Infantile Pompe's disease presenting with pulmonary infections during the newborn period

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Pompe's disease (glycogen storage disease type II) is one of over 40 lysosomal storage disorders. It is characterized by a deficiency in the enzyme α-1, 4-glucosidase (acid maltase, GAA), resulting in the lysosomal accumulation of glycogen in various organs such as cardiac and skeletal muscles, liver and brain. Pompe's disease is an autosomal recessive disorder with an incidence of 1/50,000 live births with no ethnic predilection. The gene for acid maltase is on chromosome 17q23. There are 3 variants of Pompe's disease: infantile, juvenile and adult-onset. These different expressions of the disease are probably due to severity and multiplicity of genetic mutations and level of residual enzyme activity. A splice mutation (IVS1-13T→G), commonly seen in adult-onset patients, may be helpful in delineating the phenotypes. The most severe type, namely the infantile type, with prominent cardiomegaly, hypotonia, and death prior to 2 years of age. Infants appear normal at birth but soon experience generalized muscle weakness with "floppy baby appearance," feeding difficulties, macroglossia, hepatomegaly, and heart failure due to a progressively hypertrophic cardiomyopathy. Electrocardiographic findings include a high-voltage QRS complex and a shortened P-R interval. Death usually results from cardiorespiratory failure or aspiration pneumonia.[1] Although there is currently no curative therapy for Pompe's disease, the ongoing studies and clinical trials on recombinant enzyme replacement therapy (ERT) and on gene therapy show successful results.[2,3]

A 4.5-month-old girl baby was admitted due to persistent respiratory difficulties. In history, the respiratory symptoms began with tachypnea at 2 weeks-age and she was hospitalized for 20 days. Chest x-ray showed pulmonary right lower lobe infiltration and the size of heart was defined as normal (**Figure 1a**). She was hospitalized for the second time with pneumonia at 2.5-month-age. She was from the third pregnancy of parents who are second-degree relatives. The first baby had died of hydrocephalus. The second pregnancy was terminated because the fetus developed a hydrocephalus. On her third admission at 4.5 months of age; the weight was 4900 g (5th percentile), the length was 62 cm (25th percentile), and the head circumference was 40 cm (25th percentile). Her heart rate was 132 beats/minute. Her respiratory rate was 60 per minute and with mild retractions and respiratory difficulties. She had poor head control, weakness and hypotonicity. On her chest auscultation rales was heard bilaterally. The heart was rhythmic and no murmur could be heard. The liver was palpated 5 cm below the costal margin. The laboratory findings were as follows; normal complete blood count, serum glucose, electrolytes, blood urea nitrogen, creatinine, serum and urine amino acids, lactate, pyruvate and ammonia. The following serum enzymes were elevated aspartate transferase (AST) was 260 U/L, alanine transferase (ALT) was 183 U/L, alkaline phosphatase was 447 U/L, Lactate dehydrogenase (LDH) was 915 U/L and creatinine phosphokinase (CK) was 611 U/L. Chest radiography revealed cardiomegaly (**Figure 1b**). Electrocardiography showed a regular sinusoidal rhythm with a short P-R interval of 7 milliseconds, large QRS complexes of >5 milliseconds and remarkable biventricular hypertrophy. Echocardiography findings were consistent with hypertrophic cardiomyopathy. Leukocyte lysosomal enzyme assay yielded a α-1, 4-glucosidase (acid maltase) level of 0.44 nmol/minute per milligram protein (normal range 1.2-4.4 nmol/minute per milligram protein). She was put on supportive managements, such as antibiotics, beta-blocker, salbutamol, parenteral nutrition, and mechanic ventilations. Unfortunately, she was lost at sixth month of age.

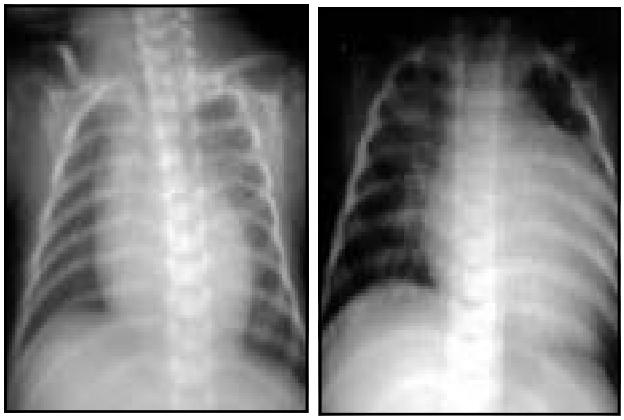

Figure 1 - Chest radiograms showing **a)** normal cardiac size at 22nd day and **b)** showing cardiomegaly in 5th month.

The presentation of Pompe's disease with pulmonary infections alone is unusual. Babies with Pompe's disease usually appear normal at birth. But, soon experience generalized muscle weakness, feeding difficulties, macroglossia, hepatomegaly, and heart failure due to a progressively hypertrophic

cardiomyopathy.[1] There were no symptoms or findings to consider Pompe's disease as the diagnosis during the newborn period in this case. Hypotonia, hepatomegaly and cardiomegaly were determined at 4.5 months of age (**Figure 1b**). After these findings were established, a storage disease (particularly, Pompe's disease, because of the cardiac involvement) was considered. Aside from the increased muscle enzymes (ALT, AST, LDH and CK), typical ECG and echocardiographic findings, the definitive diagnosis were made with decreased level of leukocyte acid-maltase activity. Leukocyte acid maltase activity was minimal but no zero; however, she had received multiple transfusions prior to blood sampling for enzyme activity.

In a review of the literature, we could not find any Pompe's disease case presenting with pulmonary infection during the neonatal period without findings due to other organ involvement. We found a few cases report of the disease manifesting in the newborn period with cardiac involvement.[4,5]

There was no cardiomegaly in our case first month of age (**Figure 1a**), but a few months later it was manifested (**Figure 1b**). Although the babies with Pompe appear normal during newborn period, the function of muscles may be deficient. This deficiency may have led to the expansion of the chest insufficiently with a resultant tendency to pulmonary infection. Pompe's disease can present with variable manifestations. Very early atypical manifestations as in our case may delay the diagnosis and specific management.

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