A RARE CASE OF POMPES DISEASE PRESENTED AS FLOPPY INFANT
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Abstract: Glycogen storage disease (GSD) are due to mutation of genes that codes for proteins involved in glycogen synthesis. Pompes disease, also referred as acid maltase deficiency or glycogen storage disease type is an autosomal recessive disorder caused by a deficiency of lysosomal enzyme acid glucosidase (GAA). It was the first recognised lysosomal storage disease and is the only glycogen storage disease that is also a lysosomal storage disease. In pompes disease, lysosomal glycogen accumulates in many tissues, with skeletal, cardiac and smooth muscles prominently involved. We report a case of pompes disease occurred in an 11 months old male child presented with flappiness of limbs and motor developmental delay since 5 months of age. This was one of the very rare cases reported in India.

Keyword: Pompes disease, Glycogen storage disease, Lysosomal enzyme. An eleven months old child, 2nd born of third degree consanguinous parents came with a history of floppiness and motor developmental delay. His antenatal and perinatal periods were uneventful. On examination, the child had a generalised hypotonia, areflexia and there was no organomegaly. Chest examination reveals no significant heart murmur, but his apex beat was shifted to left. Brachial and femoral pulses were normal. There was no cyanosis or clubbing noted. Flaccid extremities with frog position and absent deep tendon reflexes were found on neurological examination.

ECG taken shows short PR interval, high QRS voltage and prominent Q waves in left precordial leads. Then echocardiogram done shows hypertrophic cardiomyopathy. With all these clinical and laboratory findings, Pompes disease was suspected. Since the estimation of acid alpha glucosidase enzyme level in blood or skin fibroblast was the gold standard for the diagnosis of Pompes disease, it was estimated in blood and found to be very low.

| QUANTITATIVE ALPHA GLUCOSIDASE ACTIVITY BY FLUOROMETRY IN BLOOD |
|---------------------------|-----------------|
| Patients value            | 14 mmol/hr      |
| Normal value              | >60 mmol/hr     |

PCR for SMN gene -1 deletion was done and found to be negative. Based on these clinical and biochemical findings, a diagnosis of Pompes disease was made. The child was planned for enzyme replacement therapy with human recombinant acid alpha glucosidase and on follow up.

Discussion: Pompes disease is an autosomal recessive disorder due to deficiency of acid alpha glucosidase results in intra lysosomal accumulation of glycogen leading to progressive muscle dysfunction. Due to the presence of weakness and hypotonia, it has also been classified as neuromuscular disease or metabolic myopathy. Great phenotypic variability has lead to the creation of types based on the age of onset and degree of organ involvement. Based on these the type of Pompes disease are infantile, childhood, juvenile and adult form. Patients as originally described by PJ Pompe, a Dutch pathologist, in 1932 who exhibit rapidly progressive disease characterized by prominent cardiomegaly, hepatomegaly, failure in the first year. This represents the most severe end of the disease spectrum and is often referred to as classic infantile Pompe disease. Incidence data are limited with reports ranging from 1 in 14,000 to 1 in 300,000 depending upon ethnicity or the geographic area studied. In India the exact incidence of the disease was not known but studies suggest it may be 1 in 40,000 livebirths, due to
the difficulty in confirmation of diagnosis. Patients with the infantile variant form (nonclassic infantile Pompe disease) with slower progression and less severe cardiomyopathy but presenting in the first year of life as described originally by Hers1 and, more recently, by Slonim et al.7 and which has also been variably classified in the literature with the infantile or childhood forms Late-onset form that includes childhood, juvenile, or muscular variant that is a heterogeneous group usually presenting later than infancy and typically not including severe cardiomyopathy. Adult-onset form characterized by a slowly progressive myopathy predominantly involving skeletal muscle that can present as late as the second to sixth decade of life. A chest x-ray and electrocardiogram (EKG) are valuable screening tests in the diagnostic algorithm for infantile Pompe disease and an echocardiogram is a valuable next step. Chest x-ray shows massive cardiomegaly. ECG shows a short PR interval as well as very tall QRS complexes. Late onset cases rarely display cardiomegaly on a chest x-ray or ECG which minimizes their utility in these patients. In Infantile Pompe disease echocardiogram typically reveals a hypertrophic cardiomyopathy with or without left ventricular outflow tract obstruction in the early stages of the disease. In the late stages of Infantile disease, patients may have impaired cardiac function and a dilated cardiomyopathy.

DIFFERENTIAL DIAGNOSIS:
1. Acute Werdnig-Hoffman disease (Spinal Muscular Atrophy I)
2. Hypothyroidism
3. Endocardial fibroelastosis
4. Myocarditis
5. Congenital muscular dystrophy
6. Glycogen storage diseases: IIIa (Debrancher deficiency)/Cori or Pompe disease and IV (Branching enzyme deficiency/Pompe disease) Cardiomegaly, myopathy, elevated creatine kinase (CK)
7. Mitochondrial/respiratory chain disorders
8. Danon disease
9. Idiopathic hypertrophic cardiomyopathy
10. Peroxisomal disorders

DIAGNOSIS:
The clinical diagnosis is traditionally confirmed by the virtual absence (infantile-onset) or markedly reduced (late-onset) GAA activity in tissues such as cultured fibroblasts from skin biopsy, muscle biopsy, purified lymphocytes, mononuclear cells and lymphoid cell lines. New methods have been developed that assay GAA activity in dried blood spot (DBS) extracts. Isolation of GAA from DBS extracts by immunocapture 8 or competitive inhibition of MGA (maltase gluco amylase) activity using maltose9,10,12 or acarbose11,12 have been used to remove the interfering MGA activity. In general, GAA enzyme activities of <1% of normal controls are seen in the infantile form of Pompe disease. In the late onset forms, activities from 2 to 40% of normal controls are seen. Muscle biopsy in Pompe disease shows the presence of vacuoles that stain positively for glycogen. In advanced stages of the disease, glycogen accumulation is seen both in the lysosomes and dispersed in the cytosol. Quantitatively, muscle glycogen content is elevated up to tenfold above normal in infantile Pompe disease and to a lesser extent in late onset patients. Mutation Analysis. While enzyme activity analysis remains the diagnostic test of choice for individuals with Pompe disease, mutation testing has important uses. It is particularly useful in the identification of carriers when a familial mutation is known. Pompe disease is a multi-system disorder and is best managed by a multidisciplinary team led by a physican with experience managing this disorder. Specific enzyme replacement therapy with recombinant human acid alpha glucosidase has been recently introduced. It can prevent the deterioration of abnormal cardiac and skeletal muscle function. Enzyme replacement therapy should be initiated as soon as possible preferably <6 months of age in a dose of 20mg/kg given every 2 week along with rehabilitation.

REFERENCES