Glycogen Storage Disease Type II (Pompe Disease)

Genetics

-GAA (α –glucosidase)

-AR

Clinical findings/Dysmorphic features

-Infantile-onset: Cardiomyopathy <12 months; ~4 mths: hypotonia, muscle weakness, macroglossia, hepatomegaly, feeding difficulties, FTT, hypertrophic cardiomyopathy, HL

-Late-onset (0-70 years):

--> onset < age 12 months: proximal muscular weakness, delayed motor development, lordosis, kyphosis/scoliosis, respiratory insufficiency without cardiomyopathy

--> onset > age 12 months: proximal muscle weakness and respiratory insufficiency; sleep disordered breathing, clinically significant cardiac involvement is uncommon

Etiology

-Incidence: African Americans 1:14,000, US 1:40,000, European 1:100,000

Pathogenesis

-α –glucosidase cleaves α 1,4 and α 1,6-glucosidic linkages during degradation of glycogen

-Deficiency --> abnl storage of nl glycogen in tissues (mainly skeletal, smooth, cardiac muscles)

-α –glucosidase is located in the lysosomes (functions in acidic pH)

Genetic testing/diagnosis

-NBS: acid alpha-glucosidase (GAA) enzyme activity on dried blood spots

-GAA activity in lymphocytes/cultured fibroblasts (< 10% of normal)

-Elevated creatine phosphokinase (CPK) (10x normal): (as high as 2000 IU/L; normal: 60-305 IU/L) – normal in late onset (also in DMD/BMD)

-GAA: Seq 83-93%, InDel 5-13%; c.-32-13T>G is most frequent pathogenic variant

Others

-ERT: Myozyme and Lumizyme are FDA approved (work well --> live longer --> HL)

-Pseudodeficiency allele common in Asians; only GSD classified LSD; unlike other GSDs: not associated with hypoglycemia

-6-mth-old boy with severe hypotonia, massive cardiomegaly, progressive weakness and markedly elevated CPK