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Anomalous origin of the left coronary artery from the pulmonary artery with large anterior myocardial infarction and ischemia: successful tunnel repair and concomitant heterotopic heart transplantation as biological bridge to recovery

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Sir: The anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) causes myocardial ischemia, infarction, and cardiac failure, leading to a high mortality rate of 90 % in infancy [10]. Early diagnosis and surgical repair may prevent further myocardial damage. Transposition of the anomalous coronary artery to the aorta and creation of a tunnel within the pulmonary artery to connect the ostium of the left coronary artery to the aorta has become a standard surgical technique with good results. The extent of myocardial ischemia significantly influences surgical mortality rates [9].

A 4-month-old female infant was referred to our cardiac center with mild symptoms of cardiac failure, holosystolic heart murmur with propagation to the left axilla, and signs of myocardial infarction on the ECG. Echocardiography revealed severe hypokinesia of the anterolateral wall, an increased density of this part of the ventricular wall and the anterior papillary muscle, and severe mitral regurgitation. The origin of the left coronary artery could be visualized neither from the aorta nor from the pulmonary trunk.

The diagnosis of ALCAPA was confirmed by cardiac catheterization, which showed that the left coronary artery was filled by collaterals from the right coronary artery. The left ventricular ejection fraction was calculated as 19 % (Table 1). SPECT imaging using a Tl-201 tracer and persantin showed a large area of diminished myocardial perfusion of the anterolateral wall indicative of scaring after myocardial infarction, but also a large area of tracer redistribution compatible with myocardial ischemia.

Because of the severely impaired left ventricle, standard surgery for ALCAPA repair seemed to be too hazardous. We decided to transplant a heart heterotopically with the intention of removing the allograft after sufficient recovery of the native heart, since a pediatric left ventricular assist device was not available and our experience with extra-corporeal membrane oxygenation was rather limited at that time.

On 4 September 1991, a suitable donor heart without a major HLA mismatch became available. For ALCAPA repair, direct implantation of the coronary artery into the aorta was impossible, and therefore tunnel repair was performed. Heterotopic heart transplantation followed, with the donor pulmonary artery connected to the patient's right atrium to augment left ventricular function only.

The postoperative course was uneventful. Immunosuppression consisted of OKT3, cyclosporin A, azathioprine, and steroids. On postoperative day 10, an acute rejection episode was treated with bolus steroids. Cardiac catheterization at day 36 confirmed excellent allograft function. The ejection fraction was 76 %, and the coronary arteries were normal except for a circumscript narrowing of the left main stem (Fig. 1 a). The left ventricular function patient's native heart showed significant improvement, with an ejection fraction of 54 % and a cardiac index of 2.6 l/min per m^2; however, mitral regurgitation was still significant (Table 1). No ischemic myocardium was evident in the Tl-201 SPECT. Due to the mitral insufficiency, we did not dare to explant the graft, and we discharged the patient after 68 days.

Immunosuppression was converted to a dual regimen including cyclosporin A and azathioprine, with steroids being discontinued after 48 days. Cyclosporin A levels, as measured by whole blood fluorescence polarization immuno-assay, ranged from 86 to 432 ng/ml (mean 198) in the 1st year, from 73 to 350 ng/ml (mean 149) in the 2nd year, and from 72 to 288 ng/ml (mean 156) in the 3rd year after transplantation. The patient was monitored by serial echocardiography, which gave no evidence of acute rejection episodes. The absence of cytomegalovirus infection was confirmed by serial serological and cultural examinations. Coronary angiography 1.5 years after transplantation showed diffuse narrowing of all major epicardial branches compatible with transplant vasculopathy, while left ventricular function was still excellent. The degree of mitral regurgitation remained unchanged. The child grew well and developed normally.

On 7 June, 1995, the patient was readmitted for fever of unknown origin. The child seemed moderately compromised but revealed no signs of infection. An ECG demonstrated only one type of QRS morphology, in contrast to previous recordings where two QRS types represented the patient's two hearts. Echocardiography showed complete arrest of the allograft with thickening of the ventricular wall. The cyclosporin A level was 135 ng/ml; the leukocyte count (2900 µl) and the ratio of T helper/suppressor cells (3.3:1) were in an acceptable range. Elevated D-dimer levels (2.0 mg/l) indicated activation of the coagulation system. Cardiac catheterization confirmed cardiac arrest of the donor heart and severe vasculopathy (Fig. 1 b), as well as an excellent recovery of the patient's own heart, with a left-ventricular ejection fraction of 75 % and a cardiac index of 3.1 l/min per m^2. Since transesophageal echocardiography led us to suspect thrombus formation in the atria of the allograft, urgent graft explantation was neccessary. Pathologic examination of the explanted graft confirmed severe occlusive vasculopathy and revealed disseminated, focal myocardial necrosis of both ventricles. Moreover, a mild acute diffuse rejection grade I B [1] was evident. The postoperative course was uneventful. During the following 9 months, the patient did not present with further abnormal findings except for moderate mitral regurgitation, which was shown by echocardiography.

The extent of preoperative myocardial damage in ALCAPA determines perioperative morbidity and mortality [9]. As our patient had extensive myocardial necrosis and ischemia, standard surgical repair seemed to be too hazardous. However, recovery of left ventricular function was likely, since there was a considerable amount of hibernating myocardium. As ventricular support devices for small children were not available at our institution at that time, and as they offered only poor success rates, we decided to perform ALCAPA repair simultaneously with heterotopic heart transplantation to temporarily support left ventricular function. The feasibility of adjuvant

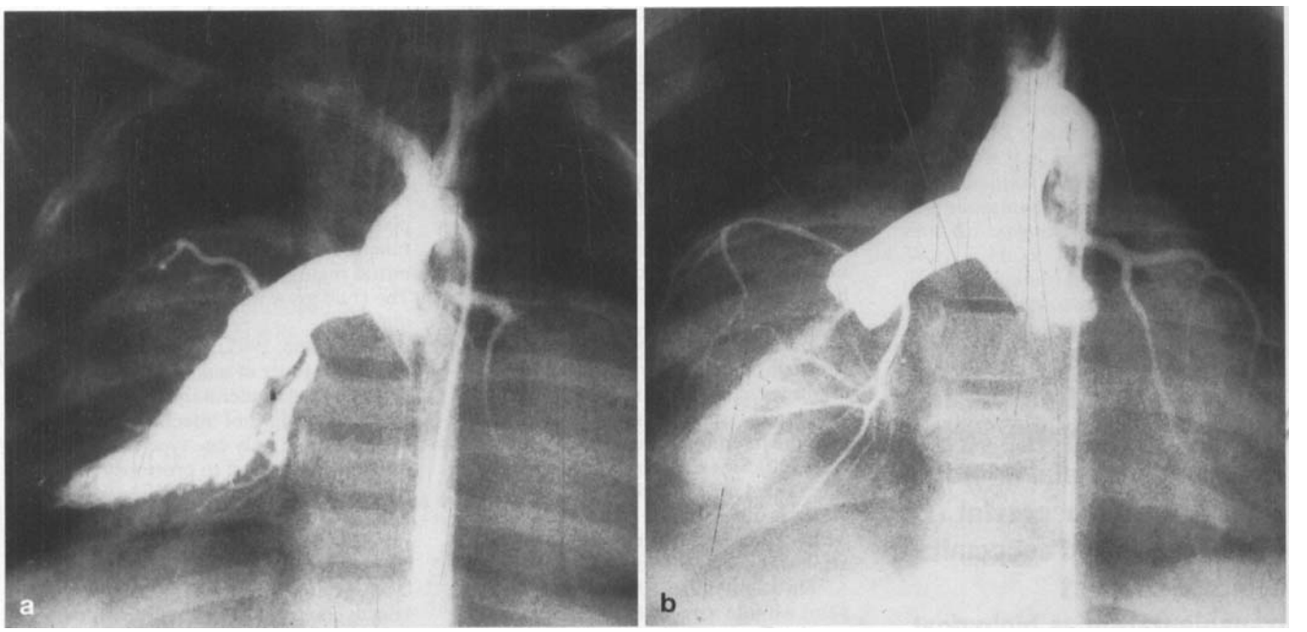

Fig. 1 **a** Left ventricular angiocardiography of the donor heart 5 weeks after transplantation demonstrates normal size and distribution of the coronary arteries aside from a mild narrowing at the origin of the left coronary artery. **b** Aortic root angiography 1 day prior to explantation reveals diffuse narrowing of both coronary arteries and a mild aortic regurgitation of the donor heart. The aortoaortic anastomosis is widely patent. The former anomaly-originating left coronary artery is filled from the ascending aorta through an intrapulmonary artery tunnel

Table 1 Findings revealed by cardiac catheterization (*LV* Left ventricle, *EF* ejection fraction, *CI* cardiac index, *EDP* end-diastolic pressure, *LCA* main stem of the left coronary artery, *LAD* left anterior descending coronary artery, *RCA* right coronary artery, *preop* preoperative, *po* postoperative)

Catheterization	First preop	Second 5 weeks po	Third 1.5 years po	Fourth 4.7 years po
Native LV				
EF (%)[a]	19	54	83	75
CI (l/min per m^2)[b]	–	2.6	3.9	3.1
EDP (mmHG)	18	4	9	10
Graft LV				
EF (%)[a]	–	76	70	0
EDP (mmHG)	–	4	6	–
Diameter[c] (mm)				
LCA	–	2.4	1.4	1.5
LAD	–	1.1	1.0	1.0
RCA proximal	–	1.8	1.4	1.2
RCA distal	–	2.0	0.9	1.0

[a] Ejection fraction was determined by the area/length method
[b] Cardiac index was measured by thermodilution
[c] Diameter of the coronary arteries was measured by quantitative coronary angiography

native heart surgery during heterotopic heart transplantation had already been proven in adults [2, 3, 5]. Orthotopic transplantation was not considered because of the large area of ischemic but viable myocardium [7]. A waiting period of several months could readily be accepted, as our patient exhibited only mild symptoms of congestive heart failure.

We routinely use triple drug immunosuppression and induction therapy with monoclonal or polyclonal antibodies. In pediatric transplantation, we try to wean the patients from the steroids as early as possible and maintain the cyclosporin level at 100–150 ng/ml after 12 months. Patient monitoring consists of serial echocardiography and analysis of T-cell subsets, while endomyocardial biopsies are carefully avoided. Since we did not find any evidence of acute rejection in the follow-up, we maintained a low level of immunosuppression (< 150 ng/ml) and a T-helper/suppressor-cell ratio of 3:1. With this regimen the patient grew well and developed normally. No hazards related to immunosuppression occurred.

The pathophysiology of transplant vasculopathy is still unknown. Increasing evidence suggests that low levels of immunosuppression and an increased number of mild rejection episodes may contribute to the process [4]. No specific risk factors, such as multiple acute rejection episodes, cytomegalovirus infection, or major HLA mismatch, were present in our patient. Considering the excellent graft function in spite of considerable transplant vasculopathy, the significant recovery of the native heart, and our intention to reduce the side effects of immunosuppression, we did not alter the drug regimen. The ensuing graft deterioration was expected to occur, even though we could not predict when.

Our case readily demonstrates that patients with congenital heart disease and severely impaired ventricular function with the potential of recovery may benefit from

temporary left ventricular assistance. Since mechanical bridging in small infants is still a very demanding task, heterotopic heart transplantation may be considered as an alternative, even if only a few patients can undergo a combined operative procedure due to the tremendous shortage of donor organs [6, 8]. Management of immunosuppression for biological bridging should be based on the rationale that over-immunosuppression may be more harmful in this setting.

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