Transient Neonatal Tricuspid Regurgitation: Possible Relation With Premature Closure of the Ductus Arteriosus

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Normal fetal circulation requires patency of the ductus arteriosus. Prenatal ductal closure causes profound circulatory changes, such as massive tricuspid regurgitation. After delivery, the clinical picture of these severely distressed cyanotic newborns usually improves rapidly as the circulation is no longer dependent on ductal patency after onset of respiration. This case report deals with a newborn infant with severe tricuspid regurgitation and a large atrial right to left shunt who was treated with prostaglandin E₁ infusion at 12 hours of age and in whom cardiac angiography revealed no evidence of either patent or functionally closed ductus arteriosus and no anatomic cardiac abnormalities at 30 hours of age.

On the basis of physiologic and morphologic observations in this infant, the possible role of premature ductal narrowing or closure in the pathogenesis of transient neonatal tricuspid regurgitation is discussed. It is recommended that documentation of ductal presence or absence should become part of the diagnostic evaluation of newborns with transient tricuspid regurgitation.

Transient neonatal tricuspid regurgitation with a right to left atrial shunt has been reported frequently (1–5) and should be considered in the differential diagnosis of cyanotic newborns with massive tricuspid regurgitation. Premature closure of the ductus arteriosus may play an important role in pathogenesis of this entity, but reports of isolated prenatal ductal closure have been few (6,7). This paper presents an infant with transient tricuspid regurgitation whose clinical course and hemodynamics are consistent with closure of the ductus arteriosus before birth.

Case Report

The mother, a 25 year old primipara, had a full-term uncomplicated pregnancy. No medications, including salicylates, were taken. The fetal membranes ruptured 16 hours before delivery. Induced labor was complicated by brief type 2 deceleration and meconium staining. The delivery was vaginal with vertex presentation.

Birth weight was 2,480 g. The Apgar scores were 8 and 9. Cyanosis and a harsh grade 3 to 4/6 systolic murmur were first noted at 7 hours of age. The arterial partial pressure of oxygen (PaO₂) was 32 torr with the infant breathing 30% oxygen. The chest roentgenogram revealed 3+ cardiomegaly with a cardiothoracic ratio of 0.84 (Fig. 1A). The electrocardiogram revealed sinus rhythm, right axis deviation and biatrial and right ventricular hypertrophy. Prostaglandin E₁ infusion at a rate of 0.1 µg/kg per min was started at 12 hours of age and the infant was transferred to this hospital.

Shortly after admission, the arterial PaO₂ was 50 torr with the infant breathing 40% oxygen while receiving prostaglandin E₁ infusion. A harsh murmur at the lower left sternal border was consistent with tricuspid regurgitation. The second heart sound was well split.

Cardiac catheterization was performed at 30 hours of age with continuous prostaglandin E₁ infusion. Except for a right to left shunt at the atrial level, the hemodynamic findings were normal. However, a right heart angiogram revealed massive tricuspid regurgitation with dilated right atrium and right ventricle (Fig. 2). In the left ventricular angiogram (Fig. 3), the ascending aorta, aortic arch and isthmus appeared dilated. No remnant of the ductus arteriosus was noted. The diagnosis of premature closure of the ductus arteriosus with prenatal right ventricular failure and secondary tricuspid regurgitation was suspected. The ben-
The prostaglandin E₁ infusion was discontinued after the catheterization. The cardiac status improved rapidly and at 3 days of age, the heart size appeared much smaller (Fig. 1B). The murmur became progressively softer and the cyanosis disappeared. At 2 months of age, the infant had no apparent residual cardiovascular abnormalities on physical examination, electrocardiogram or chest roentgenogram.

**Discussion**

**Distribution of fetal circulation.** During normal fetal circulation (Fig. 4A), the left ventricle supplies about 15% of thoracic flow by way of the aortic isthmus, and the right ventricle contributes 85% of the thoracic aortic flow by way of the ductus arteriosus (8). Anatomically and functionally, the pulmonary trunk, the ductus arteriosus and the descending aorta represent a wide and continuous arterial channel.

As long as the ductus is the principal supplier of blood flow to the thoracic aorta, the aortic isthmus remains a distinct and comparatively narrow segment.

In contrast, in fetal hearts with reversed ductal flow (pulmonary atresia, for example), the entire proximal aortic channel including the isthmus is larger than normal, the latter becoming anatomically indistinguishable from the thoracic aorta (9). This occurs because in pulmonary atresia the combined right and left ventricular output enters the ascending aorta and the total blood flow to the thoracic aorta passes through the aortic isthmus.

Similarly, in the event of a normal fetus surviving prenatal ductal closure, the combined ventricular output (except for the small pulmonary blood flow) will enter the ascending aorta and there should be no isthmic hypoplasia.

In a normally structured heart, fetal survival in case of ductal absence or early closure is unlikely. However, ductal absence need not be fatal in the presence of a large interventricular or aortopulmonary communication providing an alternate egress from the fetal right ventricle into the aorta (10,11). The anatomic complex of ventricular septal defect, fetal pulmonary regurgitation, rudimentary pulmonary valve and aneurysmal proximal pulmonary artery branches may be an example of agenesis of the ductus arteriosus (12).
Circulatory changes after experimental prenatal ductal closure or constriction. Ductal constriction or obliteration in a normal fetus during late pregnancy (Fig. 4B) also need not be fatal. Animal experiments by Haller et al. (13) and Levin et al. (6) helped to elucidate some of the profound changes in circulation after prenatal surgical or pharmacologic constriction of the fetal ductus arteriosus. Haller et al. (13) ligated the ductus arteriosus in fetal puppies. Intrauterine survival 5 to 10 days after ductal ligation was monitored, but no puppies were delivered alive. Venous angiography before ductal ligation showed the contrast agent passing from the right ventricle to the descending aorta and from the left ventricle to the ascending aorta; this produced a radiolucent hiatus in the isthmic segment of the aorta. After ductal ligation, there was no increase in pulmonary artery perfusion, but instead an increase in atrial right to left shunting occurred and immediate opacification of the ascending aorta was observed. Autopsy revealed a dilated and hypertrophied right ventricle and the dimension of the pulmonary trunk was 3 to 4 times the size of the aorta. Unfortunately, the morphologic features of the tricuspid valve were not described.

Levin et al. (6) produced constriction of the fetal ductus arteriosus in ewes 3 weeks before term delivery by administration of indomethacin. Ductal constriction produced an increase in pulmonary artery pressure that was reversible with administration of prostaglandin E₁. There was significant thickening of the pulmonary arteriolar media suggesting that as more blood was diverted toward the pulmonary arteries because of the constricted ductus, the pulmonary arteriolar resistance increased proportionately to maintain the same low fetal pulmonary perfusion rate. The authors speculated that there may be a relation between prenatal ductal constriction, excessive arteriolar medial hypertrophy and persistent fetal circulation in the newborn. In the majority of ewes, there were degenerative changes in the right ventricular myocardium, especially in the papillary muscles. On the basis of these and other observations of Levin et al. (6,14), it is tempting to consider that transient tricuspid regurgitation in the newborn is the result of prenatal or premature perinatal ductal constriction. Boucek et al. (1) reported on three newborn infants under 4 days of age with transient tricuspid regurgitation and cyanosis in whom the ductus was found constricted and carried a small left to right shunt.

Tricuspid regurgitation secondary to prenatal ductal closure. Arcilla et al. (7) suspected intrauterine ductal closure as the cause of massive tricuspid regurgitation in a newborn whose mother was treated with salicylates for rheumatoid arthritis during the last 2 weeks of pregnancy. Cardiac angiography at 4 hours of age revealed a ductus arteriosus that was slightly patent at the pulmonary end and closed at the aortic end. The pulmonary trunk, right ventricle and right atrium were moderately dilated. There was tricuspid regurgitation and an atrial right to left shunt. The pressures in the right ventricle and right atrium were elevated. Cyanosis and tricuspid regurgitation resolved within days, and recatheterization at 3 months of age showed no abnormalities. It also appears plausible, as Schiebler et al. (15) speculated, that postnatal closure of ductus arteriosus in infants with excessively hypertrophied pulmonary arteriolar media could produce transient tricuspid regurgitation if closure occurs too rapidly.

Bucciarelli et al. (2) studied four neonates less than 4 days of age undergoing cardiac catheterization for tricuspid regurgitation. Patency of the ductus arteriosus was not documented in any patient. Two other neonates with similar clinical presentation died; at autopsy, the tricuspid valve was anatomically normal and the ductus arteriosus was only probe patent in both. The authors attributed the tricuspid regurgitation in these patients to right ventricular dysfunction resulting from hypoglycemia noted in two of their four cases.

Role of prostaglandin E₁ therapy. Prenatal ductal closure implies either an effect of prostaglandin antagonists or failure of end-organ response to endogenous prostaglandin.
Figure 4. Schematic illustration of distribution of fetal circulation (after Rudolph [8]). A. Normal fetus with widely patent ductus arteriosus; the ductus contributes 85% (59/69 ml) of flow in the descending thoracic aorta, while only 15% (10/69 ml) flows through the relatively hypoplastic isthmus (IST). B. With no functioning ductus arteriosus, most of the systemic venous return enters the left atrium, left ventricle and ascending aorta. The entire flow in the descending aorta passes through the isthmus (69/69 ml), which is of the same caliber as the surrounding aorta. LL = left lung; LV = left ventricle; RL = right lung; RV = right ventricle.

In either event, little or no response to administration of prostaglandin should be anticipated in neonates with suspected premature ductal closure. However, in neonates with a normal ductus, ductal dilation after infusion of prostaglandin E₁ should be expected within the first 96 hours of age, especially if cyanosis and respiratory distress are present. Freed et al. (16) reviewed the extensive multicenter experience with prostaglandin E₁ in infants with ductus-dependent cyanotic or acyanotic congenital heart disease. The best ductal response to prostaglandin E₁ occurred in infants under 4 days of age who weighed less than 4 kg at birth. The authors also found that when angiography in these patients revealed complete ductal closure as early as 3 days of life, the ductus could not be reopened with prostaglandin E₁ infusion.

Neonatal response to prostaglandin E₁ may be helpful in diagnosing premature closure of the ductus arteriosus. Graham et al. (17) performed cardiac catheterization in a 1 day old infant with tricuspid insufficiency, normal right ventricular pressure, a large atrial right to left shunt and no evidence of ductal patency. This infant underwent a second catheterization at 4 days of age with the hope that prostaglandin E₁ infusion might open the ductus. The ductus remained closed but the patient’s condition improved presumably because of the pulmonary vasodilating effect of prostaglandin E₁.

Other causes of neonatal tricuspid regurgitation. Despite the report of Arcilla et al. (7) in 1969, premature closure of the ductus arteriosus is not generally considered one of the causes of tricuspid regurgitation in cyanotic newborns. Rowe and Hoffman (3) attributed transient tricuspid regurgitation and sometimes mitral regurgitation to myocardial ischemia resulting from severe pulmonary vasoconstriction. Papillary muscle infarction, especially involving the right ventricle, was reported as a frequent neonatal autopsy finding by Setzer et al. (4). The lesion was more common in mature neonates dying with meconium aspiration syndrome. Similarly, Donnelly et al. (5) reported tricuspid regurgitation in neonates as a result of papillary muscle damage. Most infants had severe asphyxial episodes presumably leading to development of tricuspid regurgitation.

Unless unequivocal ductal patency or reactivity to prostaglandin E₁ is demonstrated, it may not be unreasonable to consider the microscopic changes of the right ventricular myocardium, especially in the papillary muscles, as resulting from acute prenatal right heart failure induced by premature closure or constriction of the ductus arteriosus. Prenatal ductal closure explains both the severe pulmonary vasoconstriction leading to excessive medial hypertrophy, and the injury of the right ventricular myocardium due to increased afterload and tricuspid regurgitation.

Diagnostic criteria for neonatal ductal constriction or closure. In a neonate with a structurally normal heart, the following diagnostic criteria for prenatal or premature perinatal constriction or closure of ductus arteriosus are suggested: 1) Massive tricuspid regurgitation and atrial right to left shunt. 2) In the presence of these, a minimally patent or closed ductus arteriosus that fails to respond to infusion of prostaglandin E₁. 3) A dilated ascending aorta and aortic arch and absence of normal neonatal hypoplasia of the aortic isthmus. 4) Transient nature of the tricuspid regurgitation (this observation can only be made in retrospect).

References


