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Tricuspid valve insufficiency as a complication of endomyocardial biopsy

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Abstract. The purpose of this study was to investigate the occurrence of major tricuspid insufficiency caused by endomyocardial biopsy in heart transplant recipients. Endomyocardial biopsy was used for the detection of rejection and Doppler echocardiography was performed at regular intervals. Six of 96 heart transplant patients (6.3%) had sudden appearance of large tricuspid regurgitation, all of which were directly related to a preceding biopsy. Chordal tissue was identified histologically in biopsy samples of all six patients. All patients developed symptoms of right ventricular failure which was confirmed by right heart catheterization. Three patients subsequently underwent valvuloplasty for ruptured chordae tendineae of either of the three leaflets. Two of these three patients were free from symptoms during follow-up, but the third patient developed moderate tricuspid regurgitation and clinical symptoms. It is concluded that endomyocardial biopsy, although it is the most useful tool for detection of rejection, should be used with caution with regard to anatomical structures and the risk of damage to the tricuspid valve must not be neglected. It is also concluded that valvuloplasty of the tricuspid valve can be successfully performed in a transplanted heart.

Key words: Chorda tendineae rupture – Echocardiography – Endomyocardial biopsy – Heart transplantation – Tricuspid insufficiency

Percutaneous endomyocardial biopsy was introduced by Caves et al. in 1972 and was an important contribution to the detection of rejection after heart transplantation [4]. The technique is still the preferred method for diagnosis of rejection in the transplanted heart and is regarded as safe with a low morbidity and mortality. Complications such as transient arrhythmias, transient bundle branch block, transient nerve palsies, puncture site bleedings and endocarditis occur in low frequency. Major complications are rare, cardiac perforation, pneumothorax and tamponade being reported in less than 0.4% [4, 5]. Henzlova et al. recently reported coronary artery–right ventricular fistulas in four out of 74 patients after endomyocardial biopsies [8].

Rupture of chordae tendineae of the tricuspid valve as a complication of endomyocardial biopsy has recently been reported by Braverman et al. [3] in five heart transplant recipients.

The aim of the present study was to investigate the occurrence of large tricuspid valve insufficiency secondary to chordal destruction caused by the bioptome when obtaining endomyocardial biopsies in heart transplant recipients.

Patients and methods

Between January 1988 and August 1991, 96 orthotopic cardiac transplantations were performed in 78 men and 18 woman at our center. Ages ranged from 16 to 63 (mean 43) years.

To detect rejection episodes, weekly endomyocardial biopsies were used during 6 weeks post-transplantation. Thereafter, biopsies were obtained every fortnight for 6 weeks, monthly for 3 months, and then every 3 months. Biopsies were also occasionally obtained when rejection was clinically suspected.

In the standard technique for right ventricular biopsy a bioptome (Caves–Schultz) is percutaneously introduced into the right internal jugular vein through an introducer, and guided by fluoroscopy. The bioptome is advanced with its jaws closed until it reaches the right ventricular septal endocardium. The bioptome is withdrawn 1 cm, and with its jaws opened, it is readvanced into the septal endocardium. The jaws are then closed, and the bioptome is withdrawn with the biopsy [4]. Wnen the standard approach offered difficulties the right femoral vein was punctured. In rare cases the left subclavian vein was used.

Doppler echocardiography was performed after each biopsy for the first 2 months and then at the yearly follow-up. We used an Acuson-128 or Acuson-128XP (Acuson, Mountain View, Calif., USA) equipped with a 3.5 or 2 MHz phased array transducer to obtain two-dimensional echocardiographic recordings. The three patients who were subjected to tricuspid valvuloplasty were also investigated through the transoesophageal approach using a 5 MHz transducer. The degree of tricuspid regurgitation was semiquantitated by colour-flow Doppler and by continuous-wave Doppler on the basis of the systolic regurgitant flow relative to the area of the right atrium as well as on the basis of the intensity of the regurgitant jet (Table 1) [3, 7, 13].

The sudden occurrence of large (grades 3–4) tricuspid valve regurgitation was regarded as a possible adverse effect of a preceding biopsy. In these patients the biopsy samples were histologically re-

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Table 1. Semiquantitative grading of tricuspid regurgitation by echocardiography

Degree of insufficiency	Grade	Echocardiography findings
Minor	0.5	Weak not holosystolic jet
Mild	1	Weak holosystolic jet detectable
Moderate	2	Syst. jet < 50% right atrial area
Moderate to severe	3	Jet > 50% right atrial area
Severe	4	Jet filling right atrium completely

Table 2. Frequency and grading of echocardiographically estimated postoperative tricuspid regurgitation in 96 consecutive patients

	Grading of tricuspid insufficiency				
	< 0.5	1	2	3	4
No. of patients	28	24	27	10	2
%	29.2	25	28.1	10.4	2.1

Echocardiography was not performed in five patients

Table 3. Development and grading of tricuspid insufficiency as estimated by echocardiography and the number of biopsies in three patients who underwent valvuloplasty

Patient number	Tricuspid regurgitation			No. of biopsies[a]
	Before chordal rupture	After chordal rupture	After valvuloplasty	
1	0.5	4	3	17
2	2	3–4	2	16
3	0.5	4	0.5	5

[a] Number of biopsies taken between the last normal echocardiography and the one which first showed a large tricuspid regurgitation

evaluated for the presence of chordal tissue [11, 12]. The biopsies were processed, sectioned and stained as recommended by the International Society for Heart Transplantation [2].

Case reports

A total of 9790 biopsies were obtained during 1780 different procedures. During the first year a mean of 18 biopsies/patient were obtained, with a range of 12 to 27 biopsy procedures for every heart transplant recipient. The following maximum degrees of tricuspid regurgitation were estimated by echocardiography: in 28 patients grade < 0.5, in 24 patients grade 1, in 27 patients grade 2, in 10 patients grade 3, while two patients were judged as having grade 4. Five patients had no echocardiographic evaluation because of early mortality (Table 2). Of nine patients with a large tricuspid regurgitation (grade 3–4), this appeared suddenly in six. In these patients chordal rupture with a prolapse of the tricuspid leaflet into the right atrium was echocardiographically visualized in three cases. In all six patients, chordal tissue, and in three cases papillary muscle, was found histologically. Quite a few samples contained fibrous tissue, which was interpreted as previous biopsy site. This fibrous tissue was not surrounded by endocardium as were the fragments of chordae tendineae when tangenitally sectioned or cross-sectioned. All patients had clinical symptoms of right ventricular failure such as fatigue, dyspnoea, liver tenderness, pitting oedema, and elevated liver enzymes. Right heart catheterization confirmed a moderate right ventricular failure. Pulmonary artery pressures at rest were 31.6 mm Hg ± 6.2 (systolic), 10.6 mm Hg ± 1.3 (diastolic) and 17.0 mm Hg ± 1.0 (mean). Exercise pulmonary artery pressures were 47.8 mm Hg ± 6.2 (systolic), 16.8 mm Hg ± 4.6 (diastolic) and 29.8 mm Hg ± 4.3 (mean). The three patients who subsequently underwent valvuloplasty because of suspected rupture of chordae tendineae are described in detail below.

Case 1

A 51-year-old man who underwent heart transplantation for end-stage ischaemic heart disease had a pulmonary vascular resistance of 4/2 (undilated/dilated) Wood units. One month postoperatively only minimal tricuspid regurgitation was found (grade 0.5) and the patient had no clinical symptoms. Five months later regurgitation grade 4 and prolapse of the septal leaflet of the tricuspid valve were detected. The patient had pitting oedema, dyspnoea, fatigue, liver tenderness and elevated liver enzymes. Chordal tissue and papillary muscle were found histologically from one biopsy taken in the interval between the last normal and the first pathological echocardiographic investigation. During this interval two moderate rejections were treated with high dose methylprednisolone and antithymocyte globulin, respectively. Furthermore, two mild rejections were treated with bolus doses of methylprednisolone. Altogether, the patient was subjected to 17 biopsy procedures between the last normal echocardiography and the one which first showed a large regurgitation. One year after the transplantation, valvuloplasty with a Carpentier's ring no. 32 was performed via a sternotomy. Ruptured septal chordae tendineae were noticed. Postoperatively, echocardiography showed tricuspid regurgitation grade 2, which 6 months later had increased to grade 3 concomitant with appearance of symptoms like fatigue and oedema.

Case 2

A 45-year-old man with end-stage ischaemic heart disease and a pulmonary vascular resistance of 5/2.8 Wood units underwent heart transplantation. One week after transplantation tricuspid regurgitation grade 2 was present. This increased to grade 3 4 months postoperatively with a prolapse of the septal leaflet into the right atrium and clinical symptoms of oedema and fatigue (Fig. 1). Chordal tissue and structures from papillary muscle were found in three biopsies from the same occasion. During that time 16 biopsies were taken and a moderate rejection was treated with antithymocyte-globulin. Two mild rejections were treated with bolus doses of methylprednisolone. The patient subsequently underwent valvuloplasty via sternotomy and received a Carpentier's ring no. 34. Some chordae tendineae of the septal leaflet were ruptured. The tricuspid regurgitation was postoperatively been graded 2, and the patient was currently doing well and free from symptoms.

Case 3

This patient is a 41-year-old man with ischaemic heart disease who received a transplant in 1984, and another 7 years later due to chronic rejection. He had a complicated second postoperative course with renal insufficiency, wound rupture and mediastinitis. Echocardiographically, the tricuspid regurgitation was estimated at grade 0.5. It was technically difficult to perform the endomyocardial biopsy because of a rotation of the heart. The patient developed signs of vascular rejection and was successfully treated with plasmapheresis four times. After a biopsy 4 months postoperatively tricuspid valve regurgitation of grade 4 was suddenly detected and echocardiography showed evidence of chordal rupture of the tricuspid valve with leaflet prolapse into the right atrium. Histologically, connective tissue like chordae tendineae was found in the biopsy taken immediately preceding the echocardiography (Fig. 2). Clinical symptoms such as pitting oedema, dyspnoea, and fatigue occurred. Valvuloplasty was performed via a right thoracotomy and cannulation of the femoral artery and caval veins and a Carpentier's ring no. 32 was inserted. Chordae tendineae from the lateral part of the anterior tricuspid leaflet and the lateral part of the posterior tricuspid leaflet were found to be ruptured. Postoperatively the patient had renal insufficiency and underwent dialysis. One month postoperatively there was no tricuspid regurgitation and the patient was doing well.

Discussion

After heart transplantation tricuspid regurgitation of varying degree is found. Initially this can be caused by in-

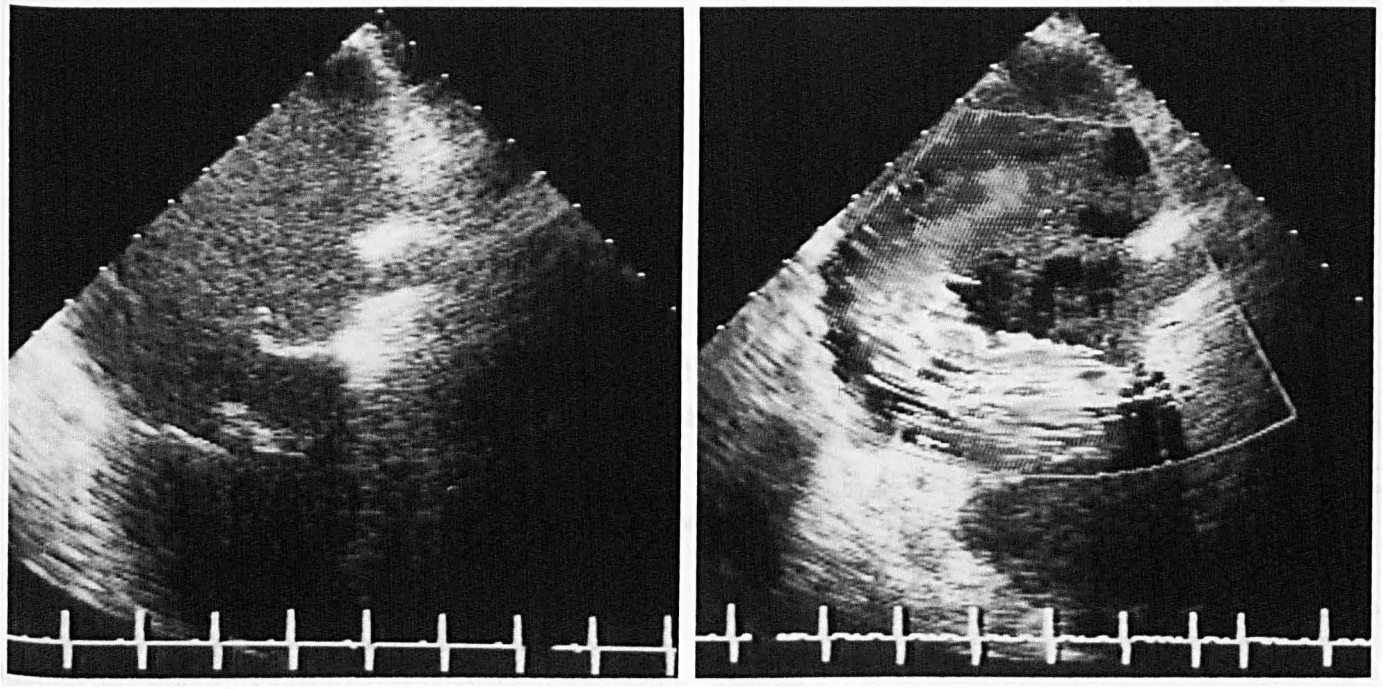


Fig. 1. **a** Doppler-echocardiographic evaluation of case 2 before valvuloplasty. **b** The regurgitant jet filling up the right atrial area. **c** Schematic illustration of the echocardiography: RA, right atrium; RV, right ventricle; LA, left atrium; LV, left ventricle

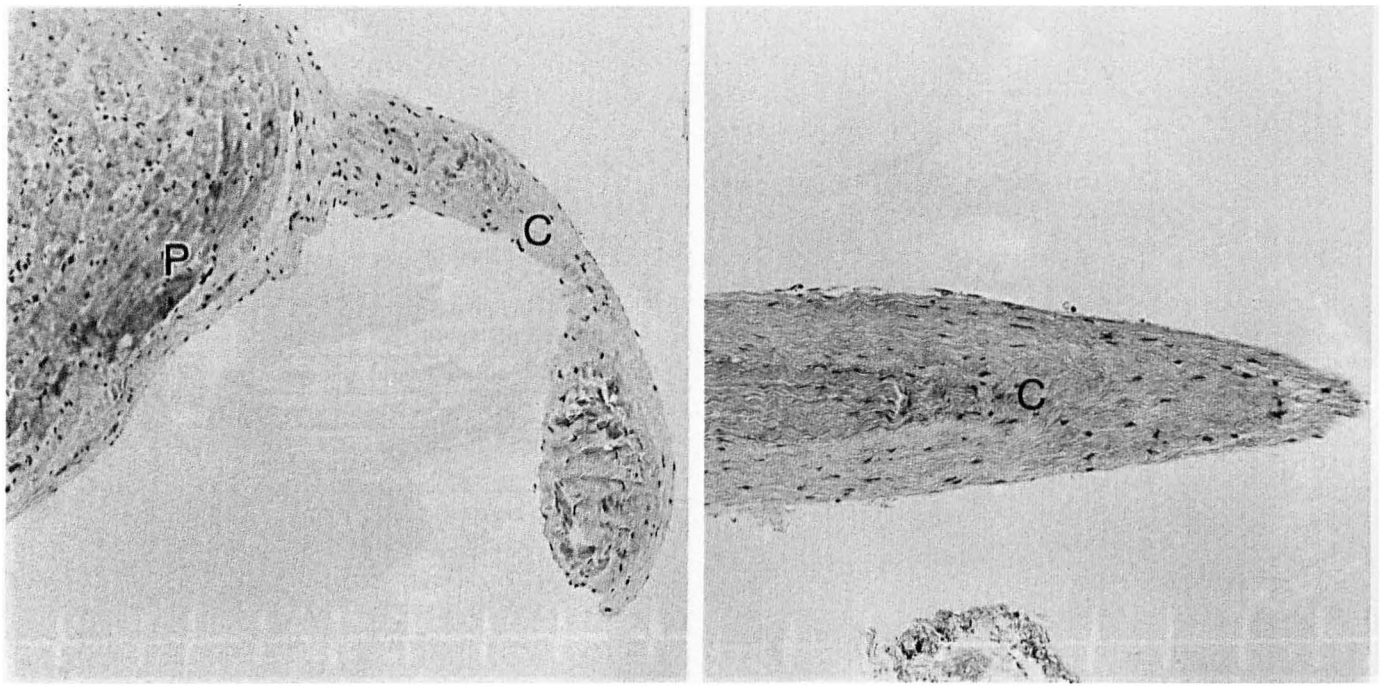
creased pulmonary vascular resistance to which the donor heart is not accustomed. The presence of tricuspid regurgitation in transplant recipients has been discussed in the literature, among others by Herrman et al. [9]. They did, however, not see any correlation in their study between the number of biopsies and tricuspid regurgitation.

Akasaka et al. recently reported a high frequency of tricuspid insufficiency in heart-lung transplant recipients, although these patients did not undergo endomyocardial biopsies. The authors speculated that the reason for atrioventricular valve regurgitation could be undetected rejection of low grade resulting in papillary muscle dysfunction [1].

In our study we found moderate to severe tricuspid regurgitation in 13% of heart transplant patients. Of all patients in our series, 6.3% had tricuspid regurgitation caused by endomyocardial biopsy as determined from the sudden occurrence and histological findings. This is an incidence similar to that reported by Braverman et al. [3] from 1442 biopsies obtained on 440 separate occasions. They did not report any clinically significant consequences from the biopsy damage, whereas in our patients the ruptured chordae tendineae was a severe complication that resulted in valvuloplasty in three patients (3.1%).

There are special anatomical features in the right ventricle to have in mind when considering the risks of endomyocardial biopsy. Thus, there are long chordae tendineae and short papillary muscles anchored at different levels and unevenly spread out in the whole ventricle making it theoretically possible for a bioptome to catch chordae tendineae at any point.

The technique of performing endomyocardial biopsy has been well described [4]. The importance of approaching the right ventricular septum with closed bioptome jaws so as not to catch chordae tendineae has been stressed, but even if these measures are taken, the jaws have to be opened at some point. Since fluoroscopy does not reveal the presence of chordae or papillary muscle, it is impossible to detect if they have been caught in the bioptome. It is not possible to recognize or differentiate the specific tissue that has been caught in the bioptome jaws. The fact that, in our study, chordal tissue or papillary muscle were found in the biopsy samples from all six patients with suspected biopsy damage of the tricuspid valve points to the importance of an immediate echocardio-



a b

Fig. 2 a, b. Endomyocardial biopsy samples from a heart transplant patient showing papillary muscle *(P)* and chordal tissue *(C)*

graphical follow-up in patients with either post-biopsy symptoms or histological findings of chordal tissue to avoid severe undetected tricuspid valve regurgitation. Whether there were histological findings of chordal tissue in patients with a lower degree of tricuspid regurgitation was not investigated, but since no patient had clinical symptoms or showed echocardiographical signs of chordal rupture it was not considered necessary.

Miller et al. have proposed transthoracic echocardiography-guided biopsies as an alternative to fluoroscopy guidance. They pointed out several advantages, such as elimination of cumulative radiation exposure for the physician and the patient, a greater amount of information on ventricular function and pericardial effusion, avoidance of the expense and congestion of operating theatres and catheterization laboratories, and, most important, that it allows the physician to obtain endomyocardial biopsies safely from the entire right ventricular surface, including the free wall, apex and septum [10].

Although endomyocardial biopsy is the most useful tool for the detection of rejection it should be used with careful consideration of anatomical features and consciousness of the risk of damage to the tricuspid valve. It is also concluded that valvuloplasty of the tricuspid valve can successfully be performed in a transplanted heart.

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