Journal of Neuromuscular Diseases 1 (2015) S53
DOI 10.3233/JND-159047
IOS Press

Poster Abstract: Diagnostic

Alpha Glucosidase Assay on Dried Blood Spot in the Early Diagnosis of Infantile Pompe Disease

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Infantile-onset Pompe disease (IOPD) presents with hypotonia, muscle weakness, motor delay, cardiomyopathy, feeding problems, and respiratory insufficiency. An early diagnosis is important to start enzyme replacement therapy (ERT) early.[1]

Alpha-glucosidase (GAA) enzyme assay on dried blood spots (DBS) allows a diagnosis of Pompe disease (PD) more simple and fast. GAA assay on DBS is reliable, non-invasive, sensitive, and specific. It is a quick and cheap test, and requires only a very small quantity of blood to be collected, which allows for a non-invasive test in a newborn who presents a clinical suspect of PD. In the last 6 years, we identified 9 children affected by IOPD by GAA assay on DBS in tandem-mass spectrometry (MS/MS): 8 of them presented classic IOPD and 1 presented non-classic IOPD. At diagnosis, all patients showed cardiomyopathy. Five patients diagnosed in the first month of life (range 2–20 days; mean 10.2 days; median 9 days) showed cardiomyopathy: two of them presented respiratory distress. Four patients diagnoses in the infantile age (range 2–15 months; mean 8 months; median 6.5 months) presented hypertrophic cardiomyopathy and hypotonia. The GAA activity on DBS was near absent in all the patients, ranging from 0 to 0.2 μmol/L/h (n.v. 2.31–27.4). The GAA activity in lymphocytes was confirmed to be low in all the patients (range 0–0.8 nmol/mg/h, n.v. 11–32). Molecular analysis of the GAA gene confirmed the diagnosis of PD in all the patients. Five patients are being followed up at our department, and ERT was started at diagnosis at a standard dose of 20 mg/kg every 2 week. All these patients demonstrated a progressive improvement of cardiomyopathy. The individual response to ERT was different in the group of patients due to CRIM-status, development of rhGAA specific antibodies, age of presentation, and rate of disease progression, in accordance with literature data.[2] In IOPD, an early diagnosis is important to start early ERT, which has been shown to be effective in treating patients with IOPD and late-onset PD. GAA assay on DBS is a reliable, non-invasive, sensitive, and specific test for newborns and infants in the firsts months of life with signs or symptoms of PD. There is a PD newborn screening pilot program in the Tuscany and Umbria regions.

REFERENCES

[1] Kishnani PS, Hwu WL, Mandel H, Nicolino M, Yong F, Corzo D, et al. A retrospective, multinational, multicenter study on the natural history of infantile-onset Pompe disease. J Pediatr 2006; 148:671-676.
[2] Wang RY, Bodamer OA, Watson MS, Wilcox WR; ACMG Work Group on Diagnostic Confirmation of Lysosomal Storage Diseases. Lysosomal storage diseases: diagnostic confirmation and management of presymptomatic individuals. Genet Med. 2011 May;13(5):457-84.

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ISSN 2214-3599/15/$27.50