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Correspondence

Letter to the Editors: Concerning "Divergent clinical outcomes of alphaglucosidase enzyme replacement therapy in two siblings with infantile-onset Pompe disease treated in the symptomatic or pre-symptomatic state" by Takashi M et al.

Dear Editors,

We read with interest the article by Takashi M et al. that recently appeared in *MGM Report*. Because many open issues remain about the outcome of infantile Pompe disease (IPD), we describe here our experience with two IPD siblings born to related parents and treated with enzyme replacement therapy (ERT) in the symptomatic and the pre-symptomatic state.

In the symptomatic child with severe respiratory insufficiency and hypertrophic cardiomyopathy, no detectable alpha-glucosidase acid (GAA) activity and homozygous substitution c.1A > G on the *GAA* gene, ERT (α-glucosidase, 20 mg/kg) was started at 6 months of age. Cardiomyopathy improved but not muscular function, and he underwent tracheostomy and gastrostomy. Early evaluation of IPD in his newborn sister showed hypertrophic cardiomyopathy, absent plasma GAA activity, CRIM negative (CN) status and the same genotype. As reported by Banugaria et al. [1], we performed immune tolerance induction (ITI) with rituximab and methotrexate and intravenous immunoglobulin before ERT (at 30 days). Her cardiomyopathy resolved after 1.5 months, and respiratory and neurological examinations appeared normal at the last evaluation (7 months). ERT effectively and rapidly reduces glycogen cardiac accumulation [2,3,4], regardless of CRIM status, but its early commencement does not prevent later anti-rhGAA IgG antibody formation [1,5,6]. Thus, in our older case, as in his sister, ERT effectively reduced cardiomyopathy, but anti-rhGAA IgG production reduced the therapeutic efficacy, worsening the neuromuscular outcome. Patients described by M. Takashi could be CRIM positive due to the presence of a missense mutation. Therefore, their outcome would depend more on the age at the start of ERT than on the CRIM status. We think that IPD patients should be screened as early as possible for CRIM status before ERT. In CN patients, it is important to do ITI and ERT to reduce anti-rhGAA IgG [7] production and to improve the natural history.

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Rita Ortolano*
Federico Baronio
Riccardo Masetti
Arcangelo Prete
Alessandra Cassio
Andrea Pession
Department of Woman, Child Health and Urologic Diseases, AOU S. Orsola-Malpighi, Bologna, Via Massarenti, 11, 40138 Bologna, Italy
*Corresponding author.
E-mail addresses: rita.ortolano@aosp.bo.it (R. Ortolano), federico.baronio@aosp.bo.it (F. Baronio), riccardo.masetti@aosp.bo.it (R. Masetti), tmoped@aosp.bo.it (A. Prete), alessandra.cassio@unibo.it (A. Cassio), andrea.pession@unibo.it (A. Pession).

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