Cardiac Hypertrophy in an Infant of a Diabetic Mother: A Case of Reversible Cardiomyopathy

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ABSTRACT
Diabetes Mellitus (DM) is a chronic metabolic disorder characterised by insulin deficiency or resistance and/or β-cell defects. High Body Mass Index (BMI) at conception, undiagnosed pregestational diabetes, and poor glycaemic control significantly affect the foetal heart, foetoplacental circulation and foetal growth. Myocardial hypertrophy and cardiac defects are more prevalent in Infants of Diabetic Mothers (IDMs). Cardiac Hypertrophy (CH) is characterised by a significant thickening of the interventricular septum, reduction in the size of the ventricular cavity, systolic and diastolic dysfunction and subaortic stenosis. A term neonate born to a mother with pregestational insulin-dependent Type I Diabetes Mellitus (T1DM) developed respiratory distress soon after birth, and Echocardiography (ECHO) showed Asymmetric Septal Hypertrophy (ASH) and Left Ventricular Outflow Tract (LVOT) obstruction. The baby responded well to oral propranolol, which was continued for four weeks, resulting in the resolution of CH at four months of age on follow-up. The present case underscores the importance of ECHO, even in infants born to mothers with good glycaemic control.

CASE REPORT
A term male neonate was born to a 29-year-old G2P1L1 mother by elective caesarean section (indication: previous caesarean birth) at 38+3 weeks of gestation. The baby cried immediately with Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores of 8 and 9 at one and five minutes, respectively and weighed 3.89 kg (>95th percentile). The mother had insulin-dependent T1DM for the past nine years and had good glycaemic control, and her Glycated Haemoglobin (HbA1c) was 5.9% in the third trimester. Foetal ECHO done at 24 weeks of gestation was normal. The patient had no history of fever, urinary tract infection, or rupture of membranes prior to delivery. The baby had respiratory distress soon after birth and was shifted to the Neonatal Intensive Care Unit (NICU). On examination, the baby was plethoric with features of macrosomia (hairy pinna, thick skin folds, and broad shoulders). Sepsis screen and blood culture were sent, and antibiotics (piperacillin and amikacin) were started. Chest X-ray showed streaky opacities and cardiomegaly (cardiothoracic ratio of 0.70) [Table/Fig-1]. The baby required Fraction of Inspired Oxygen (FiO₂) of 0.35 to maintain saturation of 91%-95%. Laboratory investigations showed haemoglobin of 16.5 gm/dL, White Blood Cell (WBC): 9,200/cumm, platelets: 1.9 lakhs/cumm, and high C-reactive Protein (CRP) (13 mg/L). Cardiovascular examination revealed a grade III murmur in the lower parasternal area. ECHO at 26 hours of life showed asymmetrical septal hypertrophy, Interventricular septal thickness end diastole: 1.1 cm (z-score=5.1; range 0.26-0.53), Posterior wall thickness end diastole (LVPWd) thickness 0.5 cm (z-score=2.8; range 0.21-0.4), aortic flow 1.0 m/sec, pulmonary flow 1.0 m/sec, moderate LVOT obstruction with a gradient of 40 mmHg, systolic anterior motion of the mitral valve, Mitral E 0.7m/sec, Mitral A 0.8m/sec, and a tiny closing ductus arteriosus [Table/Fig-2]. ECHO showed normal diastolic function (E/A 0.87, e’ 0.087, E/e’=8.04).

The infant was started on oral propranolol (1 mg/kg/dose every 8 hourly) with monitoring of blood sugar, heart rate, and blood pressure. The baby responded well to oral propranolol, which was continued for four weeks, resulting in the resolution of CH at four months of age on follow-up. The present case underscores the importance of ECHO, even in infants born to mothers with good glycaemic control.

Keywords: Cardiomegaly, Diabetes, Hyperinsulinaemia, Macrosomia, Propranolol

[Table/Fig-1]: Chest radiograph showed streaky opacities suggestive of wet lungs and cardiomegaly (CT ratio 0.70).

[Table/Fig-2]: ECHO at 26 hours of life showed Asymmetric Septal Hypertrophy (ASH), Interventricular Septal Distance (IVSd): 1.1 cm, Left Ventricle Posterior Wall Dimension (LVPWd): 0.5 cm; IVSd/LVPWd=2.2 and markedly diminished left ventricular cavity.
pressure. Respiratory distress decreased, and the baby was in room air within 48 hours of starting propranolol. Repeat sepsis screen was negative, and antibiotics were stopped at 72 hours. The baby was discharged on day six of life on oral propranolol. Follow-up ECHO at four weeks of life showed IVSd 0.7 cm (z-score=2.9), LVPW thickness 0.4 cm (z-score=1.6), resolution of LVOT obstruction, and propranolol was discontinued [Table/Fig-3]. Follow-up ECHO at eight weeks of life showed IVSd 0.5 cm (z-score=1.4). The baby had normal growth and development at four months of age with complete resolution of CH on ECHO [Table/Fig-4].

DISCUSSION

Despite advances in perinatal care, babies born to mothers with diabetes have high morbidity and mortality [1]. Maternal hyperglycaemia causes foetal hyperglycaemia, hyperinsulinæmia, macrosomia and CH. Babies born to mothers with T1DM are at a high risk of developing HCM, followed by Type 2 Diabetes Mellitus (T2DM) and gestational diabetes [2]. In infants of IDM, HCM occurs in 50% of infants born to T1DM and 25% of T2DM [3]. HCM and congenital hypertrophy are different disorders with varied aetiology. In HCM, the heart muscle is thickened with disruption of myocardial structure, unrelated to hypertension, valvular, or systemic disease [4]. CH seen in IDM, Congenital Hyperinsulinism (CHI), leprechaunism, and congenital generalised lipodystrophy is secondary to hyperinsulinæmia [5]. CH is reported in 40% of infants with CHI, 61% of infants with leprechaunism, and in 48% to 61% of patients with congenital generalised lipodystrophy [5]. On ECHO, CH is defined as a diastolic septal or left ventricular wall thickness of ≥2 Standard Deviations (SD) above the mean (z-score ≥1.96, corrected for age, gender, and body size), and ASH is defined as an interventricular septum thickness of ≥6 mm and an IVSd/LVPW ratio of ≥1.3 [6].

The CH is symptomatic in 5%-12.1% of IDM, while 40% have asymptomatic CH on ECHO [7]. HbA1c correlates poorly with CH, because even transient spikes in glucose can cause cardiac overgrowth. CH involves both ventricles, but septal hypertrophy is more evident due to a greater number of insulin receptors in that area [5]. During embryogenesis, hyperglycaemia is teratogenic and can cause structural defects. In late gestation, foetal hyperinsulinæmia increases protein and fat synthesis, glycogen deposition, and leads to hyperplasia and hypertrophy of cardiomyocytes [8]. IDM babies should undergo an ECHO, within the first 48 hours of life to assess cardiac function and identify structural malformations. ECHO parameters such as myocardial thickness, shortening fraction, myocardial performance index (Tei index), and mitral and tricuspid valve ratio of the early (E) to late (A) diastolic filling are used to assess cardiac function [9]. Thickening of the Interventricular Septum (IVS) and ventricular walls can cause systolic and diastolic dysfunction. Increased left ventricular mass can lead to dynamic LVOT obstruction, by causing the anterior mitral leaflet to appose the IVS. Typically, affected infants recover within two to three weeks, and CH resolves in 6-12 months, as insulin levels normalise. Ujuani et al., reported a case of CH with LVOT in a term infant, where the LVOT resolved in two to three weeks, similar to the index case [10]. Monda E et al., studied 60 IDMs and reported that, CH resolved in one year in 52%, two years in 72%, three years in 79%, and in 100% of cases by six years of age [11]. When CH does not improve or worsens, further evaluation is needed to rule out metabolic disorders like Pompe disease and genetic disorders like Noonan syndrome. ECHO helps differentiate hyperinsulinæmia, which causes ASH or LVOT obstruction, from concentric hypertrophy seen in metabolic and neuromuscular disorders [12].

Management of LVOT obstruction includes maintaining adequate intravascular volume and β-adrenergic blockade. β-blockers like propranolol decrease heart rate, reduce myocardial oxygen demand, improve coronary perfusion, and decrease LVOT obstruction [13]. The index case had an IVSd of 1.1 cm (z-score=5.1) and moderate LVOT obstruction with a gradient of 40 mmHg, which was treated with propranolol. Dasgupta S et al., reported a term IDM with IVSs of 1.2 cm (z-score=4.5) and LVOT obstruction with a gradient of 25 mmHg, treated with propranolol and milrinone [14]. Milrinone, due to its inotropic and lusitropic effects, is used as an adjunct to propranolol with good outcomes [14]. Inotropes like dopamine and dobutamine are contraindicated, as they can increase dynamic LVOT obstruction [15]. Despite good maternal glycaemic control, this baby developed CH, probably due to transient spikes of hyperglycaemia and the effects of insulin on the placenta.

CONCLUSION(S)

The CH in IDM is reversible, but requires monitoring and follow-up. Babies born to mothers with pregestational diabetes and poorly controlled diabetes are at a high risk of CH. A β-blocker like propranolol is recommended for symptomatic neonates. If CH does not resolve or worsens, further evaluation is necessary to rule out metabolic and genetic disorders. With the increasing prevalence of diabetes worldwide, healthcare personnel needs to be more vigilant in detecting and managing DM during pregnancy. Nutritional adaptations in intrauterine life can lead to obesity, diabetes, and cardiovascular diseases in adulthood. The present case emphasises the importance of performing an ECHO, even in infants born to diabetic mothers with good glycaemic control.

REFERENCES


