Original Research

Pericardiectomy for Radiation-Induced Constrictive Pericarditis

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Constrictive pericarditis, pericardiectomy.

Introduction: Of oncological patients who have undergone chest radiation therapy, 20% develop radiation-induced constrictive pericarditis. The purpose of this study was to review our clinic's experience of such cases, focusing on survival and the functional outcome.

Methods: Six patients with a history of previous radiation therapy, aged 33-61 years, most of whom had symptoms of heart failure, underwent radical (2 patients) or partial (4 patients) pericardiectomy.

Results: All patients were completely free of cardiovascular events during the 8 years covered by the study. Among the postoperative complications the most serious was low cardiac output syndrome in 4 patients, which was treated successfully.

Conclusions: Radiation-induced constrictive pericarditis is a clinical entity that should be taken into account in the differential diagnosis of oncological patients who show signs of heart failure. Surgery is the only effective treatment. The results are satisfactory, but always depend on associated damage to the myocardium as a result of radiation and on the underlying cancer.

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Thoracic irradiation for hematological malignancy, breast cancer, bone marrow transplantation, or less frequently other diseases, can cause radiation-induced heart disease. Pericardial involvement is most commonly seen, with an incidence of 7-20%, followed by valvular disease, coronary disease, involvement of endocardium, myocardium and conduction abnormalities.[1] Constrictive pericarditis develops when a progressive fibrotic reaction of the pericardium compresses the myocardium and impairs filling of the ventricles during diastole. The aim of this study is to review our institutional experience of operation for radiation-induced constrictive pericarditis and to focus on survival and functional outcome.

Methods

Six patients who underwent pericardiectomy for radiation-induced constrictive pericarditis at Theagenio Cancer Hospital between 2000 and 2008 were reviewed, with the diagnosis confirmed at surgery. Their medical records were studied with attention to clinical features, invasive and noninvasive preoperative investigations, early postoperative course, pathological findings and long-term follow up.

Radical pericardiectomy was defined as wide excision of the pericardium anteriorly between the two phrenic nerves and from the great arteries superiorly to the diaphragm inferiorly, posteriorly to the left phrenic nerve to the left pulmonary veins

and including the pericardium on the diaphragmatic and posterior surfaces of the ventricles. The atria and *venae cavae* were decorticated only if the dissection could be accomplished easily without risk of hemorrhage. Pericardiectomy was considered partial if both ventricles could not be decorticated because of dense myopericardial adhesions.[2]

Results

The ages of the patients (2 males and 4 females) ranged from 33 to 61 years. The two males had a history of Hodgkin's lymphoma and the 4 females a history of breast cancer. All of them had received mediastinal or chest wall radiotherapy of 40-50 Gy. The interval between irradiation and pericardiectomy ranged from 6 months to 5 years. The duration of symptoms prior to diagnosis of constrictive pericarditis varied from 1 month to 3 years. Three patients had been asymptomatic for more than 2 years after radiotherapy. The presenting symptoms were chronic heart failure in 4 patients, chest pain in 4 patients, abdominal symptoms in 2 patients, atrial tachyarrhythmia in 2 patients, pleural effusion in 2 patients and cardiac tamponade in 1 patient.

Preoperative disability was categorized according to the NYHA functional class. At the time of diagnosis of constrictive pericarditis, two patients were in Class II, 3 patients were in Class III and 1 patient was in Class IV. Results of the various preoperative investigations and subsequent detected abnormalities are summarized in Table 1.

Partial pericardiectomy was performed through a left anterolateral thoracotomy in 4 patients and a radical pericardiectomy through median sternotomy in 2 patients (Figure 2). Cardiopulmonary bypass was not used in any case. Pericardiectomy provided excellent relief of symptoms in all patients. In all cases, the pathology report on the resected pericardium showed fibrous tissue with dense collagen and lymphoid cell aggregation, while there was no neoplastic pericardial infiltration (Figure 3).

Low cardiac output syndrome was the most common complication of pericardiectomy (4/6 patients), but there were no clinical or hemodynamic findings to suggest persistent constriction as the underlying cause. These patients required augmentation of atrial filling pressures by intravenous administration of fluids combined with inotropic drugs. In nearly

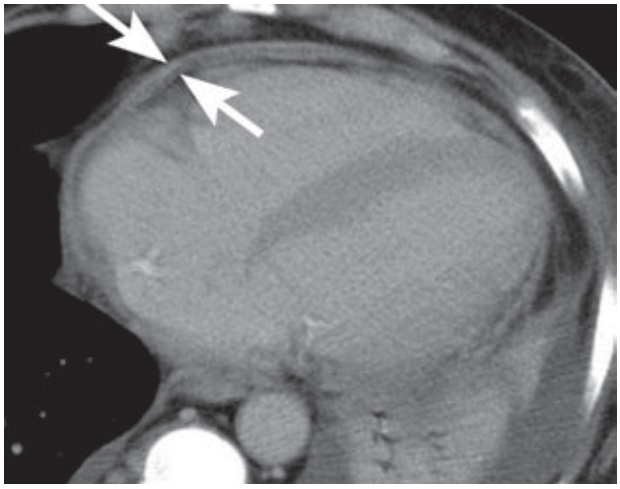

Figure 1. Computed chest tomography revealing thickened pericardium (white arrows) in a case of post-radiation constrictive pericarditis.

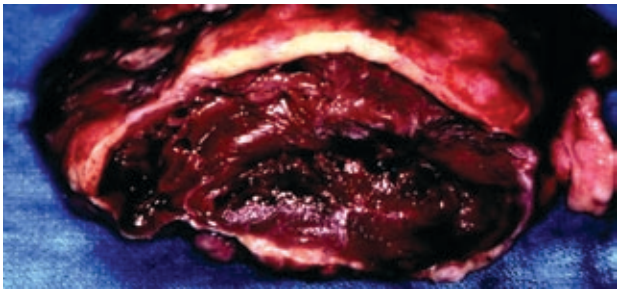

Figure 2. Macroscopic appearance of a resected pericardium.

Table 1. Results of preoperative investigations.

Study	No. of patients	Abnormality detected	No. of patients
Chest X-ray	6/6	Pericardial calcification	1/6
Electrocardiography	6/6	Low voltage QRS	4/6
		Atrial arrhythmia	2/6
Echocardiography	6/6	Pericardial thickening	4/6
		Pericardial effusion	4/6
Computed tomography	6/6	Pericardial thickening (Figure 1)	4/6
Cardiac catheterization	6/6	Elevation of end-diastolic pressures (dip-and-plateau pattern)	6/6

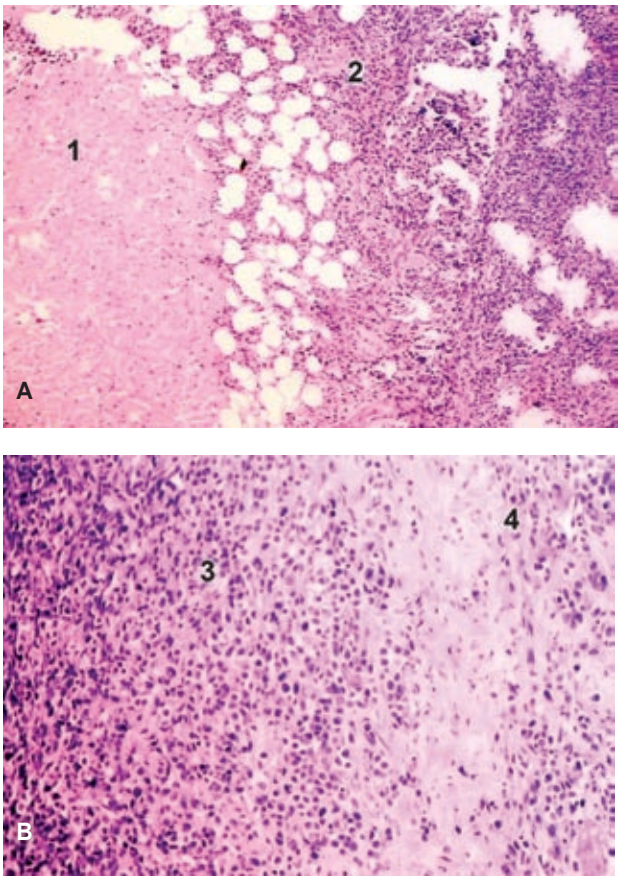

Figure 3. Irradiated necrotic pericardium (1) consisting of fibrous tissue (2) with dense chronic inflammatory infiltration (3, 4). (Magnifications: A – H-E × 100; B – H-E × 200).

all cases (3/4) of low cardiac output syndrome an immediate improvement of cardiac function and peripheral perfusion was noted after the start of treatment. In one case intra-aortic balloon pump insertion was necessary and this resulted in significant improvement in hemodynamic function. Intra-aortic balloon counterpulsation was continued for three days.

The 6 patients were followed for up to 8 years. The late survival following pericardiectomy is presented in Table 2. There was complete freedom from any cardiovascular event for all patients during follow up.

Discussion

Mediastinal irradiation is a well known cause of pericardial disease. Cardiac structures are exquisitely sensitive to the effects of radiation, which often become manifest years later.[3,4] In addition, improved cancer cure rates have resulted in greater longevity and thus the likelihood of developing cardiovascular sequelae.

Although the constrictive effects of chronic pericarditis occur in relation to all four cardiac chambers, the only consistent significant hemodynamic abnormality is the impairment of ventricular diastolic filling. Clinical signs and symptoms often develop insidiously.

The clinical features of constrictive pericarditis are due to impaired cardiac filling, which leads to reduced diastolic compliance. This usually causes an enlarged atrium, a relatively small ventricular chamber, thickened pericardium, odd septal movement and shortened isovolumic relaxation time.[5] However, an occult condition has also been described that can be difficult to diagnose.[6] Klein et al evaluated the use of transesophageal echocardiography to classify patients with diastolic dysfunction.[7] They studied 181 patients with diastolic dysfunction through transesophageal echocardiography. In this cohort, restrictive physiological features were the main cause of diastolic dysfunction for 71 patients, while constriction was responsible in 45 patients without effusion and 9 patients with effusion. A mixed constrictive and restrictive pattern was found in 21 patients. Transesophageal echocardiography is a reliable guide for assessment of the extension of fibrosis.

According to the international literature, the role of tissue imaging is extremely important for differential diagnosis. Sengupta et al proved that in constrictive pericarditis, Doppler tissue imaging in the short axis provides unique diagnostic information and

Table 2. Late survival and causes of death.

Patient (age, years)	Primary disease	Survival	Cause of death
Male (33)	Hodgkin's lymphoma	42 months	Still alive
Male (46)	Hodgkin's lymphoma	34 months	Progressive disease, septic shock
Female (42)	Breast cancer	14 months	Progressive disease
Female (49)	Breast cancer	22 months	Progressive disease
Female (60)	Breast cancer	38 months	Still alive
Female (61)	Breast cancer	88 months	Still alive

reliably differentiates constrictive pattern form control cases and most other causes of abnormal septal motion.[8]

In 1928, Churchill first performed a successful pericardiectomy for constrictive pericarditis.[9] He achieved exposure of the pericardium by using a curved left parasternal incision and resected anterior portions of the left third to seventh ribs and their adjacent costal cartilages. Since then, a number of different operative techniques and approaches have been described and controversy continues as to what constitutes the best approach. The operative approach used by Churchill is now of historical interest. The choice between median sternotomy and left anterolateral thoracotomy seems to be a matter for the surgeon's personal preference.

Median sternotomy allows a more radical clearance of pericardium overlying the right atrium and *venae cavae*. The disadvantage of the mid-sternal approach is that extensive manipulation of the heart is necessary to permit complete decortication of all surfaces of the left ventricle, particularly the diaphragmatic surface. Many surgeons routinely use cardiopulmonary bypass for pericardiectomy. A disadvantage of this approach is the potential for increased bleeding related to cardiopulmonary bypass, and especially for oncology patients there is high risk of disseminating malignancy. In our small series, cardiopulmonary bypass was not necessary in any case. Probably it is only indicated when there is a coexistent cardiac abnormality that requires correction. Left anterolateral thoracotomy offers excellent exposure of the anterolateral and inferior aspects of the left ventricle with minimal manipulation and retraction of the heart. If necessary, the incision can be easily extended across the sternum and onto the right side of the chest. Currently, we prefer left anterolateral thoracotomy as the incision of choice, because it offers superior exposure of all areas of ventricular pericardium and is well tolerated by most patients.

Another important issue has been the extent of pericardial resection that is necessary for clinical and hemodynamic correction of the constriction. All agree that failure to decorticate the anterolateral and diaphragmatic surfaces of both ventricles will lead to a less than optimal result.

Consistently good late results have been reported in many large series of patients undergoing pericardiectomy for constrictive pericarditis, but there is little discussion of radiation-induced constrictive pericarditis in the international literature. Osawa et al reported 2 cases treated surgically with good early but poor late results. One patient died six months later due to radiation-induced pneumonitis and the other was still alive 3 months after surgery.[10] In contrast, Ni et al reported 2 cases of patients who underwent pericardiectomy for post-irradiation constrictive pericarditis with very poor early results.[11] The hospital mortality was 100%. One patient died of multi-organ failure on the sixth postoperative day. The second died of biventricular failure 3 months later. According to the authors, the poor results in these patients, compared with patients having pericardiectomy for other reasons, seem to be due mainly to the various kinds of radiation-induced damage to the heart as a whole. This damage includes coronary artery disease, myocardial fibrosis, atrioventricular conduction disturbances and valve dysfunction, with the result that postoperative impaired cardiac performance is usually secondary to permanent preoperative myocardial dysfunction rather than to unrelieved constriction.[12] This is also supported by our finding that postoperative low cardiac output syndrome is a very common complication in these patients.

Radiation-induced pericardial disease should be a differential diagnosis in oncology patients suffering from chronic heart failure symptoms, pericardial thickening and effusion or pleural effusion. These patients should be examined by appropriate noninvasive (echocardiography, transesophageal echocardiography) and invasive procedures (cardiac catheterization). Early pericardiectomy has been advocated immediately after the diagnosis has been confirmed.[13] The surgical outcome is not always favorable.[14] Post-irradiation pericardium and fibrosis is very difficult to peel surgically and there is often associated myocardial involvement. Both of these features often result in a continuation of symptoms even after surgical resection of the pericardium.[15] Surgical results will continue to improve in such difficult cases only if the diagnosis is established early and pericardiectomy is performed before marked constriction causes myocardial damage.

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