Severe Infundibular Pulmonary Stenosis and Coronary Artery Stenosis with Ventricular Tachycardia 24 Years after Mediastinal Irradiation

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Abstract

A 28-year-old man developed severe infundibular pulmonary stenosis (PS), coronary artery stenosis with sustained ventricular tachycardia (VT) 24 years after mediastinal irradiation (total amount of 40 Gray) for non-Hodgkin's lymphoma. Repair of right ventricular outflow tract and coronary artery bypass graft procedure were performed. Infundibular PS was successfully relieved after operation and VT was also controlled by medication. Mediastinal irradiation often causes various cardiac complications after a latent period. Therefore, continuous careful observation is mandatory in patients with the history of mediastinal irradiation. (Internal Medicine 44: 963-966, 2005)

Key words: mediastinal irradiation, infundibular pulmonary stenosis, non-Hodgkin's lymphoma, coronary artery disease

Introduction

Mediastinal irradiation is a useful therapy for Hodgkin's/non-Hodgkin's lymphoma, breast cancer and other various malignant tumors. However, cardiac injuries following radiation are often reported involving the pericardium (1, 2), conduction system (2, 3), myocardium (1, 2), coronary arteries (1, 2) and cardiac valves (1, 4-6). Here, we report a case of severe infundibular pulmonary stenosis (PS) and coronary artery stenosis and moderate aortic valve stenosis with VT 24 years after mediastinal irradiation for non-Hodgkin's lymphoma.

Case Report

A 28-year-old man presented to our hospital with faintness and convulsion. At the age of 4 years, he was diagnosed with non-Hodgkin's lymphoma with mediastinal lymphadenopathy. He received irradiation therapy to the mediastinum (40 Gray (Gy)) and the cranium (18 Gy), combined with chemotherapy. At the age of 13 years, mild infundibular PS was initially diagnosed. At the age 18, ultrasound echocardiography (UCG) showed progression of infundibular PS with a pressure gradient (PG) of 65 mmHg and subsequent administration of atenolol was started to relieve the pressure gradient. However, as he went to China for his university programs, he did not come to our hospital for over 10 years.

The electrocardiogram (ECG) on admission showed regular sinus rhythm, undetermined axis deviation, first-degree AV block, and complete right bundle branch block with right ventricular (RV) hypertrophy (Fig. 1A). Sustained VT with faintness was also documented (Fig. 1B), but it was immediately converted to sinus rhythm by direct current cardioversion. Subsequent administration of amiodarone effectively suppressed the recurrence of VT. On chest X-ray, cardiomegaly was noted with a cardiothoracic ratio of 60%. UCG demonstrated severe infundibular PS, moderate aortic stenosis (AS) and a moderate amount of pericardial effusion. Ejection fraction (EF) was 65%. Thoracic computed tomography with contrast enhancement revealed a RV outflow tract stenosis and no recurrence of lymphoma.

Cardiac catheter examination revealed severe infundibular PS (PG=80 mmHg), and moderate AS (PG=40 mmHg); significant stenosis of the coronary arteries was also observed (Fig. 2). As the indication of surgical therapy was suggested, coronary artery bypass graft (CABG) was concomitant with

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Figure 1. Electrocardiogram on admission. A: Electrocardiogram on admission showed regular sinus rhythm, undetermined axis deviation, first-degree AV block, and complete RBBB with RV hypertrophy. (PQ interval =280 msec., QRS duration =160 msec.). B: Sustained ventricular tachycardia (rate =187~250/min) documented on admission day in the II lead.

right ventricular outflow tract repair (RVOTR). Saphenous veins were grafted to distal left circumflex artery and distal right coronary artery. RVOTR was done as myocardiectomy of infundibular posterior wall and covered with Gortex^R sheet at the anterior wall side. The postoperative clinical course was uneventful. After operation, amiodarone administration was continued, and there were only a few ventricular premature contractions on Holter electrocardiogram.

Pathological specimens obtained from the resected infundibular myocardium revealed fibrous thickening of endocardium and subendocardium, interstitial myofibrosis with disarrangement of myocytes.

Discussion

Mediastinal irradiation has been used for mediastinal neoplasms and favorable results of this therapy have led to a long-term patient survival rate. However, some of these patients have suffered from acute or late cardiac involvements such as pericarditis, myocarditis, coronary artery disease, valvular dysfunction, and arrhythmias. Radiation techniques have improved over the last 40 years, and they can reduce the adverse effects on the heart. Nevertheless it is difficult to narrow radiation fields for infants because of their small stature.

Although the precise incidence is uncertain, radiation-

induced valvular diseases have been well described (1, 4-6). In the old literature, Brosius (4) reported necropsy patients who received more than 35 Gy for classical radiation method to the mediastinum. Valvular lesions were found in 13 of 16 cases (80%) after irradiation (mean 55 months). Recently, Heidenreich reported (5) significant valve disease was noted in 29% of asymptomatic patients who were treated with 43.0±0.3 Gy radiation to the mediastinum with a current technique for Hodgkin's disease more than 20 years after radiation. Hull (6) reported 415 patients who received mediastinum (classical and current technique) or carotid or subclavian artery irradiation with mean 33 Gy for Hodgkin's lymphoma. A twenty-five patients (6.2%) developed significant valvular dysfunction after a median of 22 years. In this report, left sided valve involvement was more frequent than right sided involvements, despite the fact that right sided valves are located in the anterior portion. This may be related to higher pressure of the left side (4-6).

Regarding infundibular PS, only one case reported radiation-associated severe infundibular PS in which infundibular PS was repaired by surgery. Velebit (7) reported a 30-year-old man who had received total 38.40 Gy of mediastinal irradiation for Hodgkin's disease. Infundibular PS had developed after 8 years and RVOT repair was performed. In this case, just below the valve was a region of retraction creating an obstruction to outflow. No significant residual PG

Figure 2. Results of cardiac catheterization and pathological finding. A: Aortogram shows 90~75% stenosis of right coronary artery ostium at the segment #1 (arrows). **B and C:** Coronary arteriogram shows 90~99% stenosis of the Left Circumflex artery proximal #11 segment (bold arrows) and 50% stenosis of the left anterior descending artery proximal #6 segment (narrow arrow). **D:** Ventriculogram showed enlarged RV and stenosis of Right Ventricular outflow tract (narrow arrows). RV: right ventricle, PS: infundibular pulmonary stenosis, PAV: pulmonary valve (dotted arrow). **E:** Pathological findings of the resected infundibular myocardium. The specimen revealed fibrous thickening of endocardium and subendocardium and interstitial myofibrosis with disarrangement of myocytes (Azan stain; original magnification $\times 100$).

was observed after the operation. Tissue samples of the pulmonary artery show marked fibrotic change of the pericardium. We also confirmed fibrous thickening of the endocardium and subendocardium from the resected infundibular myocardium specimen.

Radiation therapy also causes coronary artery stenosis. It is reported that the radiation therapy highly induced the coronary artery stenosis even in younger patients. The dominant lesions were coronary ostium including right and left coronary arteries and epicardial vessels. The angiographical characteristics were often long, smooth, concentric and tubular (8). In Brosius's postmortem report of 16 patients, 6 (38%) had significant coronary major artery stenosis (4). According to Hull, 42 out of 415 (10.4%) patients developed coronary artery disease (CAD) after irradiation (mean 9 years, mean 35 Gy). Traditional risk factors such as male gender, hypertension, hyperlipidemia and age were significantly associated with the development of CAD. At least one cardiac risk factor was present in all patients who had developed CAD (6). In the present case, the patient is so young that it is hard to consider as the generally described atherosclerotic stenosis, although he has one risk factor of

smoking.

Conduction system disturbance is often found after mediastinal irradiation. A common abnormality of ECGs is right bundle branch block and it suggests that the right ventricle might receive a higher exposure of radiation than the left ventricle (2). Slama (3) reported 6 cases of atrioventricular (AV) block and confirmed the blocked site was in the infranodal regions. Pathologically, patchy fibrosis in the infranodal region was observed.

No report has mentioned the incidence and type of arrhythmias after mediastinal irradiation, particularly fatal ventricular arrhythmias. In the present case, we could not determine the precise exact origin of VT due to the lack of 12 lead ECG during VT. However, two possible causes of VT were considered; the first, myocardial fibrosis due to irradiation might be a potential risk for arrhythmogenic substrates. Pathological findings of resected myocardial specimens were supportive of this consideration. Secondly, myocardial ischemia due to coronary artery disease might be another cause inducing VT.

Conclusion

We reported the first case of progressive infundibular PS, coronary artery stenosis, and VT after 24 years of mediastinal irradiation for non-Hodgkin's lymphoma. Surgical repair of PS and CABG were successfully performed. Careful observation is necessary to prevent other cardiac injuries occurring with a long-term latency.

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