To the Editor: Pompe disease, a rare autosomal recessive disorder due to alpha-1,4-glucosidase (GAA) activity deficiency caused by its gene mutation, can cause an excessive lysosomal glycogen storage in muscular tissues. Pompe disease has two major clinical forms: infantile-onset and adult-onset forms. Without treatment, most infantile-onset patients die from respiratory and cardiac failure within the 1st year of life. A small percentage of infantile-onset patients, known as an atypical infantile form, present abnormalities in the 1st year and reveal a slower progression with less severe or an absence of cardiomyopathy. For this form, it is not easy to make a differential diagnosis with idiopathic hypertrophic cardiomyopathy. Here, we report a case of atypical infantile-onset Pompe disease from a Chinese family based on genetic and enzyme activity analyses.

A 5-month-old girl was admitted to hospital with oliguria for 10 days. Family history did not reveal any consanguinity. No family history of hypertrophic cardiomyopathy or sudden death was presented. Laboratory studies showed alanine aminotransferase (ALT) level of 121.2 U/L, aspartate aminotransferase (AST) level of 180.3 U/L, and lactate dehydrogenase (LDH) level of 630.8 U/L. Echocardiogram revealed hypertrophic cardiomyopathy with left ventricular posterior wall (LVPW) thickness of 9 mm and interventricular septum (IVS) thickness of 9 mm. A diagnosis of hypertrophic cardiomyopathy was made at that time, and the patient was given diuretic and supportive treatments. After 7 days, the patient’s situation was improved and she was discharged from the hospital.

One year later, the patient was admitted again to the hospital with gross motor delay. Neurological examination revealed weak limb muscles with Medical Research Council score of 4/5. Laboratory tests demonstrated ALT level of 190.0 U/L, AST level of 319.3 U/L, LDH level of 576.1 U/L, creatine kinase level of 980.0 U/L, and brain natriuretic peptide level of 291.26 pg/ml. Echocardiogram revealed left ventricular dilation (diameter of 27 mm in systole and 36 mm in diastole), LVPW thickness of 9 mm and IVS thickness of 12 mm [Figure 1a]. Reduced systolic and diastolic functions with an ejection fraction of 51% and delayed isovolumetric relaxation time (IVRT) of 102 ms were determined, respectively. Cardiac magnetic resonance imaging confirmed a significant increase of the left ventricular wall thickness and IVS thickness. Abdominal ultrasonography detected that medium hepatomegaly with the liver edge below the right rib of 3.7 cm. Electromyogram of the quadriceps femoris muscles was normal. Based on the clinical observations, the patient and her families were recommended to take genetic tests to find out the cause of the disorder. The results of next generation sequencing revealed a homozygous mutation at c.2015G>A (p. R672Q) in exon 14 of GAA gene [Figure 1b], which causes an abnormal splicing and an amino acid change from arginine to glutamine. All of the proband’s parents and grandfathers carried this mutation. The subsequent blood GAA enzyme activity was 1.51 μmol·L⁻¹·h⁻¹ at pH 3.8, significantly lower compared to the normal range. The diagnosis of Pompe disease was finally established based on genetic and biochemical analyses.

It was first reported in 1998 that the mutation was associated with the reduced GAA activities, however, it has never been reported in the mainland of China. A child from two heterozygous parents has a 25% probability to become homozygous. In this case, the clinical manifestations, laboratory analysis, imaging findings, genetic tests, and enzyme activity detections are consistent with atypical infantile-onset Pompe disease. At the early stage of the disorder, it is difficult to distinguish cardiomegaly due to Pompe disease from idiopathic hypertrophic cardiomyopathy without GAA enzyme activity tests or genetic analysis. In pediatric patients, in the setting of undetermined left ventricular hypertrophy or cardiac dysfunction, Pompe disease should be taken into consideration in the diagnostic algorithm and the determination of the etiology. Furthermore, early GAA genetic tests are recommended.
tests and enzyme biochemical analysis are important for the
diagnosis of the disease and genetic advising for patients and
their families.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient
consent forms. In the form, the patient/patient’s guardians have
given consent for their images and other clinical information to be
reported in the journal. The patient/patient’s guardians understand
that their names and initials will not be published and due efforts
will be made to conceal their identity, but anonymity cannot be
guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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