Pediatr Cardiol 21:271–274, 2000
DOI: 10.1007/s002460010057

Pediatric Cardiology

Transient Neonatal Cyanosis: Unusual Presentation of Right-Sided Cardiac Masses

C.I. Mesia, A. Forman, M.T. Donofrio

Department of Pediatrics: Division of Pediatric Cardiology, The Medical College of Virginia of the Virginia Commonwealth University, Richmond, P.O. Box 980026, Richmond, VA 23298-0026, USA

Abstract. We report a case of a neonate with multiple cardiac masses, cyanosis, and a heart murmur. Arterial desaturation was the result of right-to-left shunting at the foramen ovale level caused by tricuspid regurgitation. Three right-sided cardiac masses were detected by echocardiography. By 2 weeks of age the patient had complete resolution of his cyanosis and improved tricuspid regurgitation following the normal decrease in pulmonary vascular resistance. At 2 years of age, he has no cardiovascular symptoms and the masses are calcified and have no hemodynamic consequences.

Key words: Neonatal cyanosis — Cardiac masses — Tricuspid valve — Rhabdomyoma

Cyanosis in the neonate is a diagnostic emergency requiring rapid identification of the etiology to direct treatment and avoid deterioration. An unusual case of multiple cardiac masses in an infant with extreme cyanosis and a heart murmur in the absence of congenital heart disease is reported. We discuss the mechanism of transient cyanosis and the possible etiology of these cardiac masses.

Case Report

A term male neonate, the product of a normal pregnancy and delivery, presented with extreme cyanosis immediately after birth. Apgar scores were 3, 6, and 9 at 1, 5, and 10 minutes, respectively. After vigorous resuscitation, oxygen saturation level determined by pulse oximetry was 60% in a 100% oxygen hood and improved to 80% (paO_2 = 31 mmHg) after intubation and mechanical ventilation. On physical examination, weight was 3835 g, heart rate 135 beats/min, blood pressure 76/44 mmHg, and respirations 53/min. General appraisal revealed a cyanotic newborn in no respiratory distress. On cardiac examination he had a quiet precordium with a nondisplaced PMI. Heart sounds were normal and a grade 3/6 systolic regurgitant murmur was heard maximally in the tricuspid area. No clicks or diastolic murmurs were heard and pulses were easily palpated. Lungs were clear to auscultation and no organomegaly was documented.

A transthoracic echocardiogram with color-flow Doppler demonstrated normal segmental anatomy and right to left shunting across the patent foramen ovale (Figure 1). The tricuspid valve was redundant, prolapsed in systole and had a 0.4 × 0.9 cm echogenic mass attached to the posterior leaflet (Figure 2A). This mass did not obstruct inflow but did prevent complete closure of the valve causing moderate tricuspid regurgitation (Figure 1). Two additional echogenic masses were seen, a 0.3 × 0.7 cm bright mass in the right ventricular apex (Figure 2B) and a 0.4 × 0.8 cm mildly obstructive mass in the left pulmonary artery (Figures 3A and 3B).

Following the echocardiographic diagnosis, the patient was extubated and removed from O_2 within 24 hours. Clotting studies demonstrated normal coagulation. Head and renal ultrasounds, hearing screen, and genetic evaluation were normal. The patient was discharged from the hospital at five days of age when his oxygen saturation was 80% on room air and his heart murmur was softer.

On a subsequent follow up visit at two weeks of age, his cyanosis had completely resolved and echocardiography demonstrated mild tricuspid regurgitation. At three months, he had minimal tricuspid dysfunction and retraction and calcification of the cardiac masses. At 2 years of age, he was asymptomatic and reached all developmental milestones. His cardiac and neurologic examinations were normal. Echocardiogram showed that the right-sided masses were still present but calcified and smaller. The tricuspid valve mass was embedded in the posterior leaflet and measured 0.3 × 0.5 cm. The right ventricular apical mass was thin and resembled a fibrous strand. The mass located in the left pulmonary artery measured 0.3 × 0.3 cm.

Discussion

The clinical presentation of this patient with cyanosis and a heart murmur immediately after birth appropriately prompted the diagnostic evaluation for cyanotic congenital heart disease. Two-dimensional echocardiography was a valuable tool in the diagnosis of cardiac masses and tricuspid regurgitation as the cause for cyanosis.

Correspondence to: M.T. Donofrio

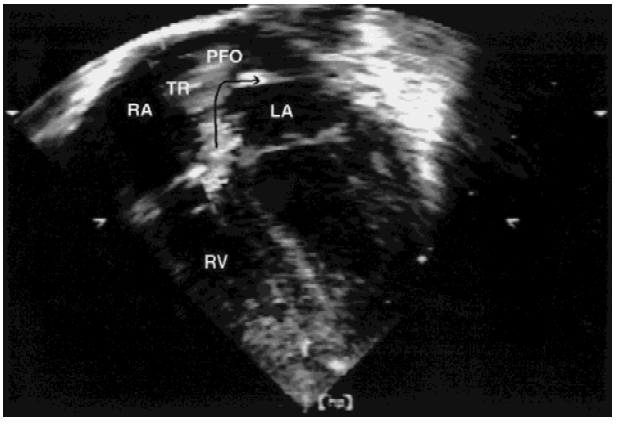

Fig. 1. Apical four-chamber view with color-flow Doppler demonstrates severe tricuspid regurgitation (*TR*) and right-to-left shunting across the patent foramen ovale (*PFO*). *Arrow* denotes direction of shunt. *LA*, left atrium; *RA*, right atrium; *RV*, right ventricle.

Rapid recognition of the etiology of cyanosis directed the course of management. The mechanism of cyanosis is similar to the one in Ebstein's malformation in which severe tricuspid regurgitation increases the right atrial pressure causing right-to-left atrial shunting. The degree of cyanosis improves as the magnitude of tricuspid regurgitation diminishes with the normal decrease in pulmonary vascular resistance after birth [5].

In newborns, a variety of disease processes can affect the tricuspid valve apparatus directly and lead to regurgitation [5]. Depending on the degree of valve dysfunction and the presence of elevated pulmonary vascular resistance, cyanosis and congestive heart failure may appear early after birth. Congenital anomalies are rare, and among these lesions the most common is Ebstein's anomaly.

Tricuspid valve insufficiency may also be associated with Uhl's anomaly, atrioventricular canal, or severe stenosis or atresia of the right ventricular outflow tract. Occasionally, tricuspid insufficiency may occur with a structurally normal valve in the absence of associated lesions, but there is usually a history of a perinatal event resulting in right ventricular and papillary muscle dysfunction. Although we are not aware of any reports of primary tricuspid valve tumors leading to tricuspid regurgitation and cyanosis in the newborn period, a case of tricuspid regurgitation and cyanosis due to chordal rupture forming a tangled mass and resembling a tumor of the valve has been described [1].

Cardiac tumors are among the least common etiologies of cyanosis in the newborn period. The pathophysiology of cyanosis in these cases usually involves a large mass either occupying the ventricular cavity and mimicking single ventricle physiology [3, 7] or obstructing the right ventricular outflow tract and simulating pulmonary atresia [11]. Primary and secondary intracardiac tumors, both benign and malignant, are exceedingly rare in infancy and the information available is limited to a few reports [4]. Primary tumors are more common, and in newborns rhabdomyomas, fibromas, and myxomas have been described [4, 8].

Our patient had three cardiac masses detected by echocardiography—one located on the tricuspid valve, one in the right ventricular apex, and one in the pulmonary artery. All these masses calcified and regressed with time. Because of the multiplicity and regression, it is possible that the masses could be rhabdomyomas. Rhabdomyomas are the most frequent cardiac tumors in newborns, are commonly multiple, and are the only tumors that have the potential for spontaneous regression [9]. These tumors are the primary cardiac finding in children with tuberous sclerosis. Classically, tuberous sclerosis consists of the triad of mental retardation, seizures, and adenoma sebaceum [12]. However, these features may not be present in all patients, and emphasis of these limited features is misleading. It is more appropriate to recognize that the tuberous sclerosis complex presents as a wide spectrum of disease. Major diagnostic features are facial angiofibromas, nontraumatic ungual or periungual fibromas, hypomelanotic macules, Shagreen patches, cortical tuber and subependymal masses, retinal hamartomas, renal angiomyolipomas, and cardiac rhabdomyoma [12]. These clinical features, with the exception of cardiac masses, were not found in our patient. Moreover, rhabdomyomas are usually localized in the left ventricular wall; however, they can be found in the right ventricular wall and rarely on the valves [9]. We are not aware of any reports of the tumor extending into the pulmonary arteries as it did in our patient.

Alternatively, it is possible that the masses seen in this case were multiple thrombotic lesions in the right side of the heart or a primarily tumoral or thrombotic lesion of the tricuspid valve that embolized to the right ventricle and pulmonary artery. Thrombotic lesions of the tricuspid valve in full-term newborns with anatomically normal hearts have been associated with hypoxic insults as the major inciting event in the absence of an obvious coagulation disorder [10].

Neonatal hypoxia creates a unique hemodynamic state of elevated right ventricular pressure and tricuspid insufficiency which leads to high right atrial pressure, turbulence, local stasis, and endocardial damage of the tricuspid valve and sets the milieu for thrombi formation [2]. A case of a newborn with thrombotic lesions of the tricuspid valve of unclear etiology has been reported and the authors postulated that an infection or transitory hypoxia that occurred during intrauterine life caused the thrombi [6]. In our case, a viable cause for increased thrombosis was not identified

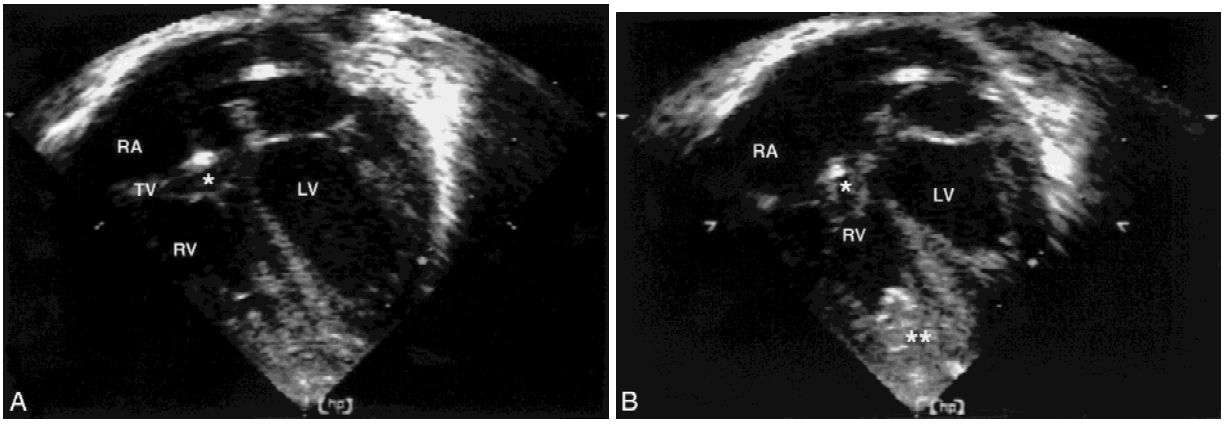

Fig. 2. (**A**) Subxyphoid coronal view demonstrates an echogenic tumor (*) attached to the posterior leaflet of the tricuspid valve (*TV*) prolapsing into the right atrium (*RA*) in systole. (**B**) Subxyphoid four-chamber view shows the same tumor (*) in the right ventricle (*RV*) and an additional tumor (**) attached to the right ventricular apex. *LV,* left ventricle.

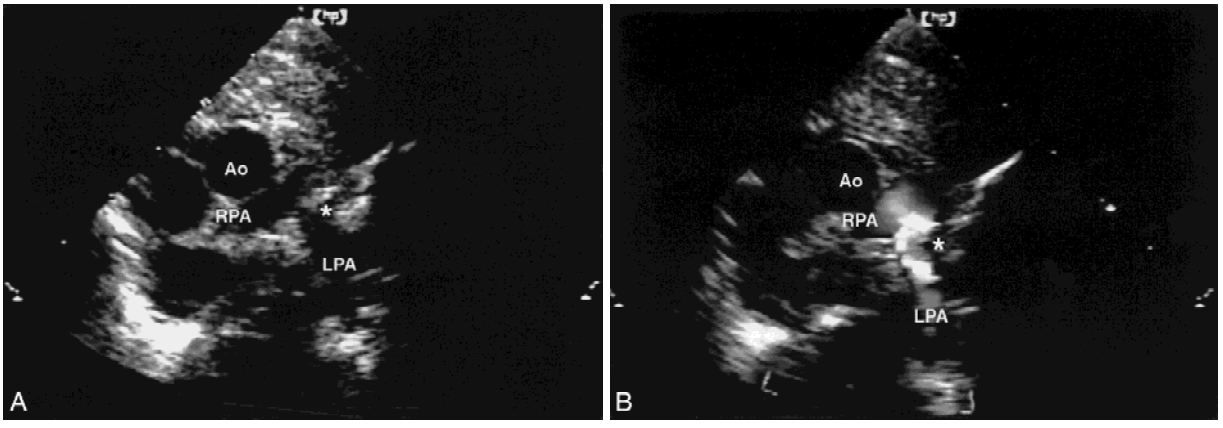

Fig. 3. (**A**) Suprasternal coronal view demonstrates a tumor (*) in the proximal left pulmonary artery (*LPA*) at the bifurcation of the main pulmonary artery. (**B**) Suprasternal coronal view with color-flow Doppler demonstrates the aliasing at the takeoff of the LPA and obstructive nature of the tumor (*). *Ao,* aorta; *RPA,* right pulmonary artery.

and there was no evidence of a significant perinatal event.

We postulate that the ultimate course of the masses in this patient, with fibrosis and calcification, is most consistent with rhabdomyomas of the tricuspid valve and/or right ventricle. The tricuspid regurgitation then created the milieu for thrombi formation before birth. Subsequent *in utero* embolization to the pulmonary artery would explain the presence of the associated mass. Pathologic confirmation of the diagnosis has not been possible due to the benign clinical course of the patient.

This case illustrates an unusual presentation of transient neonatal cyanosis associated with cardiac masses and tricuspid regurgitation. We discussed the mechanism by which cardiac masses can cause cyanosis and conclude that although cardiac thrombi and tumors are rare in infants, they should be included in the differential diagnosis of the cyanotic newborn.

References

1. Atalay S, Imamoglu A, Uluoglu O, Ikizler C (1995) Critical tricuspid regurgitation secondary to ruptured chordae tendineae mimicking a mass on the tricuspid valve in a newborn. *Pediatr Cardiol 16*:133–136
2. Bucciarelli RL, Nelson RM, Egan EA (1977) Transient tricuspid insufficiency of the newborn: a form of myocardial dysfunction in stressed newborns. *Pediatrics 59*:330–337
3. Butto F, Shachar GB, Najmabadi H, Smith G (1994) Massive cardiac tumor presenting as severe cyanosis in a newborn. *Pediatr Cardiol 15*:103–105
4. Chan HSL, Sonley MJ, Moës CAF, et al (1985) Primary and secondary tumors of childhood involving the heart, pericardium, and great vessels. *Cancer 56*:825–836

5. Epstein ML (1995) Congenital stenosis and insufficiency of the tricuspid valve. In: Emmanoulides GC, Riemenschneider TA, Allen HD, Gutgesell H (eds) *Moss and Adams Heart Disease in Infants, Children, and Adolescents: Fifth Edition.* Williams and Wilkins, Baltimore, pp 919–929
6. Hartyánszky IL, Kádár K, Hüttl T, Sápi E, Lozsádi K (1989) Thrombotic lesions of the tricuspid valve in a newborn: surgical management. *Pediatr Cardiol 10*:109–112
7. Marín-Garcia J, Fitch CW, Shenefelt RE (1984) Primary right ventricular tumor (fibroma) simulating cyanotic heart disease in a newborn. *J Am Coll Cardiol 3*:868–871
8. Nadas AS, Ellison C (1968) Cardiac tumors in infancy. *Am J Cardiol 21*:363–366
9. Nir A, Tajik AJ, Freeman WK, et al (1995) Tuberous sclerosis and cardiac rhabdomyoma. *Am J Cardiol 76*:419–421
10. Sussmane JB (1986) Thrombotic lesions of the tricuspid valve in the newborn. *Clin Pediatr 25*:225–227
11. Van der Hauwaert LG (1971) Cardiac tumors in infancy and childhood. *Br Heart J 33*:125–132
12. Weiner DM, Ewalt DH, Roach ES, Hensle TW (1998) The tuberous sclerosis complex: a comprehensive review. *J Am Coll Surg 187*:548–561

DOI: 10.1007/s002460010058

From PediHeart: *Inhaled Nitric Oxide—In Clinical Trial or in Clinical Practice?*

The molecule nitric oxide (NO) is a potent but very short-lived smooth muscle relaxant. When administered by inhalation, NO effect is limited to pulmonary arteriolar musculature. INO Therapeutics, Inc. holds a use patent on iNO and recently announced its intentions to release iNO for use in neonates with pulmonary hypertension—the only approved use—for $3000 for the first day. For other uses, one could apply to the company for free iNO on a research protocol.

The problem is apparent to clinical pediatric cardiologists who use iNO to treat postoperative pulmonary artery hypertension or to test pulmonary vaso-reactivity in the cath lab. Is this going to cost $3000 for a 15–20 minute trial? Would insurance companies pay and, if not, would our hospitals deny us the drug? Should we submit phony research protocols to get iNO for off-label use? To assess the current "standard of clinical practice," I surveyed the readership of *Pediheart.*

The following question was posed on *Pediheart* on 2/3/00. "Do you consider inhaled nitric oxide (iNO) to be a clinically proven agent to test pulmonary vaso-reactivity in the cath lab, or should iNO be on research protocol?"

Results: Sixty-five responses were received from the USA (52), Europe (9), and Canada (4). Sixty-one respondents (94%) answered "Yes" to the question, two had no opinion. Two answered "No" but their explanations suggested that their answer might actually be yes.

Conclusion: Ninety-four to 98% of respondents considered iNO to be a clinically proven pulmonary vasodilator. While iNO is FDA-approved for neonates with pulmonary artery hypertension, most practicing physicians consider that its uses extend beyond the FDA-approved condition, for example in the cath lab or in the postoperative ICU. A large body of literature confirms the clinical efficacy of iNO. This survey provides support for physicians who wish to challenge the limitations on the clinical use of iNO imposed by any regulatory agency, by third-party payers or by the company holding a use patent for iNO.

J. Deane Waldman, M.D., M.B.A.
Children's Hospital Heart Center
University of New Mexico