

Percutaneous Treatment of Congenital Heart Defects in the Rubinstein-Taybi Syndrome

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ABSTRACT

The Rubinstein-Taybi syndrome is a genetic disorder characterized by distinctive facial features, abnormalities in hands and feet, microcephaly and mental retardation. Approximately 30% of subjects with this syndrome have associated congenital heart defects.

This presentation describes two cases of patients with Rubinstein-Taybi syndrome associated with congenital heart defects: a 25-year-old patient with juxtaductal native aortic coarctation and an 11-month old infant with a large patent ductus arteriosus. Both patients underwent successful percutaneous intervention, with favorable long-term outcome.

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Key words

> Rubinstein-Taybi syndrome - Congenital heart defect - Coarctation of the aorta - Patent ductus arteriosus - Percutaneous treatment

Abbreviations

> LE	Lower extremity	RSTS	Rubinstein-Taybi syndrome
UE	Upper extremity		

INTRODUCTION

The Rubinstein-Taybi syndrome (RSTS) is a genetic, usually sporadic disorder characterized by distinctive facial features, abnormalities in hands and feet, microcephaly and mental retardation. It is caused by a microdeletion of chromosome 16p13.3, or by a mutation or deletion of the CREB-binding protein (CBP) or E1A-binding protein (p300) gene. (1)

Syndrome prevalence is one in 100000–125000 births and life expectancy is normal. Subjects with RSTS commonly develop meningiomas, other brain tumors, and leukemia. Approximately 30% of subjects with this syndrome have associated congenital heart defects, mainly patent ductus arteriosus, ventricular septal defect and atrial septal defect. (2)

This presentation describes two cases of RSTS associated with congenital heart defects (patent ductus arteriosus and coarctation of the aorta) which were successfully treated with percutaneous intervention.

CASE REPORT

Case 1

The first patient was a 25-year-old man, who was the first-born child of a couple without pathological family history. He had been born at full term weighing 3250 g. Coarctation of the aorta was diagnosed when he was

one month old and conservative management was undertaken. Due to undescended testicles and to the clinical suspicion of a genetic syndrome (distinctive facial features, abnormalities in hands and feet and mental retardation), genetic tests were performed, confirming RSTS.

At the age of 24, he was evaluated in his home town due to dyspnea and poor exercise capacity and the diagnosis of native aortic coarctation was made again. He was referred to our department to evaluate the possibility of performing a percutaneous intervention. The physical examination revealed normal S1, an ejective systolic murmur grade 2/6 heard at the lower left sternal border and at the back, and normal S2. Femoral pulses were absent. Blood pressure was 130/80 mm Hg in the upper extremities (UEs) and 80/40 mm Hg in the lower extremities (LEs). The electrocardiogram showed sinus rhythm and voltage criteria for left ventricular hypertrophy. The chest X-ray revealed mild left ventricular enlargement. Magnetic resonance imaging demonstrated neck vessels normally arising from the left aortic arch and a severe juxtaductal coarctation of the aorta with scarce collateral circulation.

Under general anesthesia, a BIB balloon (NuMed™, USA) was percutaneously introduced and insufflated and a CP stent was successfully implanted (Figure 1).

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Postsurgical controls at 15 days, 3 months and 6 months showed significant clinical improvement without differences between UE and LE blood pressure (110/60 mm Hg) and recovery of LE pulses. A chest X-ray performed during the last control showed that the stent was in its normal position with absence of fractures.

Case 2

The second patient was an 11-month old premature girl born at 34 weeks weighing 1700 g at birth, and 6300 g at the moment of consultation. The diagnosis of RSTS was made by genetic tests due to phenotypic features when she was one month old. The clinical findings included tachypnea, heavy sweating, inadequate weight gain and frequent respiratory infections. The physical examination revealed normal S1, multiple clicks, a continuous murmur grade 3/6 heard along the upper left sternal border and S2 with slightly increased intensity. The liver was palpable 2 cm below the right costal margin. The infant was under daily treatment with digoxin and furosemide. Color Doppler echocardiography showed presence of a patent ductus arteriosus with a diameter of 4.5 mm, dilated left chambers and moderate pulmonary artery hypertension.

Percutaneous closure of the patent ductus arteriosus was performed under general anesthesia. A Nit-Occlud PDA-R device (pfm™, Germany), was implanted by antegrade access achieving immediate occlusion of the defect (Figure 2). The patient was evaluated 10 days, 3 months and 6 months after the intervention. There was no residual shunting and significant clinical improvement was evident. The weight curve showed an ascending trend.

DISCUSSION

Cardiac malformations present at birth are an important component of pediatric cardiovascular disease and constitute a major percentage of clinically significant birth defects, with an estimated prevalence of 6-8 per 1000 live births. (3)

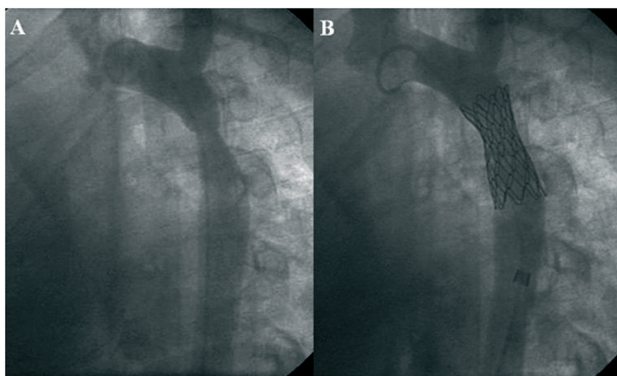


Fig. 1. Angiographies in the left anterior oblique projection (60°) before (A) and after (B) stent implant due to moderate to severe coarctation of the native aorta with scarce collateral circulation. The neck vessels arise normally from the left aortic arch. After stent implant, the aortic diameter shows significant improvement and the pressure gradient across the coarctation is no longer present.

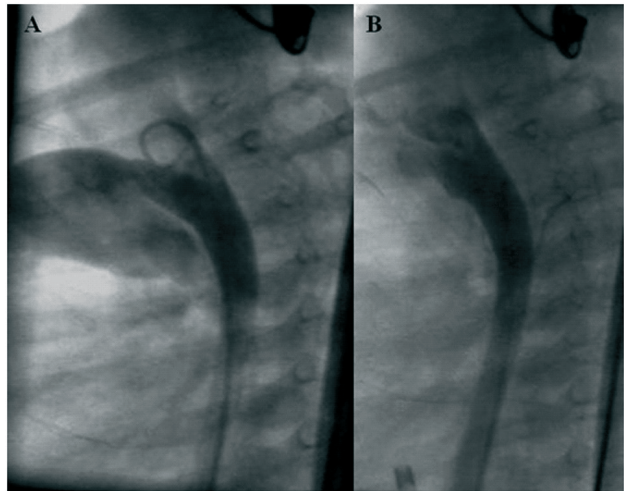


Fig. 2. Angiographies in the left lateral projection (90°) before (A) and after (B) percutaneous occlusion of a patent ductus arteriosus with an occluder device. A large patent ductus arteriosus is seen in A with well-defined aortic ampulla and a constriction near the pulmonary artery. The main pulmonary artery and the dilated pulmonary branches are well opacified. The device is seen in situ after implantation (B) with complete occlusion of the defect.

Although most congenital heart defects occur as an isolated anomaly, approximately 25% are associated with other congenital malformations or form part of a specific pattern or a genetic syndrome. (4)

Initially described by Michail et al. in 1957 as broad thumb-hallux syndrome, and then redescribed in 1963 by Rubinstein and Taybi (5), the RSTS syndrome is characterized by distinctive facial features and abnormal extremities. The facial appearance includes prominent beaked nose with the nasal septum extending well below the alae, associated with broad and short thumbs and big toes which are frequently forked. (1) The prevalence of congenital heart defects is approximately 33%. Stevens and Bhakta specifically described the incidence of heart defects among 138 subjects with RSTS included in their study, and estimated that 45 of them (32.6%) had a cardiac abnormality. Most of the patients had single defects including, in decreasing order, atrial septal defect, ventricular septal defect, patent ductus arteriosus, coarctation of the aorta, pulmonary valve stenosis, or bicuspid aortic valve. Sixteen patients had complex congenital heart defects comprising two or more abnormalities. Pulmonary valve stenosis was present as a single abnormality in only one patient. (6)

Patent ductus arteriosus accounts for about 10% of cases of congenital heart disease and is the second most common defect after bicuspid aortic valve.

Occasional cases are related to specific genetic defects as trisomies 21 and 18 and 4q-, 16p 13.3 (RSTS) and 9p- deletion syndromes. Patients with moderate to large ductus present hemodynamic impairment, with symptoms of high output heart failure and probability of developing pulmonary artery hypertension

in the long-term. Nowadays, percutaneous closure of PDA constitutes the treatment of choice for this condition with excellent outcomes, occlusion rates > 90% and infrequent complications. Surgical closure is another option and is indicated in premature patients unresponsive to the initial medical treatment, in small infants with large defects or in cases of failed percutaneous closure. (7)

Coarctation of the aorta is the fifth congenital heart defect in order of frequency, with an incidence of 1 per 2500 live births. The etiology is controversial, and family cases and association with genetic deletions have been described. Some patients may remain asymptomatic until adolescence if aortic coarctation is not severe or prominent collateral circulation has developed. The use of balloon angioplasty was first reported in 1982, with promising initial results, yet with high incidence of recoarctation and mechanical abnormalities of the aortic wall (aneurysms, dissections or significant intimal tears) during follow-up. Stent implant has improved the outcomes, reducing the incidence of recoarctation of the aorta and of mechanical abnormalities of the aortic wall. It is currently the treatment of choice in children and adults. (8) Covered stents are indicated for patients with severe coarctation of the aorta, with significant reduction in the luminal diameter of the segment where the stent is going to be implanted, coarctation of the aorta associated with patent ductus arteriosus and recoarctation of the aorta associated with aneurysms or other mechanical abnormalities of the arterial wall secondary to surgery or after previous balloon angioplasty. Stent implant is currently suggested as preferred treatment in patients > 40 years or in women with Turner syndrome. (9, 10)

So far, percutaneous treatment of congenital heart defects in patients with RSTS has been rarely described. This experience demonstrated the importance of percutaneous treatment of simple congenital heart defects with device closure of patent ductus arteriosus and stent implant in coarctation of the aorta in patients with RSTS. These procedures can be successfully and safely performed in this type of patients. We are convinced of the importance of reporting these cases to confirm that percutaneous treatment of congenital heart defects associated with a syndrome of low prevalence has favorable outcomes.

RESUMEN

Tratamiento percutáneo de cardiopatías congénitas en el síndrome de Rubinstein-Taybi

El síndrome de Rubinstein-Taybi es producido por una anomalía genética y se caracteriza por una facies típica, anomalías de manos y pies, microcefalia y retraso mental. Alrededor del 30% de los individuos afectados tienen defectos cardíacos congénitos asociados.

En esta presentación se describen los casos de dos pacientes con diagnóstico de síndrome de Rubinstein-Taybi asociado con alteraciones cardíacas congénitas. Uno de ellos, de 25 años, presentaba coartación de la aorta nativa, localizada en la región yuxtaductal, y el otro, de 11 meses de edad, mostraba un conducto arterioso permeable de tamaño grande. Ambos pacientes recibieron tratamiento intervencionista percutáneo exitoso, con evolución alejada satisfactoria.

Palabras clave > Síndrome de Rubinstein-Taybi -
Cardiopatía congénita - Coartación de la aorta - Ductus arterioso permeable -
Tratamiento percutáneo

Conflicts of interest:

None declared.

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