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Three-Vessel Coronary Artery Disease, Aortic Stenosis, and Constrictive Pericarditis 27 Years after Chest Radiation Therapy: A Case Report

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ABSTRACT

A patient with a history of Hodgkin's lymphoma presented with recurrent left pleural effusions and dyspnea on exertion 27 years after radiation therapy. Further evaluation disclosed suspected radiation-induced constrictive pericarditis, aortic stenosis and regurgitation, and severe coronary artery disease. He underwent successful 3-vessel coronary artery bypass grafting, aortic valve replacement, and pericardiectomy.

INTRODUCTION

Pericardial disease is the most frequently described chest radiation–related cardiac injury with an incidence of 50% [Applefeld 1983]. Other cardiac lesions such as coronary, carotid, or subclavian artery disease, valvular disease, conduction system disease, myocardial fibrosis, and ventricular dysfunction have been described either alone or in combination [Stewart 1984; McEniery 1987; Piovaccari 1995; Handa 2001; Hull 2003]. The actuarial incidence rates of coronary artery disease (CAD) and clinically important valvular disease at 5, 10, and 20 years after chest radiation are 3%, 6%, and 10% and 1%, 4%, and 6%, respectively [Hull 2003].

CASE REPORT

A 58-year-old man was referred for evaluation of chronic recurrent symptomatic left-sided pleural effusions. He had non-Hodgkin's lymphoma treated with chemotherapy and radiation therapy in 1976, renal cell carcinoma status post-nephrectomy in 1999, and hypothyroidism. He denied hypertension, diabetes mellitus, or hyperlipidemia. He quit smoking 27 years ago and denied any substance abuse. His father died at age 53 years from CAD. The patient was in his normal state of health until 1 year prior to presentation when he developed progressive dyspnea on exertion presumed to be due to a left-sided pleural effusion, which required repeated thoracenteses. His symptoms would resolve after each thoracentesis to recur with reaccumulation of the pleural fluid. He denied paroxysmal nocturnal dyspnea, orthopnea, chest pains, fevers, night sweats, or weight loss, but reported lower extremity edema during last admission at an outside hospital. Pleural fluid on multiple occasions was characterized as a transudate and was negative for malignancy, infection, or connective tissue disease. Results of 4 prior bronchoscopies with transbronchial biopsies were also negative. Results of pleural and pericardial biopsies were nondiagnostic. Other laboratory data included a negative antinuclear antibody, normal complement levels, erythrocyte sedimentation rate, and thyroid function.

On admission to our hospital he was not distressed and had stable vital signs. The carotid pulses were full and slightly delayed. The jugular venous pressure was around 18 cm of water with a positive Kussmaul sign. There was no pulsus paradoxus. S1 and S2 were normal and no pericardial knock or gallops were heard. There was a grade 3/6 crescendo-decrescendo systolic ejection murmur at the right upper sternal border radiating to both carotids, a grade 2/6 diastolic murmur at the left sternal border, and a grade 2/6 holosystolic murmur at the apex radiating to the axilla. The breath sounds were decreased at both bases, left greater than right. The abdominal exam was unremarkable. There was no lower extremity edema and the distal pulses were strong bilaterally. The electrocardiogram showed normal sinus rhythm with right bundle branch block and inferolateral q-waves.

The chest radiograph showed small bilateral pleural effusions that were worse on the left with atelectasis, normal pericardial and mediastinal contours, and clear lungs. Transthoracic 2-D echocardiogram showed moderate pericardial effusion with no tamponade and moderate aortic, tricuspid, and mitral regurgitations. The aortic valve was thick and calcified with an area of 0.9 cm^2 and a

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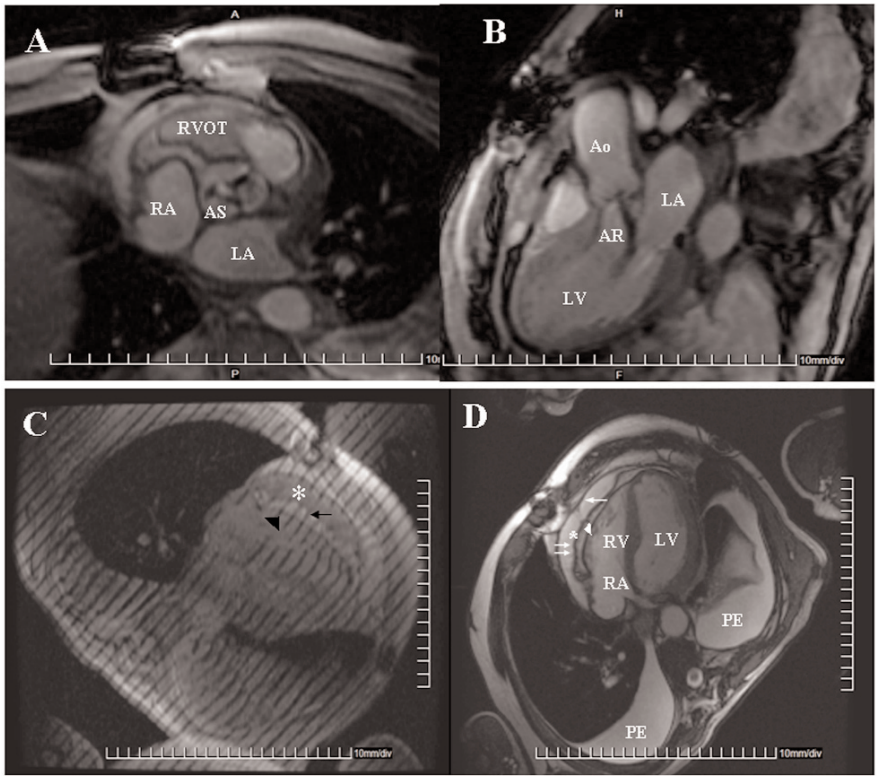

Figure 1. A, Mid-systolic gradient echo magnetic resonance image of the aortic valve showing moderate aortic stenosis (AS) with an aortic valve area of 1 cm^2 by planimetry. B, Gradient echo cardiac magnetic resonance image showing moderate aortic insufficiency (AI) in the left ventricular outflow view. C, Cardiac magnetic resonance image with tagging shows tethering of the pericardial layers (black arrow) to the myocardial surface of the right ventricular free wall (black arrowhead). D, Gradient echo steady state free precession cardiac magnetic resonance images in 3-chamber view in diastole showing a loculated pericardial effusion (*) predominantly over the right atrium and right ventricle measuring up to 2.8 cm in maximal dimensions with no evidence of tamponade. The visceral pericardium is thickened and measures up to 4 mm (double arrows). Also seen is the parietal pericardium (arrow), the sub-pericardial space (white arrowhead), and bilateral pleural effusions (PE). The inferior vena cava was dilated at 26 mm (not shown) and the left ventricular ejection fraction was 37%. RVOT indicates right ventricular outflow; RA, right atrium; LA, left atrium; Ao, aorta; LV, left ventricle.

peak gradient of 48 mmHg. Cardiac magnetic resonance imaging (MRI), done because of suspicion of constrictive pericarditis, revealed moderate aortic stenosis and regurgitation, mild left ventricular dysfunction, moderate pericardial effusion, and a thickened pericardium suggestive of constrictive pericarditis (Figure 1). Left and right heart catheterizations showed moderate aortic stenosis with a valve area of 1.06 cm^2 and hemodynamic features suggestive of constrictive pericarditis. Coronary angiography showed severe 3-vessel disease with left main involvement (Figure 2).

The patient underwent successful 3-vessel coronary artery bypass grafting, aortic valve replacement, and pericardiectomy. At surgery, the pericardium was obliterated by adhesions over the front of the heart along with evidence of acute pericarditis around the diaphragmatic surface and free wall of the heart with an element of constriction, which was not severe. The aortic valve was trileaflet with rigid fibrotic leaflets with moderate calcification. The skin over the sternum was noted to be leather-like and the bone was also quite abnormal. He had an uneventful recovery and was discharged home in stable condition.

DISCUSSION

In this case report, we describe the first successfully combined 3-vessel coronary revascularization, aortic valve replacement, and pericardiectomy in a patient with suspected radiation-associated heart disease. The patient's presentation with recurrent symptomatic pleural effusions is uncommon. In 135 patients with constrictive pericarditis, congestive heart failure was the most common presentation in 67% of patients, whereas recurrent pleural effusion was the presentation in less than 2% of patients [Ling 1999]. Severe CAD, aortic stenosis, and constrictive pericarditis have not been described in the same patient. In a cohort of 108 patients who had chest irradiation for Hodgkin's disease, cardiac disease occurred in 12 patients (11%), of whom 8 had severe CAD and 4 also had concomitant constrictive pericarditis without valvular disease [Piovaccari 1995].

McEniery et al reviewed the angiographic features of CAD developing after chest irradiation in 15 patients identified from a cohort of 19,063 patients with angiographically proven CAD. The mean age was 48 ± 13 years and the time interval from chest radiation to diagnosis of CAD was 3 to 29 years.

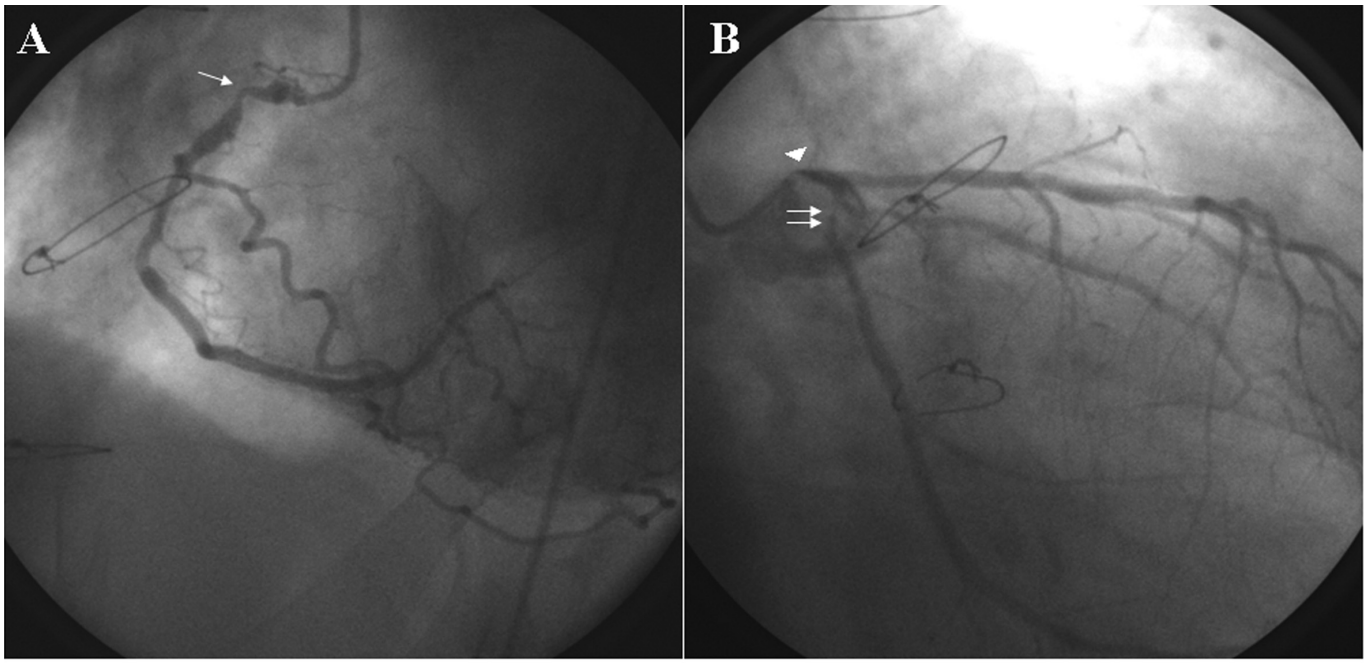

Figure 2. Coronary angiogram showing severe proximal right coronary artery stenosis (arrow) (A) and severe stenosis of the ostium of the left main (arrowhead) with dampening of pressure waveform during engagement and severe ostial-to-proximal left circumflex disease (double arrows) as well as moderate disease of the second marginal and proximal left anterior descending artery (B).

Of the 15 patients, 27% had 1-vessel disease (≥50% stenosis), 20% had 2-vessel disease, none had 3-vessel disease, and 53% had left main disease compared to 7% of the non-irradiated patients with known CAD [McEniery 1987]. Of the reported patients with either 3- or 4-vessel radiation-associated CAD, none had left main disease or the 2 other cardiac abnormalities [Carlson 1991; Handa 2001]. Radiation-related coronary lesions typically occur in patients with known cardiac risk factors [Hull 2003] and frequently involve the ostial and/or proximal coronary artery segments of the right coronary, left main, or left anterior descending arteries that are typically included in the mantle radiation field, as was the case in our patient [Piovaccari 1995; Reinders 1999; Hull 2003]. Although our patient had CAD risk factors, radiation therapy could have contributed to his CAD progression especially in view of the ostial and proximal locations of the lesions in addition to the presence of premature aortic stenosis and pericardial constriction. However, it is difficult to confirm or conclude a definite causal relation between radiation therapy and CAD.

Valvular regurgitations of any degree are the most commonly reported valvular abnormalities after chest irradiation [Carlson 1991] with the aortic valve being commonly involved due to its proximity to the radiation field [Handa 2001; Heidenreich 2003]. However, aortic valve stenosis is the most common clinically important valvular lesion [Hull 2003] and is the predominant valvular dysfunction requiring an operation [Handa 2001].

In conclusion, radiation-induced cardiac disease is common and can involve the pericardium, coronary arteries, or valves, requiring surgical intervention. Its recognition requires a high index of suspicion in patients who had chest irradiation especially after a long latency period.

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