CASE REPORT

Hypertrophic Cardiomyopathy After a Single Dose of Dexamethasone in a Preterm Infant

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Dexamethasone is widely used in preterm infants with severe pulmonary disease. Hypertrophic cardiomyopathy (HCM) is a transient side effect observed after multiple doses of dexamethasone. We report a preterm infant with myocardial hypertrophy after a single dose of dexamethasone (0.5 mg/kg) used to treat laryngeal edema secondary to prolonged intubation. A benign course was observed without left ventricular outflow tract obstruction and with recovery within 4 weeks. Myocardial effects of dexamethasone may be independent of dose and duration of treatment. The risk/benefit ratio must be carefully considered before using even a single dose of dexamethasone in preterm infants.

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1. Introduction

Glucocorticoids, in particular dexamethasone, are widely used in preterm infants with severe lung disease to facilitate weaning from the ventilator, and in the prophylaxis and treatment of bronchopulmonary dysplasia (BPD). Dexamethasone is used to treat laryngeal edema secondary to prolonged intubation. However, glucocorticoids are associated with numerous adverse effects such as gastrointestinal hemorrhage, hyperglycemia, hypertension, hypertrophic cardiomyopathy (HCM), adrenal suppression, increased risk of sepsis, psychomotor development delay, and cerebral palsy. HCM is commonly reported in infants after multiple doses of dexamethasone. It has been shown that frequency and severity of myocardial hypertrophy increase with dose and duration of treatment. Herein, we present a preterm infant with transient myocardial hypertrophy after a single dose of dexamethasone used to treat laryngeal edema secondary to prolonged intubation.
2. Case Report

A 1500-g male infant was born at 32 weeks' gestation to a 17-year-old primigravida by vaginal delivery. A single dose of betamethasone was given to the mother just an hour before delivery. Apgar scores were 4 and 8 at 1 minute and 5 minutes, respectively. The patient was intubated in the delivery room and admitted to the neonatal intensive care unit. He received two doses of surfactant for respiratory distress syndrome. On day 5, a systolic murmur was noted and a pediatric cardiology consultation was requested. Echocardiography revealed patent foramen ovale and minimal ductal shunt. The thickness of the interventricular septum (IVS) was normal at that time. Every attempt at extubation failed with worsening retractions over time. The patient was placed on a mechanical ventilator until day 10. A stridor was audible upon extubation, suggesting upper airway obstruction, and the vocal cords appeared edematous on direct laryngoscopy. A single dose of dexamethasone 0.5 mg/kg was given intravenously. The patient tolerated extubation and was followed on nasal continuous positive airway pressure for an additional 4 days and weaned to supplemental oxygen thereafter. On day 16, echocardiography was repeated because of a worsening systolic ejection murmur. Echocardiographic evaluation showed marked thickening of the IVS (6 mm) and mild thickening of the posterior left ventricular wall without outflow tract obstruction (Figure 1). Prenatal history was reevaluated for factors causing HCM. A maternal oral glucose tolerance test was normal, and drug history was unremarkable. The maternal glycated hemoglobin (HbA1c) level was 5.2%. Serum biochemistry, blood gases, and tandem mass spectroscopy analysis were normal. Serial echocardiograms were performed weekly. Maximal thickness of the IVS was 7 mm on day 23 and progressively decreased to 3 mm on day 44 (Figure 2). The baby was completely asymptomatic all the time. Supplemental oxygen was discontinued on the 30th day, and he was discharged on the 45th postnatal day. At post-discharge follow-up, cardiologic evaluation was normal.

3. Discussion

HCM is defined as septal or posterior wall thickness that is more than two standard deviations above the mean normal thickness measured by echocardiography. Myocardial hypertrophy can be encountered in infants with maternal diabetes, in utero ritodrine exposure, perinatal asphyxia, several metabolic diseases, Noonan syndrome, systemic hypertension, and familial HCM caused by mutations in genes encoding sarcomeric proteins. In our case, prenatal history was negative for maternal risk factors as well as the familial history regarding genetic and metabolic diseases. Betamethasone was started just before birth to induce lung maturity in this infant and only a single dose was given. It has been shown that a single or repeated course of prenatal corticosteroids does not alter myocardial thickness in preterm infants. The maternal oral glucose tolerance test in pregnancy and the postpartum HbA1c level were in the normal range in our patient. Furthermore, echocardiography performed on the 5th day of life revealed normal IVS and left ventricular thickness, which means prenatal and maternal causes could not be responsible for the observed myocardial hypertrophy. Our patient did not have any clinical and laboratory evidence of metabolic and genetic disorders. The reversible nature of myocardial hypertrophy makes metabolic and familial causes very unlikely.

HCM secondary to dexamethasone therapy is usually a benign condition with spontaneous recovery 2–5 weeks after discontinuation. Rarely, symptomatic left ventricular outflow tract obstruction may be observed. Why dexamethasone induces myocardial thickening and which dose and duration are safe remain unclear. At a cellular level, cardiac hypertrophy usually results from hypertrophy of myocytes by the synthesis of various intracellular cardiac proteins. The densities of insulin-like growth factor 1 (IGF1) and insulin receptors are highest in the neonatal period and decrease during infancy. An effect of dexamethasone through IGF1 or its receptors on cardiac myocytes may explain dexamethasone-induced left ventricular hypertrophy. A greater degree of hypertrophy is observed in infants receiving insulin in addition to the dexamethasone. Dexamethasone schedules for prevention and treatment of BPD have changed over time in an attempt to find the lowest possible doses with adequate therapeutic effect and to limit adverse reactions. Zecca et al reported that even a low dose and short course (1 week) therapy with dexamethasone can
have adverse cardiac effects. This is the first report of HCM in a preterm infant after a single dose of dexamethasone. Hypertrophy was more prominent in the IVS than the left ventricular wall, which returned to normal within 4 weeks. A benign course was observed without left ventricular outflow tract obstruction. The infant had no symptoms related to myocardial hypertrophy.

In conclusion, even a single dose of dexamethasone may produce a transient myocardial hypertrophy in preterm infants. Risks and benefits should be considered while using dexamethasone in preterm infants with the possible additional risk of HCM.

References