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A CASE OF INFANTILE POMPE DISEASE: A CASE REPORT AND REVIEW OF INDIAN LITERATURE.

Pediatric Medicine

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ABSTRACT

Background: Pompe disease is a metabolic disorder due to deficiency of lysosomal acid alpha-glucosidase enzyme. Deficiency of this enzyme leads to lysosomal glycogen accumulation in multiple tissues and cell types, predominantly affecting cardiac, skeletal, and smooth muscle cells, eventually causing progressive muscle destruction. The pattern of inheritance is autosomal recessive. **Clinical Description:** Our case describes a four-month-old female child, first born baby to a non-consanguineous marriage, who presented to our out-patient department with respiratory tract infection, and difficulty in swallowing for last 10 days. Clinical examination revealed hypotonia along with hepatosplenomegaly. **Management:** There was cardiomegaly evident on routine chest X ray. This significant finding was further dwelled upon and an ECG with echocardiography was planned. ECG showed short PR interval with tall QRS complex, and Echocardiography revealed a hypertrophic cardiomyopathy. Based on the above findings, the importance of ruling out possible storage disorders was considered eminent. Further tests revealed elevated CPK and LDH. Based on the clinical findings and laboratory results, the differentials of storage disorders were narrowed to Pompe disease. Dried blood spots for quantitative enzyme assay of acid alpha glucosidase (GAA) activity were tested. The result confirmed that the GAA activity was lower than the normal range, leading to a diagnosis of Pompe disease. **Conclusion:** Infantile pompe disease is fatal without specific enzyme replacement therapy. The subtle clinical features or routine findings heralding this ominous disease need to be dealt with a high index of suspicion for the same, the advantage being early diagnosis and initiation of enzyme replacement therapy.

KEYWORDS

infantile pompe disease, acid alpha-glucosidase, cardiomegaly, hypertrophic cardiomyopathy.

CASE REPORT:

A four-month-old female child presented with cough for last 10 days associated with respiratory distress for last 2 days. Antenatal history was not significant. Baby was born to a 31-year-old primigravida mother out of a non-consanguineous marriage. The mother was a booked case and had 5 antenatal visits. Antenatal ultrasound scan done in each trimester was found to be normal. Baby was born at term gestation by normal vaginal delivery and cried immediately after birth. Birth weight was 2900 grams. Regular immunizations were given as per schedule. Breastfeeding was initiated within 1 hour of birth, but the child was not able to suck properly since birth. History of feeding diaphoresis was present since birth. History and examination did not reveal any cyanosis, acidosis, or hypoglycemia. No dysmorphic features were identified. Developmental history revealed that social smile was attained, but head control was not achieved. Baby was not interested in surroundings. Anthropometry showed Weight: 4.1kg (below third percentile on WHO chart), length: 60cms, Head circumference: 40cms (appropriate for age), Chest circumference: 37cms.

On admission, the baby was tachypneic with signs of respiratory distress. (Respiratory rate: 66/minute, heart rate: 136/minute, chest indrawing present). Bilateral crepitations were present on chest auscultation. CVS examination revealed normal first and second heart sound with no murmur. Abdomen was distended. Liver was palpated 6 cms below right costal margin in midclavicular line, and it was firm in consistency with sharp border. Spleen was palpated 3 cms along the spinoumbilical margin, and it was firm. Initially the child was treated conservatively as a case of lower respiratory tract infection. On routine chest X ray, child was found to have huge cardiomegaly (Figure 1). On ultrasound examination of whole abdomen, hepatosplenomegaly was found. There were no signs of congestive heart failure. Upon careful examination, it was found that baby was hypotonic with floppy baby appearance.

Investigations:

Laboratory tests showed elevated levels of hepatic enzymes (serum aspartate transaminase and alanine transaminase were 104 U/L and 110 U/L respectively). Other routine blood investigations including complete blood count, liver function test and renal function test were normal. Elevated levels of serum lactate dehydrogenase (1272 U/L) and creatine kinase (359 U/L) were found. Electrocardiography revealed a short PR interval (0.1 second) with tall QRS complex in all leads (Figure 2). Echocardiography showed concentric LV hypertrophy, trivial TR with no significant LV outflow tract obstruction and good biventricular function (Figure 3). At this stage, storage disorder probably infantile pompe disease was considered. Dried blood spot for acid alpha-glucosidase was sent and the result confirmed that the GAA activity was only 18 nmol/hr/mg (normal reference range, > 60 nmol/hr/mg) which was clearly lower than the normal range, leading to a diagnosis of Pompe disease (1). Whole genome exome sequencing was planned, but parents didn't want to continue further evaluation owing to its poor prognosis.

Management And Outcome:

More often than not even with enzyme replacement therapy, Infantile Pompe disease is a death sentence due to its late presentation. We were unable to provide enzyme replacement therapy in our setup. Child was provided conservative management for recurrent respiratory tract infections.

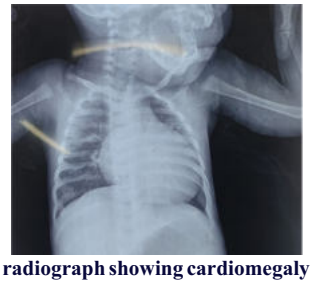

Figure 1: Chest radiograph showing cardiomegaly

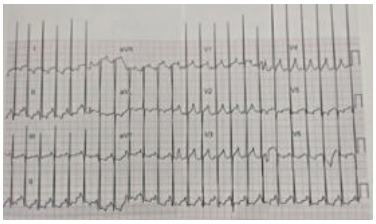

Figure 2: ECG showing short PR interval and LV hypertrophy

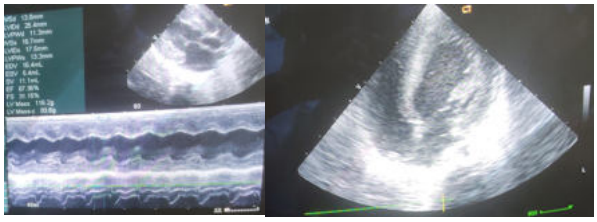

Figure 3: Echocardiography images.

(A) M mode image showing left ventricular hypertrophy.
(B) Parasternal long axis view showing eccentric LV hypertrophy.

DISCUSSION:

Pompe disease or glycogen storage disease type II is a lysosomal storage disorder in which deficiency of acid alpha-glucosidase enzyme leads to accumulation of glycogen in tissue and finally to destruction of muscles. Incidence of pompe disease is 1 in 40000 live birth globally(2). Incidence in India is unclear(3). Clinically it can present at various ages with variable symptoms. Classically, it is characterized by hypertrophic cardiomyopathy, hepatomegaly, macroglossia and skeletal myopathy manifesting as hypotonia and feeding difficulty, and death in first year of life due to cardiopulmonary failure(2). Echocardiography typically reveals a hypertrophic cardiomyopathy with or without left ventricular outflow tract obstructions in early stages of the disease. In the later stages, patients may have cardiac dysfunction and a dilated cardiomyopathy. Enzyme replacement therapy (ERT) with alglucosidase alpha is presently approved as treatment. (2).

Our case is of a four-month-old child who presented with recurrent respiratory tract infection but was subsequently found to have cardiac hypertrophy on routine chest X ray. The reason for reporting this case is to highlight the fact that in patients with unexplained cardiomegaly on chest X ray and hypertrophic cardiomyopathy on echocardiography along with recurrent respiratory tract infections in absence of congenital heart disease in early infancy, storage disorders likely pompe disease should be ruled out with a high index of suspicion. This can diagnose pompe disease before onset of frank symptoms. Pompe disease is fatal if not diagnosed early and initiation of enzyme replacement therapy in appropriate time is vital.

After thorough literature review (Google Scholar and PubMed), very few data were found on pompe disease in the form of case reports or case series in India. Table 1 gives a comparative analysis of various case reports on pompe disease in the view of rarity of this disease and the important key findings.

Table 1: Indian data on pompe disease

Study done	*Type of study*	*Key findings*
Phadke AK, et al. A rare case of infantile onset pompe disease with genetic diagnosis (4) 2020	Case report.	This case was reported in the view of its rarity.
Kumbar V, et al. Anaesthetic management of a patient with pompe disease for kyphoscoliosis correction (5) 2016	Case report.	Corrective surgery was done successfully in juvenile pompe disease patient.
Lingappa L, et al. Pompe disease. Experience from south India (6) 2013	Case report. A total of 6 patients.	Two patients among them were first to receive ERT in India. All this patient had similar presentation as our reported case.
Jegadeeswari A, et al. Two cases of Pompe's disease: case report and review of literature (3) 2012	Case report and review of literature. 2 cases.	Two cases presented with Concentric left ventricular hypertrophy similar to our case.

Enzyme replacement therapy with recombinant alglucosidase alfa is recently approved treatment modality which may alter the natural history of illness if initiated at appropriate time. In a study done by Lokesh et al there were six cases of infantile pompe disease (manifested as severe hypotonia, motor developmental delay, and respiratory distress) among which two of them were able to receive ERT through INCAP programme. But due to delay in diagnosis and initiation of treatment, ERT was not effective (6). Antenatal diagnosis of pompe disease by fetal echocardiography is an upcoming option. Early detection, confirmation of diagnosis and initiation of ERT at appropriate time has significant impact (7).

CONCLUSION:

Pompe disease is a fatal inherited disorder. Enzyme replacement therapy is helpful only if implemented early. Recurrent history of respiratory illness in an infant with failure to thrive in the presence of hypotonia, developmental delay, hypertrophic cardiomyopathy and visceromegaly warrants workup for Infantile pompe disease, at the earliest hint of suspicion and might just help in altering or slowing the course of this disease. Also, this will enable a timely genetic counselling, that can effectively anticipate the risks to future children.

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Declaration Of Consent: Proper informed consent has been taken from the legal guardians of the patient regarding the publication of the information.

Conflict Of Interests: None.

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