ORIGINAL ARTICLE

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Echo-guided endomyocardial biopsy in heart transplant recipients

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Abstract After heart transplantation the effect of immunosuppression is monitored by histopathology of endomyocardial biopsy (EMB). EMB is usually carried out under X-ray guidance. Between January 1998 and March 2003, 1,262 biopsies were collected under echo-guidance in 156 patients. The biopsy access was gained through the internal jugular vein, by the standard catheterization technique. The average time of the procedure was 17 min. Four or five specimens were obtained from each patient, with a success rate of 96%. Complications involved two episodes of partial pneumothorax in one patient, atrial flutter in another and ventricular fibrillation in three patients. Conversion from echo to X-ray guidance was indicated in 11 patients. No case of significant tricuspid regurgitation related to the EMB procedure was recorded. The echo-guided endomyocardial biopsy appears to be a prospective alternative to the conventional approach under X-ray guidance. Its duration is comparable, it eliminates X-ray exposure, enables continuous echocardiographic monitoring and can be performed at the bedside.

Keywords Endomyocardial biopsy · Echocardiography

Introduction

The collection of an endomyocardial biopsy (EMB) sample from the right ventricle was first carried out in 1973 in order to diagnose graft rejection in a heart transplant recipient in Stanford, USA [1]. The histological examination of myocardial tissue has, so far, been the only reliable method of diagnosing graft rejection. Therefore, in most centres EMB has become a routine examination in patients after heart transplantation [2, 3, 4, 5]. In European countries, there has recently been a distinct tendency to use non-invasive methods for graft rejection diagnosis, namely, cyto-immunological monitoring, intramyocardial ECG, tissue densitometry, tissue Doppler imaging or scintigraphy [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16]. Although the use of ultrasonic guidance in different interventional techniques is currently increasing, according to the recent literature data [17], its application in EMB procedures has not yet been very significant.

At the Centre of Cardiovascular and Transplantation Surgery in Brno, the technique of EMB under X-ray guidance was introduced in 1992 and under echo-guidance in 1998; by March 2003, a total of 3,248 biopsy specimens from 209 heart recipients were collected (1,986 under X-ray guidance, 1,262 under echo-guidance). Conversion to echo-guided EMB was initiated following urgent need to carry out this procedure in a patient treated in our intensive care unit. She could not be transferred to the X-ray laboratory because of her high circulation support by catecholamines, intra-aortic balloon contrapulsation and artificial ventilation. EMB

was performed at the bedside in the intensive care unit under echo-guidance. Thereafter, the use of echo-guided EMB has gradually increased and has become the preferred method at our centre [17].

Patients and methods

The first endomyocardial biopsy after heart transplantation was performed in 1992 at our institution. Until the end of 1997 a total of 1,986 EMBs was performed exclusively under X-ray control, with an average fluoroscopy time of 3.04 min. At the very end of 1997 the first EMB under echo-guidance was carried out. Between January 1998 and March 2003 a total of 1,262 echo-guided EMB collections was performed in 156 heart transplant recipients (125 men and 31 women) with a mean age of 52 ± 12 years (range 16 to 71 years).

The echo-guided EBM procedure is performed as follows: Under local anaesthesia, the first no. F7 valved introducer is inserted into the internal jugular vein and an F7 guiding catheter is advanced over a guide wire into the right ventricle. Its position in the right atrium and its optimal location in the right ventricle are subsequently verified by ultrasonography. Great care is paid to avoid damage to the tricuspid valve by forceps manipulation in the right ventricular cavity. The optimal position of the forceps is apicoseptal. Colour flow mapping of tricuspid valve flows during and after the procedure is mandatory. In order for ideal visualization of the instruments to be achieved in both the right atrium and the right ventricle an apical four-chamber view, or, in slim patients, subcostal projection, is used. Echocardiographic monitoring is carried out with an HP SONOS 1000 or Image Point ECHO device with a 2.5 MHz probe. Two persons are needed for the procedure, one invasive cardiologist and one echocardiographer, who may be a cardiologist or a technician.

The guiding catheter is repeatedly flushed with heparin containing saline. This solution also serves as an echo contrast material that improves the quality of ultrasonographic examination [18], as shown in Fig. 1. During an EMB procedure, the end part of the guiding catheter and the position of open forceps are carefully monitored [19] (Fig. 2).

Results

The average time of the procedure (from jugular vein puncture to removal of the instruments) was 17 min (range 8 to 45 min) and four or five specimens were collected from each patient. The success rate was 96%. In one patient the procedure was complicated by partial pneumothorax on two different occasions, while three patients developed ventricular fibrillation during
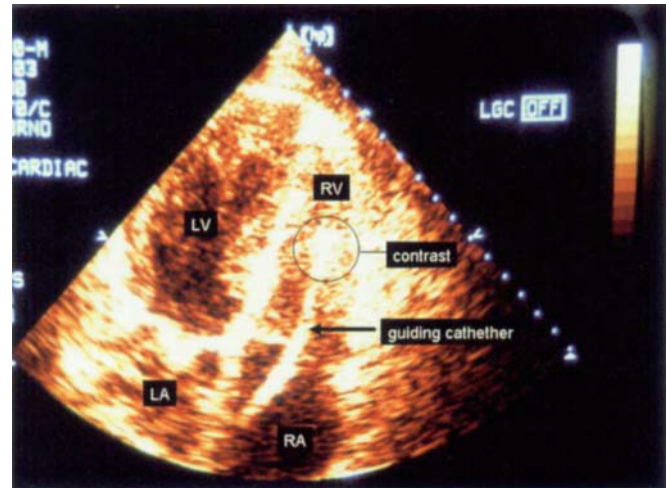

Fig. 1 Guiding catheter in the right atrium (RA) and right ventricle (RV), and saline contrast in the RV, locating the end of the catheter (LA left atrium, LV left ventricle)

catheter manipulation in the right ventricle, and one patients had atrial flutter when the catheter was withdrawn from the right atrium into the superior vena cava. No case of significant tricuspid regurgitation related to the EMB procedure was recorded. Unfortunately no exact data about tricuspid regurgitation after X-ray guided EMB in our institution are available. In 11 patients, the procedure had to be completed in the X-ray laboratory because we failed to control catheter movement through the central veins (the superior vena cava in particular) or to advance the catheter into the right atrium.

Discussion and conclusions

Ultrasonic guidance is currently used in a large number of interventions such as liver, kidney and other biopsies,
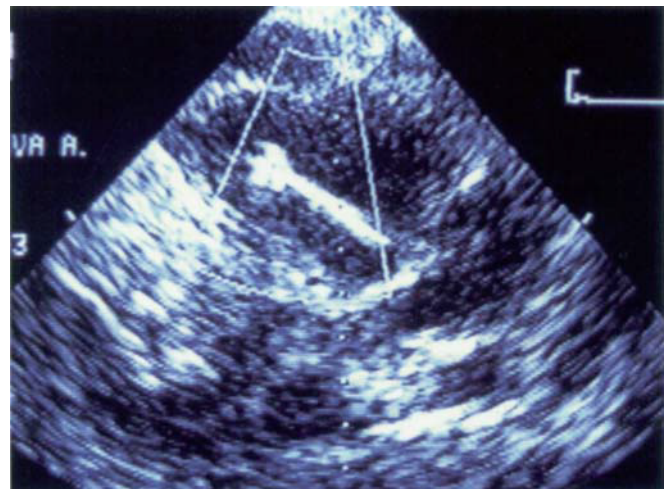

Fig. 2 Detail of the opened forceps in the right ventricle

pericardial and pleural tap or drainage. Echocardiography also helps in the insertion of stimulation electrodes or catheters through the tricuspid orifice in patients with a bioprosthesis or an annular ring. In interventional cardiology, ultrasonographic guidance is used in balloon atrioseptostomy in neonates or, in conjunction with X-ray imaging, for balloon valvuloplasty of the aorta or in interventional closure of atrial septal defect or patent foramen ovale [20].

EMB specimens for histological assessment of graft rejection are usually obtained from the right ventricle, with the use of a commercial bioptome under X-ray guidance. Most commonly, this is performed through the internal jugular vein. Great care should be paid when the bioptome tip is pushed out of the guiding catheter. The bioptome forceps is opened and a specimen is cut out during slight pressure of the opened forceps on the right ventricular endocardium. Bioptome penetration through the right ventricular wall into the pericardial cavity is a rare but potentially grave complication. Under X-ray imaging, this situation can be missed because the bioptome tip may not cross the heart shadow in certain projections. During the procedure both the patient and physician are exposed to radiation. Only one attending physician is required to perform X-ray guided EMB.

In echo-guided EMB, insertion of the instrument requires great skill. Neither the guide wire nor the catheter is well visualized in the first phase of insertion, and their passage through the venous system is without visual control. This may result in difficulties that may occasionally necessitate the use of an X-ray-guided technique. It is more convenient for the cardiologist to cannulate the right jugular vein, but left-sided access is also possible. The catheter devices are well visualized when they appear in the right side of the heart. After the guiding catheter has been inserted into the right ventricle, a small amount of saline (as echo contrast agent) is flushed through in order for the correct position of the instrument to be confirmed. Real-time echocardiography allows for monitoring of the position of the instruments in the heart cavities and eventually enables their visualization in the pericardial cavity. Two cardiologists are needed to perform this procedure, with the specialist in echocardiography being involved from the moment of jugular vein cannulation (the extra person for echo-monitoring might be an experienced technician, not necessarily a cardiologist). Should a conversion to X-ray control be indicated, the radiological unit has to be within easy reach.

The elimination of any unnecessary radiation exposure in post-transplantation patients is advisable, in respect of the fact that the risk of cancer in these patients is 100-times higher than in their age-matched controls [21].

Three categories of complications might occur in association with EMB. The first includes complications related to jugular vein cannulation. With an increasing number of EMBs being performed in a single patient, complication rates may increase because of scars in the jugular vein region. The cannulation of a central vein may also result in pneumothorax.

The second category comprises abnormalities of heart rhythm. These may be either atrial dysrhythmias, which (with the exception of atrial flutter) do not represent a serious complication, or unsustained ventricular dysrhythmias, which are almost always present during EMB as isolated ventricular premature beats or premature beats in series. A sustained ventricular tachycardia or ventricular fibrillation/flutter may also develop. This usually requires, usually, an external electric cardioversion.

The third category of complications includes mechanical damage to the heart structures, e.g. injury to the tricuspid valve, the subsequent development of tricuspid regurgitation, or perforation of the heart or central veins, which carries a risk of cardiac tamponade [22]. A critical site is the right ventricle, but perforation may also occur at the superior vena cava suture. Differentiation of these complications, particularly the identification of right ventricular perforation, is most reliably achieved by echocardiography. Under careful echocardiographic monitoring ventricular perforation can be avoided and developing haemopericardium or tamponade can be diagnosed at an early stage. Higher grades of tricuspid regurgitation in the post-transplant period are related to the classic surgical technique (Shumway), to the number of rejection episodes and to the number of EMBs performed [23, 24, 25, 26]. In this respect the echo-guided EMB is clearly superior to the X-ray technique, as the bioptome forceps and its relation to the tricuspid apparatus can be easily monitored by echocardiography. In our series no case of acute post-EMB tricuspid regurgitation was recorded.

In conclusion, real-time echocardiography facilitates the exact localization of a bioptome in the right ventricle and its position relative to the right ventricular structures and, therefore, reduces the risk of injury. It also allows for the detection of right ventricle perforation and immediate management of cardiac tamponade, should these occur. The minor disadvantages of this approach, i.e. involvement of two attending cardiologists and difficult visualization of the catheter in the proximal part of the venous system, are compensated for by elimination of radiation exposure. It eliminates radiation exposure to the patient (echo-guided EMB is the method of choice in pregnant patients [27, 28, 29]) and, particularly, the cardiologist, for whom, considering the large number of biopsies performed, this is an important factor. We estimated the average skiascopy time in 1997 for one X-ray guided EMB as 3.04 min/patient.

At our centre, echo-guided EMB has become a method of choice; roentgenography is used only when coronarography is concurrently carried out or in patients who cannot be well visualised by echocardiography.

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