycle disorders are known to be unusual causes of stroke. To date, there are several reports of ornithine transcarbamylase (EC 2.1.3.3) deficiency that presented with stroke-like episodes (Christodoulou et al 1993; Mamourian and de Plessis 1991). However, cases of citrullinaemia manifested as stroke-like episodes have not previously been described. We report two infant cases of citrullinaemia (McKusick 215700) that both initially presented with a stroke.

Case reports

Patient 1 was admitted to the hospital because of focal clonic seizures involving the right upper extremity and the right side of her face at the age of 3 months. She was drowsy and had

increased muscle tone and hyperreflexia in both right upper and lower extremities. The plasma ammonia concentration was greater than 400 $\mu\text{mol/L}$. She was diagnosed with citrullinaemia after serum amino acid analyses revealed markedly elevated citrulline concentration at 2401.3 nmol/ml (normal range 3–35 nmol/ml), and normal glutamine and arginine concentrations. Urine organic acid analysis showed increased excretion of orotic acid. An electroencephalogram showed spike discharges from the left frontotemporal area. Brain MRI demonstrated an acute ischaemic lesion in the left hemisphere (Fig. 1). The patient's refractory status epilepticus was controlled after three days of treatment with phenobarbital, valproate and vigabatrin. The ammonia concentration decreased after the administration of sodium benzoate, L-arginine, vitamin B complex, and parenteral nutrition with glucose and lipid. She could control her head by 7 months of age. Currently, at the age of 7 years, her plasma ammonia concentration has remained below 100 $\mu\text{mol/L}$ on a low-protein diet. However, she has microcephaly and severe mental retardation with normal motor development.

Patient 2 was brought to the emergency room at the age of 53 days because of generalized tonic seizures and impaired consciousness. Her height and weight were both below the 3rd centile. She was mentally comatose and had increased muscle tone and hyperreflexia in both extremities. The plasma concentration of ammonia on admission was 535 $\mu\text{mol/L}$. Serum amino acid analyses revealed a markedly elevated citrulline concentration at 1376.0 nmol/ml, with normal concentrations of glutamine and arginine. Molecular study identified a missense mutation of G324S homozygotes in the argininosuccinate synthetase (ASS) gene in both patients, which was reported in previous study (Kobayashi et al 1990). An electroencephalogram showed diffusely suppressed background activity. Brain MRI revealed acute ischaemic lesions in the right hemisphere and

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J. H. Choi · H. Kim · H. W. Yoo
Department of Pediatrics, Asan Medical Center, University of
Ulsan College of Medicine, Seoul, Korea

H. W. Yoo (✉)
Department of Pediatrics, Asan Medical Center, 388-1,
Pungnap-Dong, Songpa-Gu, Seoul 138-736, Korea
e-mail: hwyoo@amc.seoul.kr

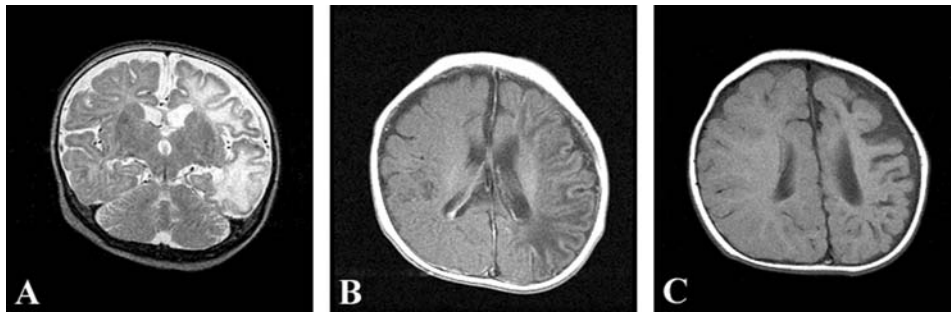
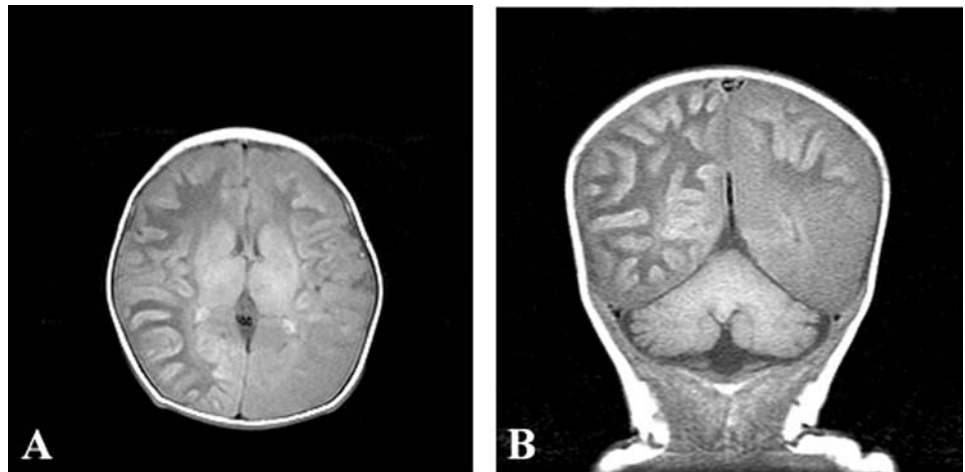


Fig. 1 (A) T2-weighted coronal image shows high signal intensity involving both the white and grey matter in the left hemisphere, suggesting infarction. (B) Gadolinium-enhanced T1-weighted axial MR image shows mild ventricular enlargement and diffuse low signal in-

tensity with decreased volume in the left hemisphere, indicating brain atrophy. (C) T1-weighted axial image of 8 months later shows severe volume loss of white matter of the left hemisphere, widening of sulci and secondary cortical atrophy.

Fig. 2 T1-weighted axial (A) and coronal (B) MR images show diffuse atrophic changes in the right hemisphere and left frontoparietal lobe, suggesting infarction.



the left frontoparietal area (Fig. 2). The serum ammonia concentration was normalized with peritoneal dialysis. However, the patient, now 6 years old, has a global developmental delay and spastic quadriplegia because of the initial brain damage caused by hyperammonaemic episodes.

In this report, two cases of citrullinaemia presenting with stroke are described, urea cycle disorders should be included in the differential diagnosis of unexplained stroke during infancy and childhood.

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