Clinical, Pathological, and Electron Microscopic Findings in Two Thai Children with Pompe Disease

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Abstract

The authors report on a Thai boy who first presented at age 7 months and an unrelated Thai girl in her neonatal period with hypotonia, cardiomegaly and hepatomegaly. Their chest roentgenograms showed markedly enlarged hearts, EKGs showed abnormally shortened PR intervals with gigantic QRS complexes, and electron microscopic studies of their skin samples showed glycogen accumulations surrounded by membranes. The boy died at age 22 months and the girl at age 9 months due mainly to cardiorespiratory failure. Autopsy of the girl showed marked accumulation of glycogen in the liver, heart and numerous additional tissues including her brain. The clinical, pathological, and electron microscopic findings of these two children are consistent with the diagnosis of Pompe disease.

Pompe disease is an autosomal recessive disorder of glycogen metabolism resulting from deficiencies in activity of the lysosomal acid α-glucosidase. Definite diagnosis of the disease can be made from a biochemical test or a mutation analysis. To the authors' knowledge, no service laboratories in Thailand offer the tests. Because Thai children have occasionally been reported to be affected by Pompe disease, an attempt to establish a definite diagnostic test for Pompe disease in Thailand should be encouraged. With a definite diagnosis, the proper genetic counseling and prenatal diagnosis could be offered to the families.

Key word : Glycogen Storage Disease, Pompe Disease, Electron Microscopy

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Pompe disease or glycogen storage disease type II is an autosomal recessive disorder of glycogen metabolism resulting from deficiencies in the activity of the lysosomal hydrolase acid α-glucosidase in all tissues of affected individuals[1]. The clinical manifestation of Pompe disease includes a range of phenotypes, all of which involve varying degrees of myopathy. The most severe type is infantile-onset disease, with hypotonia, cardiomegaly, hepatomegaly, and death due to cardiorespiratory failure, usually before the age of 2 years[2]. The deficiency of the enzyme results in accumulation of glycogen of normal structure within lysosomes in numerous tissues, most marked in cardiac muscle, skeletal muscle, and hepatic tissues[3]. Electron microscopy reveals a specific vacuoles tightly packed with glycogen particles surrounded by a single membrane[4].

The authors report two Thai children with clinical, pathologic, and electron microscopic findings characteristic of Pompe disease. With the diagnosis, proper genetic counseling and prenatal diagnosis could be offered to the families.

MATERIAL AND METHOD

Patient 1

The patient, a boy, was born at term to a 24-year-old G1P0 Thai mother and a 30-year-old nonconsanguineous Thai father. The pregnancy and labor were uncomplicated. Birth weight was 3,100 g. He had pneumonia at age 7 months. During hospitalization, hypotonia and cardiomegaly with congestive heart failure were found. Diuretics, digitalis, and enalapril were given. He was rehospitalized 4 more times for pneumonia or congestive heart failure at ages 10, 19, 20 and 22 months. He held his head up at age 3 months, rolled over at 5 months, but was not able to sit at age 10 months. At age 22 months, he measured 75 cm (-3 SD), weighed 8.0 kg (-3 SD), and had a head circumference of 46.5 cm (-2 SD). Cardiac examination revealed a systolic murmur grade 3/6 on his left upper sternal border. His liver was palpated 5 cm below the right costal margin but the spleen was not palpable.

Electrocardiogram (EKG) showed a short PR interval, large QRS voltage, signs of left atrial dilatation and biventricular hypertrophy (Fig. 1). Roentgenograms of his chest showed marked cardiomegaly. The echocardiogram showed severe ventricular hypertrophy. Electron microscopy on a skin biopsy at age 7 months showed vacuoles filled with glycogen (Fig. 2). He died of cardiopulmonary failure with septicemia at the age of 22 months. Hemoculture was positive for *Morganella morganii*.

Patient 2

The patient, a girl, was born at full-term to a 32-year-old G1P0 Thai mother and a 37-year-old nonconsanguineous Thai father. The pregnancy was complicated by maternal gestational diabetes mellitus. The patient was born by Cesarean section with forcep extraction due to fetal distress. Birth weight was 3,600 g. APGAR scores were 6 and 8 at 1 and 5 minutes, respectively. After birth, she had dyspnea requiring hospitalization for 4 weeks. Hypotonia and cardiomegaly with congestive heart failure were found. She was hospitalized three times at ages 3, 4, and 6 months for pneumonia. At age 6 months, she could hold her head up but could not roll over. Her weight was 5.3 kg (-2.5 SD). She had respiratory distress, bilateral rhonchi on both lungs, systolic ejection murmur grade 2/6 on left sternal border, and hepatomegaly.

Her liver enzymes were elevated with alanine aminotransferase (ALT, SGPT) 89 U/L (normal: 5-45) and aspartate aminotransferase (AST, SGOT) 185 U/L (normal: 15-55). EKG showed a short PR interval, massive QRS voltage, and signs of biventricular hypertrophy. Chest roentgenograms showed striking cardiomegaly. The echocardiogram showed severe ventricular hypertrophy with low left ventricular systolic function and mild tricuspid and mitral valve regurgitation. Mitochondrial DNA analysis at position 3,243, 8,344, and 8,993 was negative. She died of cardiopulmonary failure at the age of 9 months.

At the postmortem examination, the main pathology was observed in the heart, liver, and the brain. The heart was enlarged, with the weight of 195 grams (normal: 41 ± 5). The left and right ventricular walls were thickened, and respectively measured 1.8 cm and 1.0 cm. There was also marked eccentric thickening of the interventricular septum. The liver weighed 250 g (normal: 288 ± 67), showing yellow brown cut surfaces. The brain weighed 720 g (normal: 810 ± 82). Coronal sections revealed diffusely increased firmness with gray discoloration of the white matter of both the cerebral hemispheres. The gray structures were relatively intact.