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Case report

Unique neuroradiological findings in propionic acidemia

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ABSTRACT

Propionic acidemia is a rare metabolic disorder that affects the catabolism of branched-chain amino acids and oddchain fatty acids. Propionic acidemia is one of the least common organic acidemias. Presented here are manifestations not previously characterized. The first case is an infant with diffuse subcortical diffusion restriction and vermian atrophy. The second case is an adolescent with asymmetric cortical volume loss and contralateral cortical diffusion restriction. These unique brain MRI findings of propionic acidemia may aid the neuroradiologist in guiding genetic testing for occult metabolic disease.

Introduction

The organic acidemias are a group of metabolic disorders in which a build-up of organic acids in the blood takes place due to an enzyme deficiency. Since the build-up of metabolites is excreted in the urine, organic acidemias are also referred to as organic acidurias.

The amino acids valine, isoleucine, threonine, and methionine as well as odd chain fatty acids and cholesterol side chains are catabolized into the 3-carbon substrate propionyl-CoA, which under normal physiologic conditions is converted to the 4-carbon metabolite methomalonyl-CoA in the presence of the biotin-dependent mitochondrial enzyme propionyl-CoA carboxylase. The enzyme is a dodecamer of 6 alpha and 6 beta subunits, and mutation to either of the encoding genes PCCA (on chromosome 13q32.3) or PCCB (on chromosome 3q22.3) inherited in a homozygous recessive fashion can result in the accumulation of propionyl-CoA and eventually propionic acid resulting in the disorder propionic acidemia [1]. Propionic acidemia is one of the rarer organic acidemias and occurs in approximately 1 in 100,000 to 1 in 150,000 people [2].

The disease typically presents in the neonatal period. Less common forms presenting later in life, however, have been described. Clinical features of the organic acidemias in

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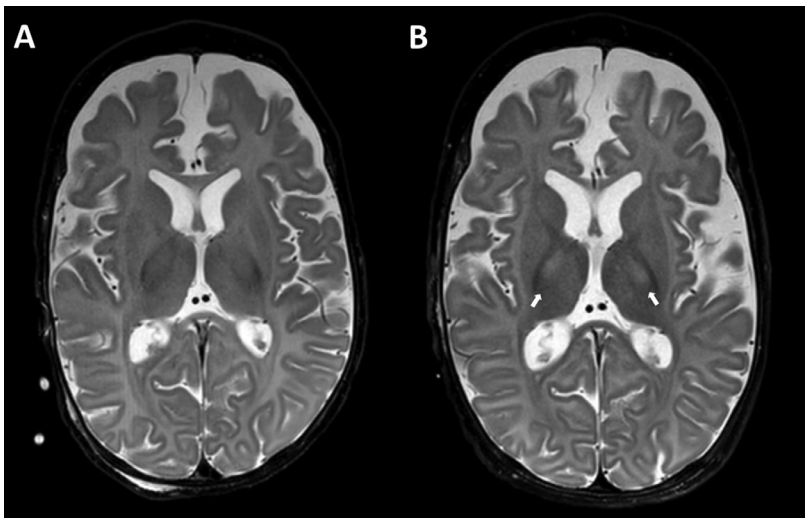

Fig. 1 – Axial T2-weighted images of the brain were acquired at 3.0 T on a Philips Ingenia MRI system. Shown here are images of a 3-month-old male at baseline (A) and during an acute propionic acidemia crisis at 5 months of age (B). White arrows in (B) indicate T2 hyperintense signal in the ventral thalami.

the newborn include poor feeding, hypotonia, vomiting, and lethargy. Patients are also prone to seizures, and propionic acidemia may manifest as failure to thrive in older children. If a metabolic crisis is left unrecognized or untreated, coma, and death can ensue.

The rarity of the disease has resulted in few published cases, but case series have been described. Common findings reported include T2/fluid-attenuated inversion recovery hyperintensity in the putamina and caudate nuclei, generalized brain swelling, and delayed myelination [3–5].

We present unique neuroradiological findings in an infant and an adolescent with different and unique manifestations of propionic acidemia exacerbation.

Case report 1: infant

The first patient was a 5-month-old male transferred to our tertiary care center with increased vomiting and lethargy. The patient had been followed by the genetics service and was known to carry an in-frame deletion of a single amino acid in the PCCA gene. He had been admitted several times previously for propionic acidemia crises, and a prior magnetic resonance imaging (MRI) obtained at 3 months of age was available (Figs. 1A, 2A, and 3A). Comorbidities included hyperparathyroidism, hypocalcemia, and *Clostridium difficile* diarrhea. His laboratory studies included a white blood cell count of 2.2 cells/mm^3, ammonia of 127 μmol/L, lactate of 2.7 mmol/L, ionized calcium of 1.19 mg/dL, and glucose of 242 mg/dL. The basic metabolic panel revealed a sodium of 132 mEq/L, a potassium of 5.1 mEq/L, bicarbonate of 13 mEq/L, blood urea nitrogen of 48 mg/dL, creatinine of 0.6 mg/dL, and a chloride of 99 mEq/L.

The child became increasingly lethargic on hospital day 4 and underwent an MRI which revealed increased T2 signal in the ventral thalami and parenchymal volume loss in comparison to the examination obtained 2 months prior with resulting prominence of the lateral ventricles and cortical sulci (Fig. 1B). There was also marked volume loss in the vermis (Fig. 2B). The most striking feature was a diffuse symmetric subcortical pattern of diffusion restriction (Fig. 3B), in addition to diffusion restriction of the basal ganglia and thalami. No seizures were observed. An electroencephalogram performed on hospital day 4 showed slowing consistent with metabolic encephalopathy. The patient was eventually discharged from the hospital after a 24-day course without additional encephalopathic changes or neurologic imaging.

Case report 2: adolescent

This child was a 15-year-old female who presented to the emergency department with a headache and increased sleepiness. She had been followed by the genetics service since birth with propionic acidemia, which had been confirmed by genetic testing during infancy. Her younger sister also had confirmed propionic acidemia. The patient's past medical history was significant for developmental delay and seizure-like activity with electroencephalography suggesting abnormal activity throughout the right hemisphere. MRI had been performed 10 months previously at age 14 during a metabolic crisis (Figs. 4A and 5A) and was repeated shortly after this admission (Figs. 4B and 5B). At admission, her ammonia level was 63 μmol/L.

Asymmetric volume loss was apparent throughout the right hemisphere with subsequent asymmetric prominence of the cortical sulci and extra axial spaces, a finding that was relatively unchanged in comparison to the previous MRI (Fig. 4). New volume loss was now apparent throughout the left cerebral hemisphere (Fig. 4B). Asymmetric cortical diffusion restriction involving the left hemisphere and right occipital lobe apparent during a metabolic crisis (Fig. 5A) had resolved (Fig. 5B).