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Diagnosis and management of fetal ductus arteriosus constriction-closure

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Abstract. Pathognomonic features of in utero premature restriction/closure of the ductus arteriosus (DA) are increased right ventricular afterload, impaired right ventricular function, and consequently tricuspid regurgitation and right heart dilation. The most common reason for constriction-closure of DA is maternal administration of non-steroidal anti-inflammatory drugs (NSAIDs) during the 3rd trimester of gestation. The idiopathic form is a rare event and, maybe, an underestimated abnormality that, if it is not promptly recognized, may result in severe fetal-neonatal compromise. We describe a case of a 38-year-old woman presenting at 34+0 weeks of gestation with a normally grown male fetus whose fetal echocardiography had shown right ventricular hypertrophy, a tortuous S-shaped DA and a significant pulmonary hyperflow. All signs were consistent of an idiopathic severe constriction of DA with a significant fetal cardiac involvement. The patient was admitted to a tertiary care center equipped with Neonatal Intensive Care Unit (NICU), and delivered by cesarean section at 34+4 weeks with a good maternal and neonatal outcome. Based on our experience and a review of the Literature we propose a management algorithm to use when dealing with preterm or early term pregnancy complicated by this fetal hemodynamic malfunction.

Keywords: Ductus arteriosus, fetal ventricular afterload, fetal pulmonary hyperflow, fetal ventricular hypertrophy, fetal ventricular overload

1. Introduction

The ductus arteriosus (DA) connects the pulmonary artery to the aortic arch during the intrauterine life and normally occludes after birth to establish the adult circulation pattern; it allows unloading of the right ventricle (RV) bypassing the high resistance fluid-filled lungs [1–3]. Patency of the ductus arteriosus is maintained during gestation by locally produced and circulating prostaglandins, especially PGE2, and low fetal oxygen saturation [4, 5]. In the third trimester of gestation, DA becomes more sensitive to constricting factors such as prostaglandins synthetase inhibitors. In fetuses born at term, the DA...
PHY OF THE HEMODYNAMIC ABNORMALITY, MAY DETERMINE HYPERTROPHICAL PRESSURE ON THE PULMONARY VASCULATURE, DUE TO THIS DEMISE [19]. IN SOME CASES THE INCREASED MECHANICAL STRESS, CARDIAC FAILURE AND ISCHEMIA AND FETAL REGURGITATION, PAPILLARY MUSCLE STRESS OR Rupture WITH HYPERTROPHY, DYSFUNCTION, DILATATION, TRICUSPID VALVE THE RIGHT VENTRICLE (RV) WITH SUBSEQUENT VENTRICULAR HYPERTROPHY AND PULMONARY HYPERTENSION. NO OTHER CARDIAC STRUCTURAL LESIONS WERE FOUND.

Considered all of the above we suggest that practitioners should think to this cardiac abnormality, especially in patients who take NSAIDs during pregnancy and/or have certain dietary and behavioral habits and obtain a formal fetal echocardiogram whenever in doubt.

2. Case report

We report the case of a 38-year-old woman, in her third pregnancy (a previous caesarean-section at 36 weeks of gestation and an abortion diagnosed at 34th weeks of gestation with preterm idiopathic constriction of ductus arteriosus). The course of pregnancy and antenatal blood tests were unremarkable until that moment. The mother’s medical history was negative for major illness such as diabetes mellitus, hypertension, and preeclampsia. During pregnancy the woman received iron supplement, folic acid and a short course of paracetamol (one 500 mg-tablet QID per 4 days) during the 33rd week because of lumbar pain. The woman did not smoke neither during pregnancy nor before.

On request of her obstetrician who noticed a fetal heart abnormality on routine ultrasound, a fetal echocardiography evaluated the two-dimensional cardiac anatomy, including outflow tracts, ductus arteriosus, aortic arch and determined the flow velocities across each valve and through the ductus. The fetal heart scans revealed a right ventricular hypertrophy, a tenuous S-shaped DA and a significant hyperflow in the high-resistance, fluid-filled lungs. Pulsed Doppler showed a significantly increased peak systolic velocity of 2.75 m/s (normal \( \leq 1.4 \text{ m/s} \)) (Fig. 1) at the junction of the DA with the transverse aortic arch, a pulsatility index (PI) lower than in normal condition (1.9), and a ductal gradient of 30 mmHg.

Test results were consistent with significant restriction of the DA and consequent severe right ventricular hypertrophy and pulmonary hypertension. No other cardiac structural lesions were found.

It was decided to give an antenatal administration of corticosteroids for lung maturity. After 3 days it was repeated the echocardiography, which confirmed the findings obtained previously (peak systolic velocity \( = 2.75 \text{ m/s} \), PI \( < 1.9 \), ductal gradient = 30 mmHg) and the signs of ventricular overload (pulmonary hypertension).

Due to the fetal cardiac condition the risks of leaving the fetus in utero appeared higher than those associated with a preterm delivery, therefore the patient was scheduled for an elective cesarean section at 34th...
weeks. A 2370 g male infant was delivered. The baby had an Apgar score of 8 at 1 minute and 9 at 5 minutes, but soon after birth he developed a respiratory distress and was immediately admitted to the neonatal intensive care unit (NICU) where he required low-flow oxygen administration by nasal cannula and parenteral fluid support.

A 6-hour postnatal echocardiogram showed a marked right ventricular hypertrophy with impaired function, a little tortuous DA, and a shunt right-to-left. The right ventricular hypertrophy was also evident at the electrocardiogram (EKG). It was decided not to use inotropes because the patient was hemodynamically stable. Chest X-ray revealed diffused enhancement of the pulmonary plot with reticular-granular lung opacities (Fig. 2).

The maternal postoperative course was absolutely uneventful. The patient went home on post-partum day 4. Oxygen supplementation and parenteral fluid support was suspended on day 4. The newborn had a complete regression of the RV hypertrophy by the end of his NICU stay (day 13) and he was discharged home on day 15. The successive follow-ups were unremarkable.

3. Discussion

Fetal ductus arteriosus preterm constriction-closure is a rare condition that may compromise, even severely, the fetal cardiac function. Before diagnosing a
Table 1

| Intrauterine ductus arteriosus restriction: parameters for the diagnosis at >27 weeks |
|---------------------------------|---------------------------------|
| Peak systolic velocity          | >1.4 m/s                        |
| Diastolic peak flow velocity    | <0.35 m/s                       |
| Pulsatility index               | <1.9 (n.r. 2.46 ± 0.52)         |

In case of DA constriction, blood circulation through the ductus is characterized by turbulence, increased systolic flow, absent diastolic flow and reduced Pulsatility Index (PI) < 1.9; PI in the normal ductus is 2.46 ± 0.52 throughout gestation. Several reports suggest that a peak systolic velocity of greater than 1.4 m/s in conjunction with a persistent diastolic peak flow velocity of greater than 0.35 m/s is evocative of DA constriction (Table 1) [27–30].

Patients with total occlusion of DA show absence of ductal flow.

Few reports of pregnancies complicated by this pathology and unrelated to medications were found in Literature. Mielke et al. [31] described a case of right atrial and ventricular dilatation and severe tricuspid valve regurgitation due to a severe S-shaped ductal arch, with a peak systolic flow velocity of 1.49 m/s; the symptoms resolved in the postpartum period.

Table 2

<table>
<thead>
<tr>
<th>Authors</th>
<th>Cases</th>
<th>Maternal factors</th>
<th>Domainular ultrasound findings</th>
<th>Delivery</th>
<th>GA Birth</th>
<th>Birth weight (g)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auer et al.</td>
<td>1</td>
<td>NSAID</td>
<td>RV dysfunction, TR, PR no flow in the pulmonary trunk</td>
<td>Cesarean Section</td>
<td>37w 3300</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Gewilling et al.</td>
<td>8</td>
<td>NSAID</td>
<td>RV dysfunction, PA dilatation</td>
<td>Spontaneous 38w 2930</td>
<td>A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hofstadler et al.</td>
<td>4</td>
<td>NSAID (20 weeks)</td>
<td>RV dilatation, TR</td>
<td>Cesarean Section</td>
<td>37w 3350</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Shastri et al.</td>
<td>1</td>
<td>NSAID</td>
<td>RV dysfunction, TR</td>
<td>Cesarean Section</td>
<td>35w 2629</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Shima et al.</td>
<td>1</td>
<td>NSAID</td>
<td>RV dysfunction, TR</td>
<td>Cesarean Section</td>
<td>38w 2816</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Soslow et al.</td>
<td>1</td>
<td>NSAID</td>
<td>RA and RV dilatation, fetal ascites, hydrops</td>
<td>Spontaneous</td>
<td>3040</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Travett et al.</td>
<td>1</td>
<td>NSAID</td>
<td>RV dysfunction, TR</td>
<td>Cesarean Section</td>
<td>38w 3942</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Lowenthal et al.</td>
<td>1</td>
<td>Bupropion</td>
<td>Tricuspid atresia</td>
<td>Cesarean Section</td>
<td>35w 32w</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

GA, gestational age; NSAID, non-steroidal anti-inflammatory drug; ACS, antenatal corticosteroids; RA, right atrium; PA, pulmonary artery; TR, pathological tricuspid regurgitation; PR, pathological pulmonary regurgitation; A, alive; D, death.
after three days. Trevett et al. [19] presented a case of a 33-week-fetus characterized by a right ventricular hypertrophy secondary to an S-shaped ductus arteriosus with distal constriction and a peak systolic velocity of 2.8 m/s. In this clinical case the fetus was monitored by weekly ultrasound for signs of fetal hydrops, then labor was induced at 38 weeks; the newborn was born with no clinical symptoms, but 3 weeks after birth a neonatal echocardiogram showed moderate right ventricular hypertrophy and minimal left ventricular hypertrophy.

Unlike the above case, in our study a right ventricular hypertrophy and a tortuous S-shaped DA with a significantly increased peak systolic velocity of 2.75 m/s, were associated with a significant hyperflow in the high-resistance, fluid-filled lungs. This abnormal fetal hemodynamic condition, even at an earlier gestational age (34 weeks), induced us to plan an urgent preterm delivery by cesarean section to optimize the neonatal prognosis.

Based on our experience and a review of literature, grouped on the gestational age at the time of diagnosis, on the management (either by careful fetal surveillance and/or by preterm induction or elective cesarean section), and on the perinatal outcomes, as described in Table 2, we propose a management-flowchart (Fig. 3) for the practicing obstetrician when dealing with pregnancy complicated by this fetal heart condition.

4. Conclusion

In our experience, in the presence of this fetal condition, the best management consists of a continuous fetal surveillance followed by an urgent preterm delivery, if specific hemodynamic and morphologic parameters indicate that the in utero fetal risks outweigh those of a preterm birth. The obstetrical conduct, presented in Fig. 3, usually results in excellent neonatal prognosis, due mostly to a good timing of delivery and a consequent exponential decrease in fetal pulmonary vascular resistance. Delaying delivery, when the hemodynamic fetal conditions are not favorable, may seriously and irrevocably affect the fetal survival-wellbeing.
Moreover, it is important to perform delivery of these high-risk newborns under optimal circumstances, in a tertiary care center with prompt resource availability.

Financial disclosure statement

No author has any potential conflict of interest.

References