Original Article

Pompe's Disease in Childhood: A Metabolic Myopathy

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Abstract

Background: Myopathy of metabolic origin in childhood occurs due to a variety of conditions. Pompe's Disease also known as Glycogen storage disease Type II, is a rare storage disorder with clinical presentation akin to spinal muscular atrophy.
Methods: A series of patients with suspected metabolic myopathy were reviewed at a tertiary care service hospital over a period of three years. The diagnosis was confirmed by estimation of acid alpha glucosidase activity.
Result: At our centre, these cases presented with generalized hypotonia, organomegaly (hepatomegaly, cardiomegaly) and congestive cardiac failure. Infantile onset, the most severe form of Pompe's disease, was the commonest form accounting for 75% of the cases. Four of the babies with infantile onset Pompe's disease expired, three due to refractory heart failure and one to fulminant respiratory infection before 15 months of age.
Conclusion: Pompe's Disease is now being increasingly diagnosed, due to definitive enzyme estimation facilities. With the recent availability of enzyme replacement therapy with Myozyme, the prognosis is likely to change for the better.

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Key Words : Metabolic myopathy; Pompe's disease; Hypotonia; Cardiomegaly; Hepatomegaly; Acid alpha-glucosidase

Introduction

Metabolic myopathy in childhood is an uncommon entity. Glycogen-storage disease type II (GSDII), also referred to as Pompe's Disease, is a rare storage disorder presenting as metabolic myopathy with multiorgan dysfunction. In our set up it was the commonest metabolic myopathy encountered. It has an incidence of 1/40000 live births with no ethnic predilection [1]. Timely diagnosis is essential for genetic counseling, antenatal diagnosis and definitive treatment with enzyme replacement therapy. We report our experience of encountering metabolic myopathies over three years and discuss babies who presented with generalized hypotonia and congestive cardiac failure in early infancy and were confirmed to be suffering from Pompe's disease by definitive enzyme estimation.

Material and Methods

Over a period of three years, all children admitted in a tertiary care service hospital, who had features suggestive of a metabolic myopathy, were enrolled in the study. In all the cases a detailed history was taken regarding adverse perinatal events, consanguinity, developmental delay and nature of symptomatology. Family history of early deaths was recorded. Detailed general and systemic examination was carried out and abnormalities noted. Multisystemic abnormalities viz cardiomegaly ± congestive heart failure (CHF), hypotonia, seizures, hepatomegaly and other organomegaly gave a clue to a possible metabolic myopathy which was then more specifically investigated. Investigations included routine blood counts, liver and renal function tests, blood sugar, serum calcium/phosphates, creatinine phosphokinase (CPK), serum electrolytes and arterial blood gas levels. Radiograph of chest, electrocardiogram (ECG) and 2 Dimensional echocardiography (2-D ECHO) was carried out in all cases with cardiomegaly/CHF. Ultrasonography (USG) of abdomen was carried out to delineate organomegaly. Electromyogram (EMG) and nerve conduction studies (NCV) were conducted when indicated. Specific enzyme assays were carried out for suspected metabolic myopathy. In case of Pompe's disease, alpha glucosidase levels were estimated. The patients were provided decongestive therapy in case of CHF. As enzyme replacement therapy is as yet unavailable in our country, only supportive management was provided. These babies were on regular follow up care wherein frequent respiratory infections were treated, decongestive therapy regulated and vitamin supplements provided.

Results

Over a period of three years, we encountered 25 cases diagnosed to be metabolic myopathies. These included Wilson's disease, mitochondrial myopathies, Barter's syndrome and Pompe's disease. The distribution of the cases of metabolic myopathies seen according to the age and frequency of presentation is shown in Fig.1. Pompe's disease was the commonest of the metabolic myopathies encountered accounting for 32% of the cases. Of these children who were diagnosed to have Pompe's disease, six were of the infantile

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variety and only two of the milder juvenile onset category who presented at two and nine years of age respectively. The clinical profile of these cases is as shown in Table 1.

Of the infantile onset Pompe's disease, two presented antenatally with cardiomegaly and reduced foetal movements detected on routine USG, who developed CHF soon after birth. Four children presented in late infancy with hypotonia, CHF, cardiomegaly and frequent respiratory infections and one child presented at two years of age with hypotonia and motor delay of six months duration. In addition, one girl with manifest features of juvenile onset disease presented with reduced mobility and hypotonia since 8 years of age. In our series of Pompe's disease, there were two girls and six boys. History of consanguinity was present in all but two of juvenile Pompe's disease. In two of the babies who presented at birth, antenatal USG in final trimester revealed cardiomegaly and decreased foetal movements. Motor delay was evident in all except in one juvenile onset case. Generalized hypotonia was a universal feature and the babies exhibited the pathognomonic frog like position (Fig. 2). Organomegaly was the hallmark of all our cases of infantile onset Pompe's disease. Hepatomegaly was a marked and universal feature in all the infantile onset cases though LFT was normal in all them. Cardiomegaly was a prominent feature in all of the babies with infantile onset disease (Fig. 3). It was associated with CHF. ECG pathognomically revealed short PR interval, tall biphasic QRS complexes and deep T wave inversions in precordial leads (Fig. 4). 2D Echo revealed non obstructive hypertrophic cardiomyopathy in all of the cases of infantile Pompe's disease. Of the clinical presentation, features observed in order of increasing frequency were hepatomegaly (71%), cardiomegaly (71%), hypertrophic cardiomyopathy (71%), CHF (71%), motor delay (85%) and hypotonia (100%).

Definitive diagnosis of Pompe's disease was based on estimation of the effected enzyme viz acid alpha glucosidase activity. It ranged from 4 to 16 nmol/hr/mg which was grossly deficient as opposed to a normal level of > 60 nmol/hr/mg. It was further observed that the deficiency was more profound in the babies who manifested the disease early with the levels rising with the age of presentation.

In our series, four out of the six cases of infantile onset Pompe's Disease babies expired. The cause of death was pulmonary haemorrhage related to CHF in the neonate. Of the remaining three cases, refractory heart failure in two cases and fulminant respiratory infection in one lead to death. Death occurred between 15 to 18 months of age in these babies. The remainder are on regular follow up.

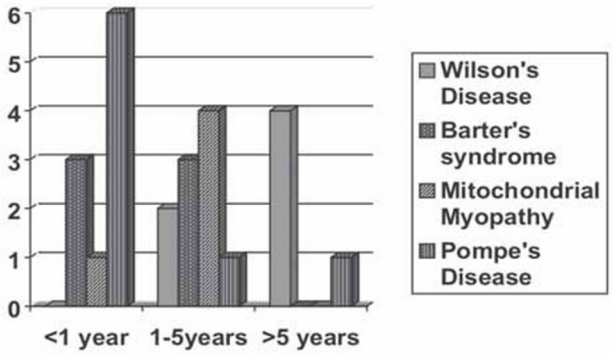

Fig. 1 : Etiological distribution of metabolic myopathies vs age of presentation

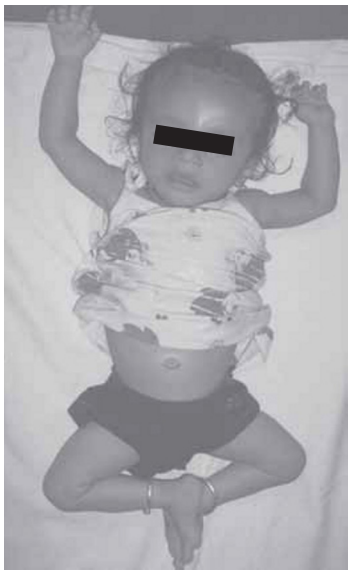

Fig. 2 : Infant of Pompe's disease with generalized hypotonia

Table 1

Clinical vs Investigative profile of Pompe's disease cases

S. No.	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case7	Case 8
Age at presentation	7 months	2 years	8 months	At birth	At birth	8 months	9 months	9 years
Symptomatic since	Birth	6 months	Birth	Birth	Birth	15 days	7 months	1 year
Sex	Male	Male	Male	Male	Male	Female	Male	Female
Consanguinity	Present	Absent	Present	Present	Present	Present	Present	Absent
Reduced fetal movements	Absent	Absent	Absent	Present	Present	Absent	Absent	Absent
Motor delay	Present	Present	Present	NA	NA	Present	Present	Absent
Generalised hypotonia	Present	Present	Present	Absent	Absent	Present	Present	Present
Hepatomegaly	Present	Absent	Present	Present	Present	Present	Present	Absent
Cardiomegaly	Present	Absent	Present	Present	Present	Present	present	Absent
Congestive heart failure	Present	Absent	Present	Present	Present	Present	Present	Absent
ECG	Giant QRS	Normal	Giant QRS	Normal	Normal	Giant QRS	Giant QRS	Normal
Echocardiography	HCM	Normal	HCM	HCM	HCM	HCM	HCM	Normal
Enzyme level nmol/hr/mgm	11	13	9	4	6	9	12	16