Congenital dilated cardiomyopathy – A rare genetic condition in infants

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ABSTRACT

A male newborn admitted in the Neonatal Intensive Care Unit due to dyspnea and cyanosis. The baby was intubated due to tachypnea. No murmurs were heard on auscultation. The ultrasound of the fetal heart before birth showed cardiac malformations. Chest X-ray showed: increased pulmonary vascular markings and cardiomegaly. The abdominal X-ray showed normal liver, spleen and intestine. Electrocardiogram showed Sinus rhythm and tachycardia.

On the first day after birth, two-dimensional echocardiography demonstrated marked hypertrophy of both ventricles (the posterior wall of the left ventricle was 33mm thick).

The baby was started on treatment with low flow oxygen support, digoxin and captoril to enhance myocardial contractility, creatine phosphate for myocardial nutrition, furosemide diuretic to reduce load, enhance feeding, monitor bilirubin, prevent neonatal jaundice, and close attention was paid to the disease changes. The baby was stable and was discharged from the hospital. After 20 days of discharge, the baby was admitted again with complains of shortness of breath and cyanosis after 20 days of discharge. The heart beat was low on auscultation with alternating tachycardia and bradycardia, with an occasional gallop rhythm. The baby was kept on ventilator assisted ventilation with the required parameters and necessary investigations were performed.

On repeating the two-dimensional echocardiography, the left ventricular posterior wall and the ventricular septum was increased compared to the previous echocardiography. A mutation on Chromosome 18, c.1921G>A was detected on gene mutational analysis. Recently, some genetic studies have shown that mutations in chromosomes 1, 11, 14 and 15, and mutations in sarcomere proteins genes are autosomal dominant.

**Keywords:** rare; dilated cardiomyopathy; chromosome 18 mutation

1. Introduction

Hypertrophic cardiomyopathy (HCMP) is a rare heart disease having a variety of causes like genetic syndromes such as Noonan syndrome and Costello syndrome, Metabolic diseases like adenosine triphosphate synthase and long-chain-3-hydroxyaxyl-CoA dehydrogenase deficiencies, family history, use of steroids, maternal diabetes mellitus, etc[1]. A study which was performed concluded that primary HCMP cases are very rare[2]. Ahead we describe a neonate with congenital HCMP without any other congenital anomalies, who presented with severe cyanosis and shortness of breath, the subsequent investigations, diagnosis and treatment.

2. Case

A 3400g male newborn was delivered by caesarean section at 38 weeks of gestation as the second child of a healthy, non consanguineous parents. His mother (gravida3 Para 2) was 27 years old and his father was 26 years old at the time of delivery. The mother was healthy and has no family history of cardiovascular or genetic disease, but her first pregnancy by terminated by drug induced abortion due to abnormal embryonic development of the fetus. Indication of
caesarean section was scarred uterus. In addition, the fetal heart ultrasound before birth showed cardiac malformations. After birth, the baby was transferred to our neonatal intensive care unit because of cyanosis and dyspnea. The Apgar scores at 1 and 5 minutes of birth were 8 and 9, respectively. The vital signs initially were body temperature 36.7 degrees Celsius, Blood Pressure 64/49mmHg, Pulse 144/min, Respiratory Rate 45/min. The baby was placed on nasal catheter oxygen inhalation because of tachypnea and cyanosis.

In the physical examination, head circumference was 34cm (less than 50th percentile) and the body length was 50cm (less than 90th percentile). The baby had no dysmorphic features. Chest and Abdomen showed no abnormal findings. The heart beat was regular with tachycardia, no murmur was heard on auscultation. Respiratory findings were normal, except for the tachypnea. There was no organomegaly and neurological examination was normal. Laboratory examination showed increased levels of transaminase, lactate dehydrogenase, creatine kinase, creatine kinase MB isoenzyme, alpha-hydroxy butyric acid dehydrogenase, thyroid function tests, normal hematological parameters. Blood culture showed no detection of bacteria. The serum Immunoglobulin M levels of Toxoplasma, Rubella, Cytomegalovirus and Herpes simplex virus were negative. An inborn error of metabolism screening test was done and the result was normal. Chest X-ray showed: increased pulmonary vascular markings and cardiomegaly. The abdominal X-ray showed normal liver, spleen and intestine. Electrocardiogram showed Sinus rhythm and tachycardia.

On the first day after birth, two-dimensional echocardiography demonstrated marked hypertrophy of both ventricles (the posterior wall of the left ventricle was 33mm thick).

The baby was started on treatment with low flow oxygen support, digoxin and captoril to enhance myocardial contractility, creatine phosphate for myocardial nutrition, furosemide diuretic to reduced load, enhance feeding, monitor bilirubin, prevent neonatal jaundice, and close attention was paid to the disease changes. With the stable condition of the baby and no surgical intervention indications, it was decided for the baby to be discharged from the hospital with special advise to prevent catching cold, avoid strenuous activities, report to the hospital immediately in case of any symptoms and regular follow up.

The baby was discharged but was admitted again with complains of shortness of breath and cyanosis after 20 days of discharge. The heart beat was low on auscultation with alternating tachycardia and bradycardia, with an occasional gallop rhythm. The baby was kept on ventilator assisted ventilation with the required parameters and following investigations resulted: normal hematological parameters, elevated liver enzymes and bilirubin, decreased level of albumin and globulin, elevated levels of serum potassium, magnesium and phosphorus with decreased levels of sodium and chloride, elevated CK-MB and procalcitonin.

On repeating the two-dimensional echocardiography, the left ventricular posterior wall and the ventricular septum was increased compared to the previous echocardiography, showing the thickness of the posterior wall of the left ventricle being 33mm.

3. Gene mutation report

Mutations on Chromosome 18, c.1921G>A, Chromosome 4 c.7117A>G, Chromosome 3 c.283G>A, Chromosome 2 c.16214T>C were detected on gene mutational analysis (Figure 1). This was performed by the company, MyGenostics.
**Figure 1:** The red arrow showing the site of gene mutation

<table>
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<tr>
<th>DSG2</th>
<th>chr18:29121197</th>
<th>c.1921G&gt;A</th>
<th>p.A641T</th>
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**Figure 2:** The red arrow showing the site of gene mutation

<table>
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<tr>
<th>ANK2</th>
<th>chr4:114276891</th>
<th>c.7117A&gt;G</th>
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4. Treatment and prognosis

During the first time admission, the baby was on low flow oxygen inhalation, Tablet Digoxin to improve the myocardial contractility, Sodium phosphocreatine for nourishment of the myocardium and Tablet Spironolactone.

During the second admission, the baby was kept on nasal oxygen inhalation, maintenance of body temperature and regular monitoring of the vitals.

The parents refused to go ahead with further investigations and treatment, and the child died at night.
5. Discussion

Hypertrophic cardiomyopathy in children can be primary or secondary. Primary cause may be due to a mutation in one of the genes[3], whereas, secondary HCMP may be as a sequelae of obstruction congenital heart disease or any inborn error of metabolism like mucopolysaccharidosis or glycogen storage disease[4]. Additionally, some HCMO cases have been reported to be occurring in association with other congenital heart diseases like ventricular septal defect and Tetralogy of Fallot[3]. As already mentioned, congenital HCMP can occur in a newborn due to mutation of protein metabolism, chromosomal abnormalities, exposure to steroids, or maternal diabetes mellitus. A study has been reported[3], in which, from among a total of 14 patients with HCMP, seven of the cases were diagnosed to be due to a genetic cause like Noonan Syndrome, Costello Syndrome, etc.; 2 cases due to a metabolic disease in the form of ATP synthase deficiency, 1 case with myopathy, and the remaining 4 cases with unexplained cause. After a 1 year follow up, it was reported that 4 of the cases died during the period.

Only a few cases if congenital dilated cardiomyopathy have been reported in the available literature[6].

In our case, the baby had no family history of HCMP, his mother was not a diabetic., his karyotype was normal. And he had no history of exposure to corticosteroids or showed any errors in the metabolism. He did not have any other congenital heart disease that could result in HCMP. Recently, some genetic studies have shown that mutations in chromosomes 1, 11, 14 and 15, and mutations in sarcomere proteins genes are autosomal dominant[4,5]. HCMP is one of the more common heritable cardiac diseases, and thus, further genetic studies of congenital HCMP are warranted.

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References