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Review Article

Flowchart for Screening of Pompe Disease

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Abstract

Pompe disease, or acid maltase deficiency or glycogen storage disease type II, is a metabolic disorder with deficiency of acid α-glucosidase.

There are two classic forms of the disease: infantile-onset Pompe disease and late-onset Pompe disease.

In IOPD, symptoms are distal muscle weakness that precede proximal muscle weakness, hypotonia, macroglossia, hepatomegaly, hypertrophic cardiomyopathy and death secondary to cardiorespiratory failure in the first 12 months of age, if not treated.

In LOPD, the age of onset is 1 years old to 50s with symptoms of respiratory insufficiency and limb–girdle weakness.

Symptoms of LOPD started in the proximal lower limb and paraspinal trunk muscles.

We can do Dried Blood screening for detection of PD and confirm later on with gene study.

After the diagnosis, we can initiate with a dose of 20 mg/kg every other week. High-dose ERT (40 mg/kg biweekly) results showed that prescription gave the best outcomes, and a dosage increase is needed upon a rise in biomarker levels.

Keywords: *Pompe Disease; Dried Blood Screening*

Introduction

Pompe disease (PD), or acid maltase deficiency or glycogen storage disease type II, is a metabolic disorder with deficiency of acid α-glucosidase (GAA).

The incidence of PD is around 1 in 40,000 live births.

There are two classic forms of the disease: infantile-onset PD (IOPD) and late-onset PD (LOPD).

LOPD is categorized into childhood, juvenile, and adult-onset PD.

Patients with residual GAA are classified as (CRIM)-positive while those that lack the enzyme completely are CRIM-negative.

In IOPD, GAA activity is absent, normally < 1% of the mean activity as compared to healthy individuals.

This absent of activity will cause distal muscle weakness that precede proximal muscle weakness, hypotonia, macroglossia, hepatomegaly, hypertrophic cardiomyopathy (HCM) and death secondary to cardiorespiratory failure in the first 12 months of age if not treated.

Patients with LOPD have still residual GAA activity and because of this, the age of onset of LOPD is 1 years old to 50s with symptoms of respiratory insufficiency and limb-girdle weakness.

Symptoms of LOPD started in the proximal lower limb and paraspinal trunk muscles. Dysfunction of the diaphragm and accessory muscles of respiration is a major cause of death in LOPD [1-8].

Dried blood screening (DBS)

As soon as we suspect of PD, we can do the DBS.

The flowchart is based on the age of presentation less or equal to 12 months of age (IOPD) or more than 12 months (LOPD). In the IOPD need to have at least two manifestations but one need to be obligatory musculoskeletal. In the LOPD, also need to have at least two manifestations with unexplained cause and with compatible EMG findings (Figure 1).

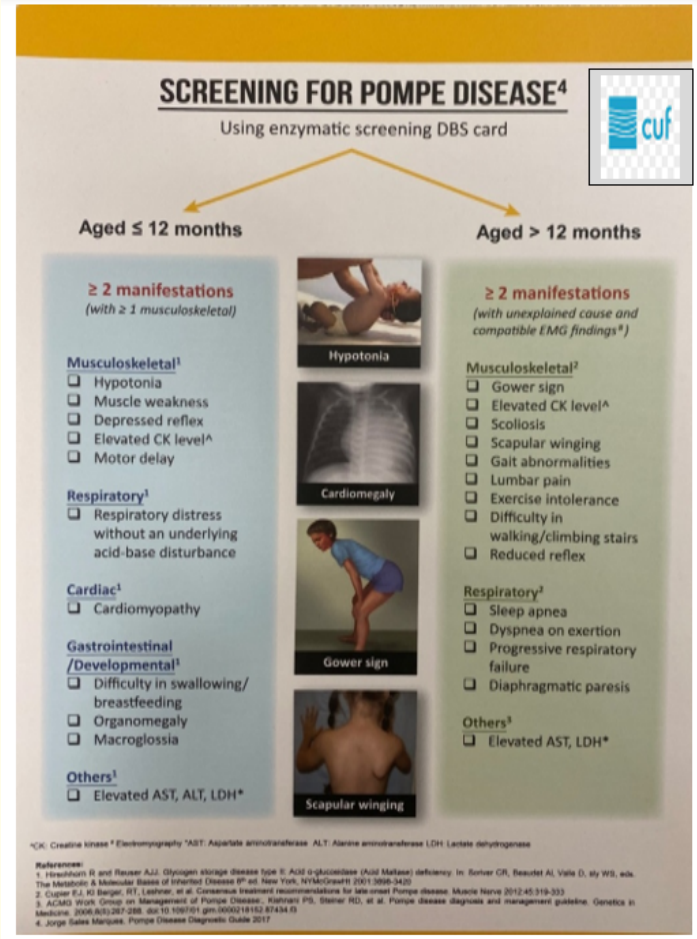

Figure 1: *Dried blood screening for Pompe disease.*

Next generation sequencing and mutation analysis

After the positive DBS we can confirm PD by using Next-generation sequencing (NGS).

Currently, there are more than 350 genes displaying pathogenicity. The variant p.Arg854Ter was found in about 50 - 60% of African Americans with IOPD and 50 - 85% of adults with LOPD have the variant c.336-13T > G.

Newborn screening for PD

ERT should be started before the onset of symptoms to avoid irreversible damage.

For this reason NBS is essential.

After the diagnosis, we can initiate with a dose of 20 mg/kg every other week.

Chien., *et al*. (2020) [9] involved 28 IOPD patients on high-dose ERT (40 mg/kg biweekly).

The results showed that prescription of a high-dose ERT immediately upon positive findings at NBS gave the best outcomes, and a dosage increase is needed upon a rise in biomarker levels [10].

Conclusion

PD is a metabolic disorder that can be treated with ERT.

When we suspect of PD, using the flowchart of DBS is recommend at the first stage for the diagnose.

The confirmation is by gene study.

Because of the autosomal recessive mode of inheritance, genetic counselling and prenatal diagnosis is the next step for the parents.

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