Chronic antepartum maternal hyperoxygenation in a case of severe fetal Ebstein's anomaly with circular shunt physiology

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ABSTRACT

Perinatal mortality remains high among fetuses diagnosed with Ebstein's anomaly of the tricuspid valve. The subgroup of patients with pulmonary valve regurgitation is at particularly high risk. In the setting of pulmonary valve regurgitation, early constriction of the ductus arteriosus may be a novel perinatal management strategy to reduce systemic steal resulting from circular shunt physiology. We report the use of chronic antepartum maternal oxygen therapy for constriction of the fetal ductus arteriosus and modulation of fetal pulmonary vascular resistance in a late presentation of Ebstein's anomaly with severe tricuspid valve regurgitation, reversal of flow in the ductus arteriosus, and continuous pulmonary valve regurgitation.

Keywords: Congenital heart disease, Ebstein's anomaly, fetal intervention, maternal hyperoxygenation

INTRODUCTION

Perinatal mortality remains high among fetuses diagnosed with Ebstein's anomaly, with reports of up to 45% in recent large multicenter series.[1] In the setting of pulmonary valve regurgitation, early constriction of the ductus arteriosus may be a novel perinatal management strategy to reduce systemic steal resulting from circular shunt physiology. We demonstrate the use of chronic antepartum maternal oxygen therapy in a case of severe Ebstein's anomaly for constriction of the fetal ductus arteriosus and modulation of fetal pulmonary vascular resistance before successful neonatal surgical repair.

CLINICAL SUMMARY

A 22-year-old mother with intrahepatic cholestasis was referred to our institution at 32 5/7 weeks gestation with a fetus with Ebstein's anomaly and severe tricuspid valve regurgitation, continuous pulmonary valve regurgitation, reversal of flow in the ductus arteriosus, mild ascites, and a small pericardial effusion [Figure 1]. Middle cerebral artery (MCA) Doppler revealed absent end-diastolic flow suggesting significant systemic steal [Figure 2]. With a cardiothoracic ratio of 0.75 and Celermajer index of 1.5, the fetus received a prognostic score of 8 based on a recent evaluation of fetuses with isolated tricuspid valve malformations; no patients in this study with a prognostic score of ≥5 survived past the first month of life.[2,3]

Given the high risk for fetal demise, maternal oxygen therapy was proposed to constrict the ductus arteriosus to reduce the aortic-to-pulmonary shunt and augment pulmonary blood flow by decreasing pulmonary vascular resistance. As alternative therapy for ductal constriction, maternal administration of nonsteroidal anti-inflammatory drugs (NSAIDs) was contraindicated due to the history of intrahepatic cholestasis. The mother subsequently consented to a trial of oxygen therapy.

A fetal echocardiogram was performed before and after a 30 min trial of maternal hyperoxygenation at

Access this article online

Quick Response Code:

Website: www.annalspc.com

DOI: 10.4103/apc.APC_20_17

How to cite this article: Arunamata A, Axelrod DM, Bianco K, Balasubramanian S, Quirin A, Tacy TA. Chronic antepartum maternal hyperoxygenation in a case of severe fetal Ebstein's anomaly with circular shunt physiology. Ann Pediatr Card 2017;10:284-7.

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6 L/min through nonrebreather facemask (FiO_2 1.0). Maternal hyperoxygenation for 30 min demonstrated increased pulmonary blood flow with an increased ratio of pulmonary artery forward: reverse velocity time integral (VTI) and pulmonary venous VTI by fetal echocardiogram; ductal constriction and reduction of systemic steal were demonstrated by restoration of continuous end-diastolic MCA flow and an acute decrease in MCA pulsatility index [Figure 3].

The mother was subsequently admitted to the hospital for maternal oxygen therapy with 6 L/min through nonrebreather facemask for 4 h, 3 times daily with serial fetal echocardiograms until delivery. After chronic maternal hyperoxygenation through 36 weeks gestation, there was evidence of moderate ductal restriction (peak instantaneous gradient of 35 mmHg) [Figure 4] and normal MCA flow.

Emergent cesarean section was performed at 36 weeks gestation for late fetal heart rate decelerations; Apgar scores at delivery were 3, 3, and 4 at 1, 5, and 10 min, respectively. Initial peripheral arterial blood gas revealed significant respiratory and metabolic acidosis with a pH of 6.9 and hypoxemia with a partial pressure of oxygen (PaO_2) of 40 mmHg.

The male infant was (i) cannulated onto veno-venous extracorporeal membrane oxygenation (ECMO) to support oxygenation, (ii) started on inhaled nitric oxide to decrease pulmonary vascular resistance, and (iii) underwent surgical ductal ligation to eliminate systemic steal as discussed during prenatal delivery planning. At 2 weeks of age, the infant underwent primary repair of the tricuspid valve and reduction annuloplasty, with right atrial reduction plasty. On inspection of the tricuspid valve in the operating room, there was complete absence of the posterior leaflet and a poorly developed and displaced septal leaflet; sutures were used to coapt the anterior and septal leaflets to create a functional bileaflet tricuspid valve. The infant tolerated patent foramen ovale closure with successful ECMO decannulation in the operating room, with a right atrial pressure of 8 mmHg and left atrial pressure of 5 mmHg at the end of the case. The infant was discharged home at 2 months of age

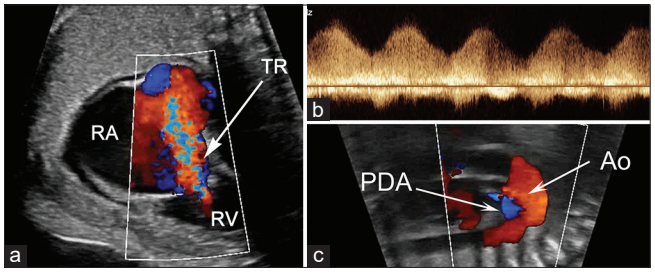

Figure 1: Fetal echocardiogram before maternal oxygen therapy. (a) Color Doppler demonstrating severe tricuspid valve regurgitation (TR, annotated by the white arrow). RA: Right atrium, RV: Right ventricle, (b) Spectral Doppler noting continuous pulmonary regurgitation. (c) Color Doppler of reverse flow (left-to-right) in the patent ductus arteriosus (PDA). Ao: Aorta

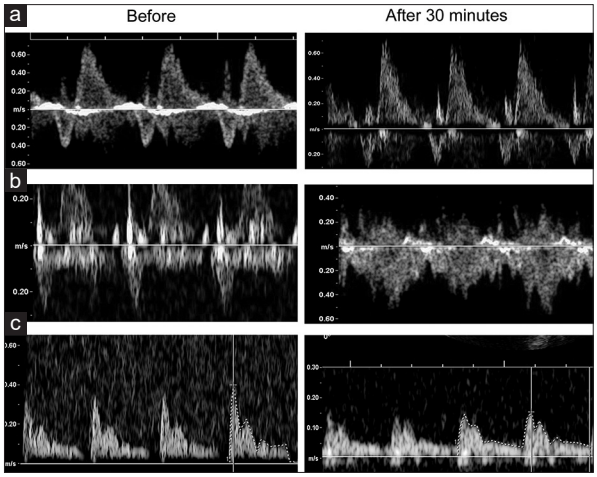

Figure 3: Fetal echocardiogram before and after maternal oxygen therapy for 30 min. (a) Increase in pulmonary artery forward (above baseline): Reverse (below baseline) velocity time integral ratio from 3.9 to 5.2. (b) Increase in pulmonary venous velocity time integral from 0.05 m to 0.14 m. (c) Acute decrease in middle cerebral artery pulsatility index from 3.1 to 1.7 attributed to ductus arteriosus constriction

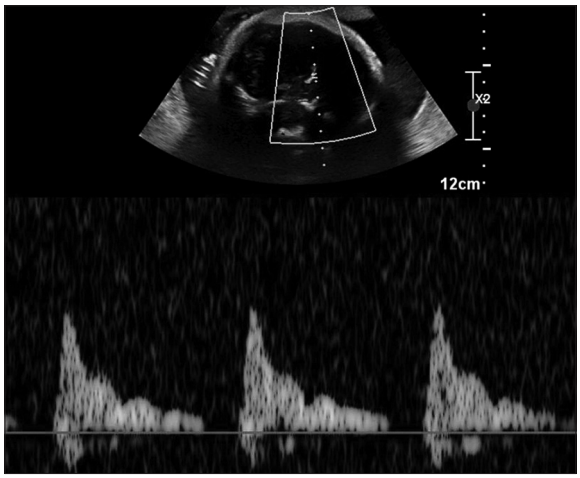

Figure 2: Abnormal middle cerebral artery Doppler profile with absent end-diastolic flow

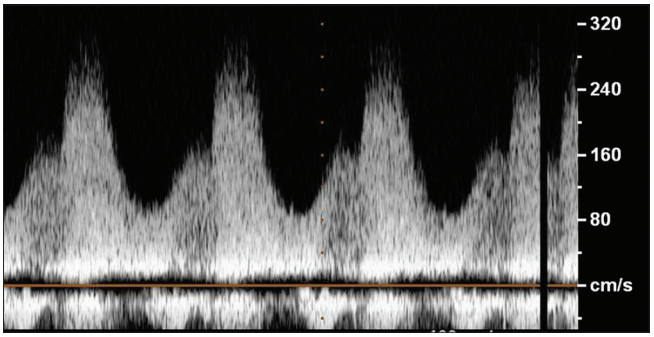

Figure 4: Spectral Doppler in the ductus arteriosus at 36 weeks gestation after 1 month of maternal hyperoxygenation demonstrating moderate ductus arteriosus restriction, with a peak instantaneous gradient of 35 mmHg

after an uneventful cardiac postoperative course. He is followed in outpatient cardiology clinic and continues to thrive with normal growth and development.

DISCUSSION

The subgroup of fetuses with Ebstein's anomaly and pulmonary valve regurgitation with circular shunt physiology is at particularly high risk for perinatal demise.[1] In this scenario, there is retrograde (left-to-right) flow across the ductus arteriosus, continuous pulmonary valve regurgitation, severe tricuspid valve regurgitation, and right-to-left flow across the atrial septal communication leading to systemic steal. The absence of end-diastolic flow in the MCA Doppler is a marker of significant systemic steal. The chronic volume load on the right side of the heart leads to marked dilation of the right atrium and ventricle contributing to cardiomegaly, pulmonary hypoplasia, and subsequent pulmonary vascular disease well-described in neonatal Ebstein's anomaly.[4,5]

There remain limited options for perinatal management of fetuses with this pathophysiology; however, neonatal studies have suggested that early ductal ligation or spontaneous ductal constriction may result in termination of the circular shunt and hemodynamic improvement.[6] While NSAIDs may be considered for fetal ductus arteriosus closure in late gestation, use of NSAIDs *in utero* carries a risk of maternal postpartum hemorrhage, fetal organ impairment, and potentially persistent pulmonary hypertension, a complication that is detrimental to neonates with Ebstein's anomaly.[7,8]

Maternal oxygen use was first described in fetuses with congenital anomalies leading to pulmonary hypoplasia such as renal agenesis, obstructive uropathy, and congenital diaphragmatic hernia; poor reactivity to oxygen administration demonstrated on Doppler assessment of pulmonary blood flow predicted neonatal demise from pulmonary hypoplasia.[9] Clinical maternal oxygen use in the setting of fetal congenital heart disease has been described as a useful diagnostic tool to determine pulmonary vasculature response in hypoplastic left heart syndrome with concerns for a restrictive or intact atrial septum.[10] More recently, chronic antepartum oxygen therapy has been used to promote aortic and mitral annular growth in patients with left heart hypoplasia.[11,12] Antepartum maternal hyperoxygenation appears to be technically feasible, with no reports of neonatal retinopathy on ophthalmologic examinations.[11]

As in neonatal life with an increase in blood oxygen-content stimulating closure of the ductus arteriosus, our case demonstrates that chronic maternal hyperoxygenation at 12 h/day in late gestation may constrict the ductus arteriosus and has a beneficial role in the management of severe fetal Ebstein's anomaly. Maternal hyperoxygenation may be additionally beneficial in fetuses with Ebstein's anomaly by reducing pulmonary vascular resistance and promoting antegrade pulmonary blood flow, demonstrated on fetal echocardiogram by the increase in antegrade: retrograde flow across the branch pulmonary arteries and pulmonary venous VTI.

We propose that a prenatal management paradigm of chronic oxygen therapy for ductal constriction combined with pulmonary vascular resistance reduction, and a brief postnatal period of vascular remodeling and oxygenation support may enable early successful repair in patients with severe Ebstein's anomaly.[13]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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