Correction of a short cardiac PR interval in a 12-year-old girl with late-onset Pompe disease following enzyme replacement therapy

To the Editor: We read with interest the article titled "Cardiovascular Abnormalities in Late Onset Pompe Disease and ERT" by Forsha et al.[1]. Ninety patients were randomized 2:1 to enzyme replacement therapy (ERT) or placebo in a double-blind protocol. Electrocardiograms and echocardiograms were obtained at baseline and scheduled intervals over a 78-week study period. Eighty-seven adult patients (median age 44 years; 51% male) were included in the final analysis of the results. At baseline 10% of the patients had a short PR interval (<120 milliseconds). Other cardiac dysfunction included ventricular hypertrophy (12%), decreased ejection fraction (7%), and enlarged left-ventricular mass (5%). These findings are in contrast to those described in infantile Pompe disease in which electrocardiograms abnormalities are universal and cardiac hypertrophy is much more prevalent and severe. The study suggested that cardiovascular parameters, including short PR interval, may not be impacted by ERT. However, the authors recognized that the relatively small sample size could be a limiting factor in detecting small differences between baseline and follow-up data. The authors concluded that long-term evaluation of the cardiac effect of ERT in a larger cohort of late-onset Pompe patients is necessary.

Because of the authors' conclusion, we would like to contribute our experience with a patient with late-onset Pompe disease, in whom ERT had a quick and prominent effect in the recovery of a short PR interval. We evaluated a 12-year-old girl for failure to thrive, proximal weakness, and fatigue of 2 years duration. Neurological examination revealed diffuse decrease of muscle mass in both the upper and lower extremities. Proximal muscle strength was 4+/5 in the upper extremities and 4/5 in the lower extremities. Deep tendon reflexes were normal in upper extremities, absent in the patellas, and decreased in the Achilles tendons. Laboratory evaluation revealed creatine phosphokinase 563U/L, aldolase 19U/L, aspartate aminotranferase 249U/L, and alanine aminotraferase 216U/L. Electromyogram and nerve conduction velocity studies were normal. Cardiac exam revealed a short PR interval of 70 milliseconds in leads II, III, V2, V4, V5, and V6. An echocardiogram was also performed, which demonstrated an intact atrial septum with no evidence of septal or free wall hypertrophy. There was adequate myocardial performance with a fractional shortening of the left ventricle of 0.42 seconds. The diagnosis of late-onset Pompe disease was confirmed by an abnormal low acid alpha glucosidase activity of 1.3 pmol/punch/hour in dried blood spot (normal range 10–49 pmol/punch/hour) and genetic studies. The patient had a c3213 T>G mutation within the first intron of the *GAA* gene (carried by her mother) and a mutation in exon 11 (c1636g>c), carried by her father, compatible with Pompe disease. Our patient remained clinically stable for 2 years with nutritional restrictions and physical therapy. ERT was initiated after an elevation of creatine phosphokinase and glucose tetrasaccharides in urine. She was treated with biweekly intravenous infusions of Lumizyme at a dose of 20 mg/kg body weight. We noticed a mild improvement in strength and she reported amelioration of her fatigue. In an electrocardiogram performed 5 months later, the PR interval was normal (140 milliseconds).

Although other studies have shown improvement of cardiac dysfunction after ERT in patients with infantile-onset Pompe disease,[2] there is a lack of literature regarding cardiac response to ERT in late-onset Pompe disease. Forsha et al.'s study[1] is one of the first to report on the cardiac response to ERT in patients with late-onset Pompe disease. Although they found that cardiovascular parameters were not affected by ERT, it is unclear in the paper whether the PR interval of two patients improved after 78 weeks of ERT or if they simply dropped out of the study. Given the small sample of patients, one should not underestimate the possible therapeutic effect of ERT on this particular cardiac parameter. On the other hand, this study did not include patients under 17 years of age, a factor to take into consideration when comparing with our case. Recently, Ishigaki et al.[3] reported a 12-year-old boy with childhood-onset Pompe disease who showed improvement in cardiac wall thickness after 8 months of ERT. This case and ours would suggest that cardiac function of childhood-onset Pompe disease (a subtype of late-onset Pompe disease) may improve with ERT.

We agree with Forsha et al.[1] that further studies are needed to evaluate cardiac effects of ERT in late-onset Pompe disease and would like to emphasize that they should include childhood- and juvenile-onset cases.

DISCLOSURE

The authors declare no conflict of interest.

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