A 5-month-old male infant born to consanguinous marriage with past history of feeding difficulties in the form of suck-rest-suck cycle, forehead diaphoresis, and poor weight gain since early infancy presented with increasing severity of respiratory distress and apathy of 2 weeks duration. Physical examination revealed tachypnea, tachycardia, severe respiratory distress with chest wall retractions, and cool peripheries. The liver edge was palpable 4 cm below the left costal margin in midclavicular line. Neurological examination showed floppy infant appearance with generalized hypotonnia and absent deep tendon reflexes. Cardiovascular system examination revealed apex impulse in right 6th intercostal space near anterior axillary line, presence of gallop rhythm, and soft systolic murmur. Chest X-ray (Figure A) was suggestive of visceral situs inversus, dextrocardia, cardiomegaly, and normal pulmonary vasculature. Echocardiogram showed peaked P waves, severe right and left ventricular hypertrophy with ST-T changes. Echocardiography (Figure B–D; Video in the Data Supplement) showed severe concentric hypertrophy of left ventricle and papillary muscles, right ventricle free wall hypertrophy with almost complete obliteration of right ventricle cavity during systole, restrictive left ventricle filling pattern, mild mitral regurgitation, mild tricuspid regurgitation, no left ventricular or right ventricular outflow tract obstruction, and thin rim of pericardial effusion. Levels of lysosomal enzyme α-1, 4-glucosidase in leucocytes were grossly deficient: with acarbose, 1.98 (normal range, 3.3–14.5 nmol/h/mg protein); without acarbose, 17.1 (normal range, 20.67–206.73 nmol/h/mg protein), and ratio of 0.11 (normal, >0.2). To summarize, this is a case of infantile-onset Pompe disease presenting with severe cardiomyopathy and generalized muscle weakness with marked biventricular hypertrophy, almost complete obliteration of ventricular cavity at the end systole with situs inversus and dextrocardia, which is probably not yet reported. Unfortunately, baby died because of cardiorespiratory failure at the age of 6 months, and parents declined postmortem examination.

Discussion

Pompe disease (Type II Glycogen storage disorder; OMIM 232300) is an autosomal recessive disorder with an incidence of ≈1/40,000 live births, caused by deficiency of lysosomal acid α-1, 4-glucosidase (GAA), resulting in lysosomal glycogen accumulation principally in cardiac, skeletal, and smooth muscle cells. Infantile-onset Pompe disease is characterized by a generalized muscle weakness, hypotonia, feeding difficulties, macroglossia, hepatomegaly, and a hypertrophic cardiomyopathy with death typically in the first year of life because of cardiorespiratory or respiratory failure. Late-onset Pompe disease (juvenile and adult forms) feature slowly progressive proximal muscle weakness without significant cardiomyopathy. Respiratory failure as a result of respiratory muscle involvement is the usual cause of death in late adulthood. Treatment options were once limited to palliative care, till the introduction of enzyme replacement therapy, which has changed the disease course considerably. Recombinant human GAA (algglucosidase alfa, [Myozyme]) at the dose of 20 mg/kg every other week improved ventilator-free survival, cardiomyopathy, growth, and motor function in patients with infantile-onset Pompe disease. Major obstacle to successful enzyme replacement therapy is development of neutralizing anti-GAA antibodies. Gene therapy with adeno-associated virus is still in experimental stage; however, this holds promise for future curative therapy for infantile-onset Pompe disease. Urinary biomarker (Glc4) can be used as both screening test and for monitoring of response to enzyme replacement therapy. Newborn screening with fluorometric and MS/MS methods in dried bloodspots has been successful in Taiwan. Carrier detection of at-risk family members is possible by mutation analysis (molecular testing) of the GAA gene (MIM# 606800) located on chromosome 17q25.2–25.3, provided familial mutation is known. Genetic counseling should be offered to young adults who are affected or are at risk of being carrier regarding mode of inheritance, risk to offspring, natural history, treatment options, and family-planning decisions. Prenatal diagnosis is a viable option for couples who had an affected child or to couples at risk for an affected child by mutation analysis of fetal DNA obtained by chorionic villus sampling (10–12 weeks gestation) or by amniocentesis (15–18 weeks gestation), provided both disease-causing alleles are identified.
familial mutation is not known, biochemical testing may be performed by measuring GAA enzyme activity in uncultured chorionic villi or amniocytes.

To conclude, expensive enzyme replacement therapy may not be affordable and feasible in all patients of infantile-onset Pompe disease, especially in developing countries; however, genetic counseling and options of carrier detection and prenatal diagnosis can be provided if future pregnancy is planned.

Disclosures

None.

References


Key Words: dextrocardia ■ hypertrophic cardiomyopathy ■ situs inversus

Figure A, Chest X-ray showing visceral situs inversus, dextrocardia, and cardiomegaly. B, Apical 4-chamber view showing marked biventricular hypertrophy with almost complete obliteration of right ventricular cavity at the end systole and mild tricuspid valve regurgitation. C, Parasternal long axis view showing severe concentric hypertrophy of left ventricle without left ventricular outflow tract obstruction. D, Parasternal short-axis view showing marked biventricular hypertrophy.
Giant Heart of Classical Infantile-Onset Pompe Disease With Mirror Image Dextrocardia
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Supplemental Figure 1. 12 lead Electrocardiogram showing peaked P waves, severe right and left ventricular hypertrophy with secondary ST-T changes
Supplemental Figure 2. Tissue Doppler imaging showing markedly reduced mitral annular septal e’
Supplemental Figure 3. CW Doppler showing RV intracavitatory gradient of 35mmHg during end systole

**Video Legend.** Apical four chamber, Parasternal long axis, Parasternal short axis and subcostal coronal views in order