

Tetralogy of Fallot and Hypertrophic Cardiomyopathy: A Rare Association

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Tetralogy of Fallot is known as the most common cyanotic congenital heart disease and has a prevalence of 10% of all congenital heart diseases. Although many other heart anomalies may coexist, the association of tetralogy of Fallot and hypertrophic cardiomyopathy is extremely rare. We report this association in a 15-month-old female, cyanotic since birth, in her first hospital admission for diagnosis and treatment of recurring cyanotic crises. In addition, a review of the literature and of the problems related to the treatment is provided.

Tetralogy of Fallot may be associated with many other congenital heart diseases, such as atrial septum defects, pulmonary valve anomalies, atrioventricular septal defect, coronary artery anomalies, some venous drainage anomalies, especially persistence of the left superior vena cava, and, rarely, anomalies of the left heart, such as left ventricular hypoplasia and aortic valve anomalies. Tetralogy of Fallot may be part of some genetic syndromes, such as the following: Down's, Klinefelter's, Di George, Goldenhar's, Robinow's, Shprintzen, conotruncal anomaly, and Cantrell pentalogy. Tetralogy of Fallot may also be associated with the use of teratogens, such as trimethadione, thalidomide, and phenylketonuria¹. When it occurs isolated, it is rarely familial¹⁻³.

Hypertrophic cardiomyopathy has been described as a primary disorder of the cardiac muscle, typically isolated, although some rare reports exist of its association with septal defects, coarctation of the aorta, and pulmonary valve stenosis, which is part of the Noonan's syndrome. One case of its association with Friedreich's ataxia has been reported. In approximately 60% of the cases, a typical genetic transmission, autosomal dominant, exists^{1,4,5}.

The association of these 2 heart diseases is extremely rare, and, in human beings, only 2 reports (3 cases) exist in English and 2 others (3 cases) in French⁶⁻⁹.

Case report

The patient is a 15-month-old mulatto female natural and coming from Itapagé, in the northeastern Brazilian state of Ceará, with a history of being born from a normal delivery in the seventh gestational month from a 22-year-old mother. Although the pregnancy was undesired, the mother denied the use of abortive drugs, medications, and the occurrence of diseases during gestation. No diabetes mellitus, cardiac anomalies, or sudden death existed in the maternal familial history, but the paternal history was completely unknown. The mother did not know the newborn's weight at birth, nor her physical examination then, but reported that the newborn was discharged cyanotic and dyspneic on her second day of life. The infant was severely undernourished and difficult to feed. The mother denied respiratory infections. She reported worsening of the cyanosis and appearance of dyspnea after crying. These manifestations subsided spontaneously. The mother also reported that the crises became more frequent, which made her look for medical assistance.

On hospital admission, the physical examination revealed an extremely cyanotic, dyspneic (FR 60mpm), afebrile, pale, irritated on handling, and undernourished child (weight: 6,300 g) with a significant motor deficit and absence of speech. The thorax showed an increased anteroposterior diameter, sternal bulging, preserved thoracic expandability, and physiological pulmonary auscultation. Cardiac auscultation evidenced a heart rate of 140 bpm, regular rhythm, cardiac sounds of normal intensity, and a systolic murmur audible in the entire left sternal margin. The abdomen was flabby, had no visceromegalies, and a right inguinal hernia was evidenced. The pulses were normal. The child also had clubbing of the fingers and her nails looked like the glass of a watch.

On admission, the electrocardiogram showed sinus tachycardia and right atrial and ventricular hypertrophy. The chest X-rays on the left posteroanterior and lateral views

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revealed cardiomegaly and a reduction in the pulmonary flow. The echocardiogram showed tetralogy of Fallot associated with severe asymmetric septal hypertrophy (figs. 1 to 4).

During hospitalization, cyanotic crises were observed and reverted with the usual treatment.

Propranolol (2 mg/kg/day) was started orally, as was the treatment for the other pediatric intercurrent events. The patient underwent palliative surgery (systemic to pulmonary artery anastomosis) and evolved with marked improvement in the cyanosis. The postoperative echocardiogram showed that the systemic-pulmonary shunt was patent.

On follow-up at the age of 2 and one-half years, the child continued to be mildly cyanotic and dyspneic, but with no cyanotic crises, and was gaining weight, although a weight-height deficit persisted. The patient also showed great motor progress, was able to communicate using simple words, and was on treatment with oral propranolol (4 mg/kg/day). The shunt was adequate.

Discussion

In English, we found the report of 3 patients with tetralogy of Fallot associated with hypertrophic cardiomyo-



Fig. 1 – In the parasternal long-axis view, a marked septal hypertrophy with perimembranous ventricular septal defect and aortic override of less than 50% is observed.

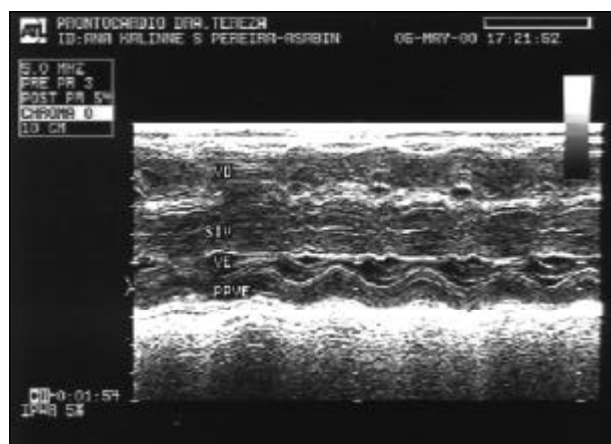


Fig. 2 – In the transverse view of the ventricles, a more marked septal hypertrophy is seen as compared with the posterior wall.



Fig. 3 – In the parasternal short-axis view, deviation of the infundibular septum to the right ventricular outflow tract is seen, causing severe infundibular stenosis with confluent pulmonary trunk and arteries.

pathy. One patient was a 13-year-old adolescent male, with a history of dyspnea and cyanosis, whose condition had worsened in the 4 months preceding the report, and who, after the hemodynamic study, began to have repetitive cyanotic crises. The patient underwent a successful aortopulmonary shunt on an emergency basis⁶. The other 2 patients were newborn infants with multiple congenital malformations, who required a systemic-to-pulmonary artery anastomosis. One of the latter patients was 3 and one-half years old at the time of the report, was on chronic use of propranolol, and the other, also on chronic use of propranolol, died suddenly at the age of 10 months⁷.

In the French literature, we found 2 studies. The first study was about a newborn with multiple congenital malformations diagnosed on echocardiography on the 10th day of life, who, because of mild cyanosis, was followed up until the age of 5 months, when, after aggravation of the symptoms, underwent a hemodynamic study and treatment with propranolol. Initially, considerable improvement was obtained, but later, the septal hypertrophy worsened, and at the age of 22 months, treatment with verapamil was started⁸. The second study was about 2 adolescents aged 14 and 15



Fig. 4 – In the apical 4-chamber view, severe asymmetric septal hypertrophy is evident.

years. The first patient had a hemodynamic diagnosis of pulmonary atresia with ventricular septal defect associated with left ventricular concentric hypertrophic cardiomyopathy, which evolved to heart failure, and the patient was treated with digitalis and diuretics. The second patient, who had been hemodynamically diagnosed with tetralogy of Fallot associated with left ventricular diffuse hypertrophic cardiomyopathy, underwent definitive correction of the tetralogy of Fallot with muscle resection and died in the postoperative period due to cardiogenic shock⁹.

The clinical treatment of tetralogy of Fallot includes an acute approach to the cyanotic crises and prophylaxis with propranolol in patients who are not considered good candidates for surgical treatment. In tetralogy of Fallot with a favorable anatomy, total surgical correction is the treatment of choice. When surgery is necessary in patients with an unfavorable anatomy, a palliative procedure with a systemic-to-pulmonary artery anastomosis is performed to increase pulmonary blood flow^{2,3}.

The clinical findings in patients with hypertrophic cardiomyopathy varies. Some patients may deteriorate progressively or die suddenly; others, however, may remain stable for many years. The beginning of symptoms during childhood is considered a poor prognostic signal. The treatment of choice of a symptomatic child with hypertrophic cardiomyopathy is the adrenergic beta-blocker due to its sympatholytic effect. This medication, however, does not have any effect on hypertrophy progression and does not eliminate the risk of sudden death. Calcium channel blockers are another effective alternative. Verapamil is associated with an increase in sudden death in children under the age of 1 year, and, therefore, is not recommended in this age bracket. Its use in other children with hypertrophic cardiomyopathy still requires deeper investigation.

Patients with arrhythmias should be treated, and amiodarone has been suggested as more effective than verapamil in reducing ventricular arrhythmias. Its use has been limited to children with refractory or lethal arrhythmias due to the risk of severe secondary effects with its chronic use. In patients with bradycardia, maintenance of atrial synchrony with a pacemaker is important. Surgical treatment has been reserved for patients with severe symptoms, with gradients of 50 mmHg or greater, when medicamentous therapy does not provide adequate relief. The use of dual-chamber pacemakers has been proposed as an alternative to surgical treatment with clinical and hemodynamic improvement. The efficacy of this treatment during childhood is currently being assessed in several centers. When medical therapy fails, another alternative is heart transplantation^{4,5}.

Management of patients with tetralogy of Fallot associated with hypertrophic cardiomyopathy differs greatly from that of patients with tetralogy of Fallot alone, whose clinical and surgical management based on safe evidence in most cases assures good long-term results. The prognosis of patients with hypertrophic cardiomyopathy, however, is poor, mainly when the symptoms appear during childhood as already mentioned.

In our case, we chose palliative surgical treatment with systemic-to-pulmonary artery shunt and maintenance of the therapy with propranolol, adequate to the pharmacological treatment of the 2 heart diseases, because we observed a better prognosis in the preceding cases undergoing this management.

In conclusion, the recognition of tetralogy of Fallot associated with hypertrophic cardiomyopathy is of great importance, because of the therapy, which has not yet been totally established, making the surgical approach difficult, and because of the still unknown long-term prognosis.

References

1. Bum F. The aetiology of congenital heart disease. In: Anderson RH, Macartney FJ, Shinebourne EA, Tynan M, eds. *Paediatric Cardiology*. London: Churchill Livingstone, 1987: 15-63.
2. Neches WH, Park SC, Etedgui JA. Tetralogy of Fallot and Tetralogy of Fallot with Pulmonary Atresia. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Paediatric Cardiology*. 2nd ed. Baltimore: Williams & Wilkins, 1998: 1383-411.
3. Zuberbuhler JR. Tetralogy of Fallot. In: Adams IH, Emmanouilides GC, Rimenschneider IA, eds. *Moss' Heart Disease in Infants, Children and Adolescents*. 5th ed. Baltimore: Williams & Wilkins, 1995: 998-1017.
4. Denfield SW, Gajarski RJ, Towbin JA. Cardiomyopathies. In: Garson A, Bricker JT, Fisher DJ, Neish SR, eds. *The Science and Practice of Paediatric Cardiology*. 2nd ed. Baltimore: Williams & Wilkins, 1998: 1851-83.
5. Maron BJ. Cardiomyopathies. In: Adams IH, Emmanouilides GC, Rimenschneider TA, eds — *Moss' Heart Disease in Infants, Children and Adolescents*; 5th ed. Baltimore: Williams & Wilkins, 1995: 940-53.
6. Rao AS, Gupta SK, Reddy KN, et al. Tetralogy of Fallot with hypertrophic cardiomyopathy — an unknown combination. *Indian Heart J* 1989; 41: 344-7.
7. Lewin MB, Towbin JA, Thapar MK, et al. The rare association of tetralogy of Fallot with hypertrophic cardiomyopathy: report of 2 neonatal patients. *Tex Heart Inst J* 1997; 24: 215-7.
8. Grinneiser O, Bourlon F, Redjimi M. Une association pathologic rare: tetralogie de Fallot et hypertrophie septale asymetric. *Arch Mal Coeur Vaiss* 1994; 77: 577-80.
9. Touze JE, Chauvet J, Mardelle T, et al. Myocardiopathie hypertrophique et tetralogie de Fallot: etude de deux observations. *Ann Cardiol Angeiol* 1986; 35: 31-4.