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### Journal
Molecular Genetics and Metabolism, 123(2)

### ISSN
1096-7192



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### Publication Date
2018-02-01

### DOI
10.1016/j.ymgme.2017.12.198

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## Variable clinical features and progression in 18 patients with Pompe disease

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Pompe disease is a lysosomal disorder caused by the deficiency of enzyme acid alpha-glucosidase (GAA) which results in accumulation of glycogen particularly in the skeletal, cardiac, and smooth muscles. The late-onset form with symptoms presenting in childhood through adulthood, is characterized by proximal muscle weakness, respiratory insufficiency, and unlike classic or infantile-onset form typically with no cardiac involvement. We report our experience with 18 adult patients (4 F/14 M) with Pompe disease at one center, several of whom had unique findings and novel mutations. Patients ranged in ages from 21-72y. (mean 52 y.) and were diagnosed at a range of 11-65 y (mean 43.4 y.) often after a history of progressive muscle disease of several years duration. Genetic sequencing revealed that 16/18 individuals had the common c.-32-13T>G mutation, and eight had 6 novel mutations: c.1594G>A, c.2431delC, c.2655_2656delCG, c.1951-1952delGGinsT, c.525_526delTG, and c.1134C>G. A male with the c.1594G>A mutation developed an intracerebral aneurysm at the age of 43 y. treated with surgery. Another male with the c.525_526delTG developed testicular cancer and is in remission. Cardiomyopathy was noted in an adult with the c.525_526 delTG mutation, and peripheral neuropathy in a male with the c. 1951-1952delGGinsT. Two siblings with the c.2655_2656delCG developed very high antibody titers, one of whom developed a severe infusion reaction. Other clinical features included scoliosis and cardiomyopathy in a young adult, BiPAP requirement in eight, tinnitus in seven, and one individual was born with partially developed hip and clubfoot. All patients currently receive alglucosidase alfa with different response rates in their muscle weakness, pulmonary function dynamometry, and functional studies. Our patient cohort illustrates the variable range of clinical features, and alert us to the importance of careful monitoring and early management of these complications. Possible genotype-phenotype associations with these novel mutation will emerge with larger studies.

doi:10.1016/j.ymgme.2017.12.198