CASE PRESENTATION

Curing lymphoma, breaking the heart - multimodality imaging for valvular heart disease secondary to mediastinal irradiation

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INTRODUCTION

Hodgkin's lymphoma (HL) has an annual incidence of 3 per 100.000 persons and became a curable disease with survival rates close to 95%, but the cardiovascular complications due to mediastinal irradiation are an important long-term treatment related morbidity, and the second cause of late mortality after second malignancy[1]. Clinical manifestations of radiation cardiotoxicity can include coronary artery disease, valvular abnormalities, pericardial disease, conduction defects, less frequently restrictive cardiomyopathy, all possibly leading to heart failure. The identified relative risk of fatal cardiovascular events is between 2.2 and 12.7, an absolute excess risk of mortality from 9.3 to 28 per 10,000 person-years of follow-up and a 4.9-fold increase in risk of heart failure in survivors of HL[1,2,3]. In a study, 22% of survivors of childhood cancer, exposed only to radiotherapy, had evidence of diastolic dysfunction and 27.4% had reduced exercise capacity (<490 m at 6 minute walk test)[4]. Ostial lesions are frequent and during the treatment for HL the most affected are the left main stem, ostial segments of the circumflex and right coronary arteries[5,6]. Radiotherapy-induced valvular heart disease affects approximately 10% of treated patients, occurs especially at cumulative doses larger than 30 Gy and has a median time to diagnosis of 22 years[7,8,9,10]. It includes fibrosis and calcification of the aortic root, aortic valve cusps, mitral valve annulus and the base and mid portions of the mitral valve leaflets[11].

CASE REPORT

We report the case of a 61-year-old woman who was admitted to hospital for progressive worsening dyspnea over the last five years, at minimal effort at present. She has a history of Hodgkin's disease with radio- and chemotherapy as well as splenectomy in 1983 (at the age of 23) with sustained remission at the hematological re-evaluation this year. In 2004 she was diagnosed with a second malignancy - thyroid cancer with subsequent total thyroidectomy and hormonal replacement therapy. She is also known for the last 9 years with severe restrictive ventilatory defect, probably due to interstitial lung disease with pulmonary fibrosis secondary to radiation therapy.

The first abnormal cardiac evaluation was performed 5 years ago and concluded to degenerative aortic valve disease (moderate stenosis and regurgitation), mild mitral regurgitation, with normal left ventricle systolic function. Clinical examination revealed normal blood pressure and heart rate, holosystolic murmurs in the second right intercostal space next to sternum, at the apex and in the Erb's point and an apical diastolic murmur. Electrocardiogram showed normal sinus rhythm and her laboratory findings were also within normal limits, except for an increased BNP of 463.9 pg/ml. The evaluation of her functional capacity by 6 minutes walking test was stopped prematurely at 5 minutes on account of dyspnea, reaching only 380 m with a slight decrease in oxygen saturation (93%).

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Transthoracic echocardiography quantified a progression of the aortic valve disease, now with severe stenosis and moderate regurgitation (Figure 1), mitral valve disease (mild stenosis and moderate regurgitation) (Figure 2), moderate tricuspid regurgitation and secondary pulmonary hypertension (PH) (estimated pulmonary artery systolic pressure (PAP) 91 mmHg), with normal left ventricular systolic function. In the absence of a clear etiology to explain the PH, right heart catheterization was performed and confirmed the PH, with a mean PAP of 50 mmHg and a PCW of 20 mmHg, confirming postcapillary PH. Therefore the patient does not meet the criteria for specific PAH treatment. Coronary angiography showed right-dominant circulation and an ostial stenosis of 60% of the right coronary artery (Figure 3).

The patient has an indication for aortic valve replacement; in the context of past mediastinal radiotherapy the preferred method is transcatheter aortic valve implantation (TAVI). A cardiac computed tomography (CT), with systolic and diastolic multiphase reconstruction, was performed for better characterization of the aortic valve and annulus assessment, as well as for planning, landing zone calcification review and aortic root measurement, in order to perform TAVI procedure. The CT (Figure 4) emphasized the severe annular calcification and described a band of calcification in the posterior wall of the LV outflow tract extended from the left coronary cusp to the mitro-aortic junction (Figure 4D). Also, calcified plaques were described from the aortic root to the level of the first third of the descending aorta, suggestive for porcelain aorta (Figure 4F).

DISCUSSION

The present case is an illustration of the echocardiographic findings of radiotherapy related valvular disease, with fibrosis and calcification of the aortic root and aortic valve cusps, mitral valve annulus and the base and mid portions of the mitral valve leaflets, but with sparing the mitral valve tips and commissures (helping the differential diagnosis with rheumatic disease). The ostial lesions of coronary arteries are frequent after radiotherapy for HL, the most exposed being the left main stem and ostial segments of the circumflex and right coronary arteries. Survivors of HL have four- to seven-fold increased risk of coronary artery disease compared with the general population. Guidelines recommend percutaneous coronary intervention only for ostial lesions of more than 70% before TAVI as a IIa indication, level of evidence C[12]. Porcelain aorta is frequently associated in this setting. Due to the extensive calcifications of the ascending aorta, mediastinal fibrosis, impaired wound healing and associated coronary artery disease, conventional cardiovascular surgery is frequently prohibited and, when having severe aortic stenosis, patients who underwent mediastinal radiotherapy are eligible for TAVI (class I indication, level of evidence B)[12]. Of note, PH is an independent risk factor for survival after TAVI. Nevertheless, TAVI was proven to lead to an acute improvement of nearly all invasively assessed variables in patients with PH, with a similar improvement in functional NYHA class compared to patients without PH, indicating a similar benefit among survivors[13].

Conflict of interest: none declared.

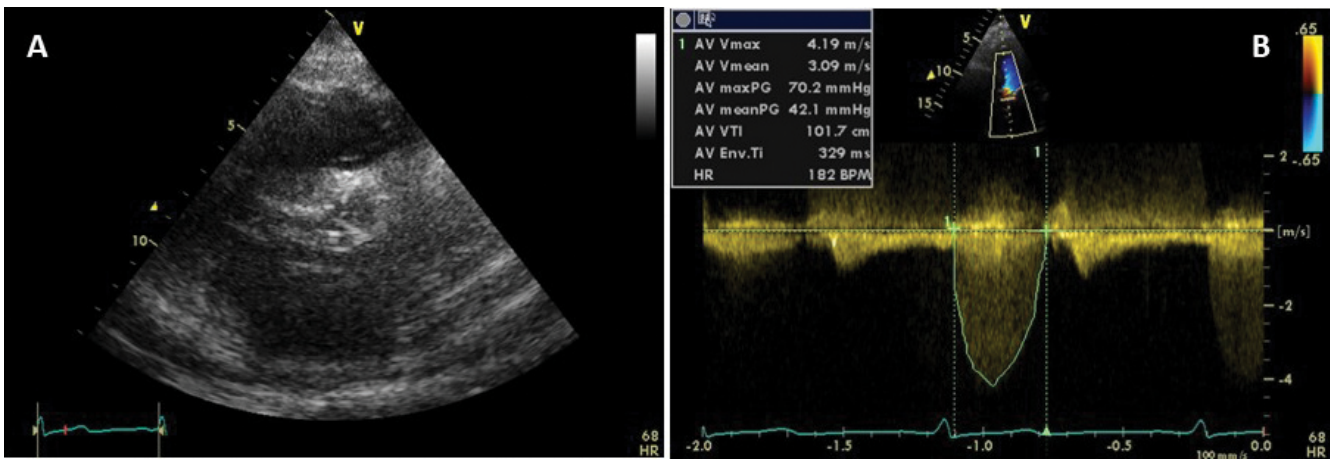

Figure 1. Transthoracic echocardiography. A. Parasternal short axis view shows tricuspid aortic valve with limited systolic opening. B. Doppler interrogation of the aortic valve flow shows high peak velocity (4.2 m/s) and mean transaortic gradient (42 mmHg).

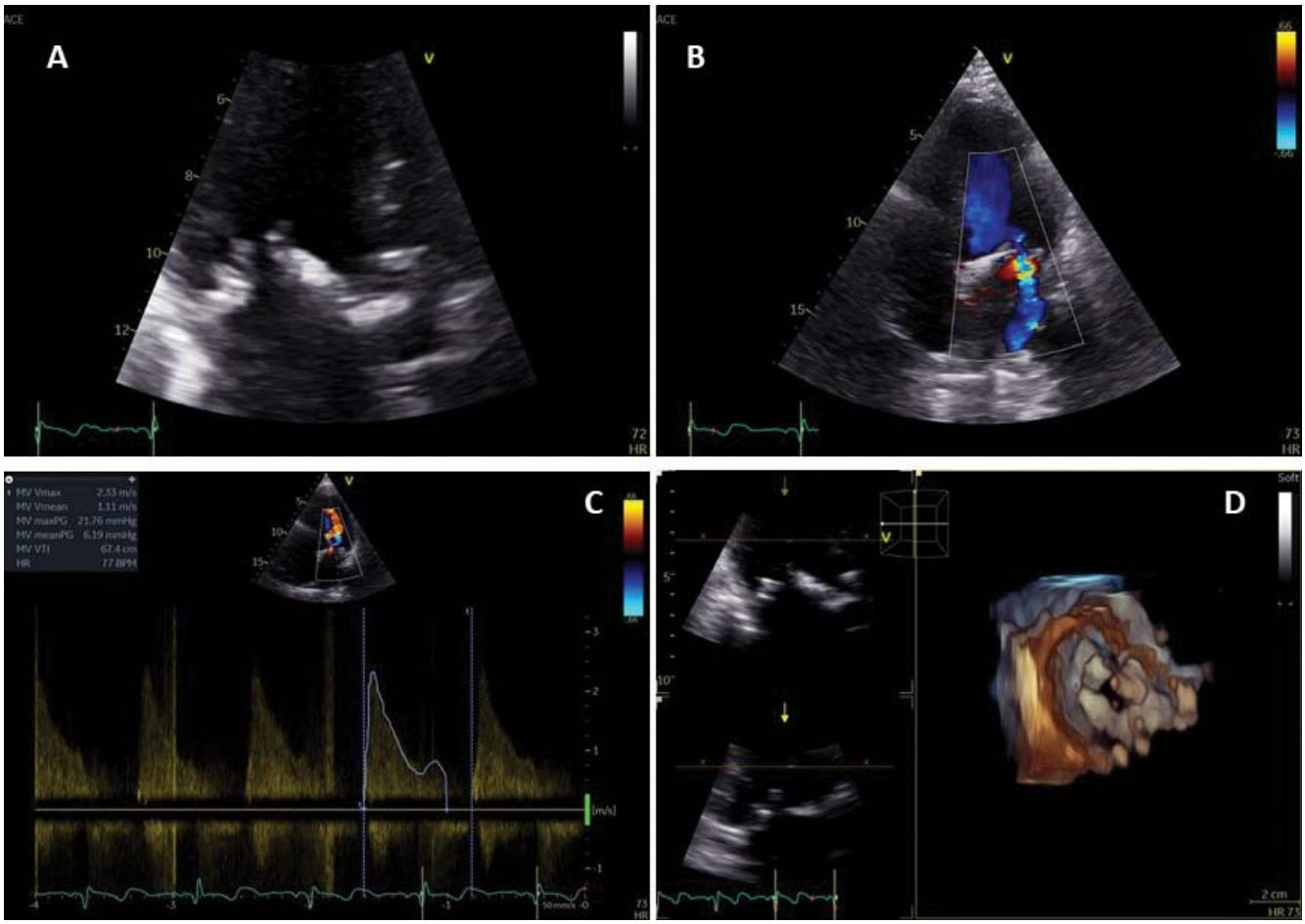

Figure 2. Transthoracic echocardiography. A. Zoomed image of apical long axis view showing mitral and aortic valve calcifications. B. Moderate mitral regurgitation. C. Color Doppler interrogation of the mitral valve shows elevated mean transmitral gradient (6.3 mmHg). D. 3D ventricular view of the mitral valve showing the limited maximal diastolic opening.

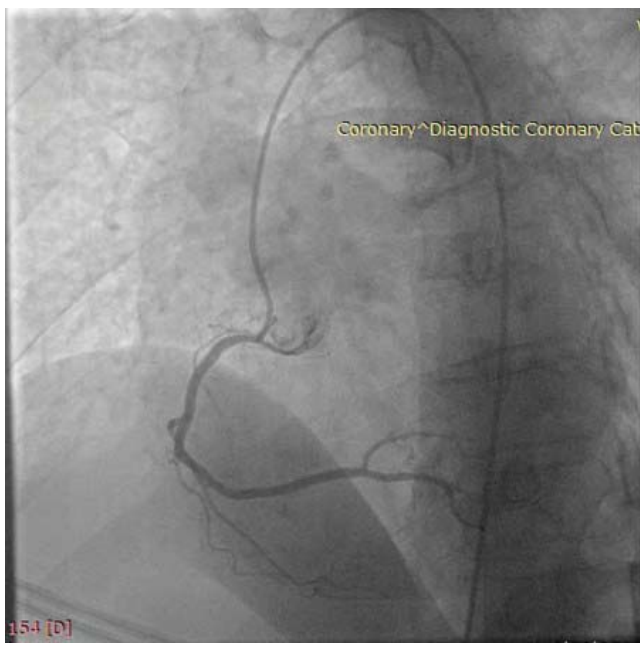

Figure 3. Coronary angiography showing 60% ostial stenosis of the right coronary artery.

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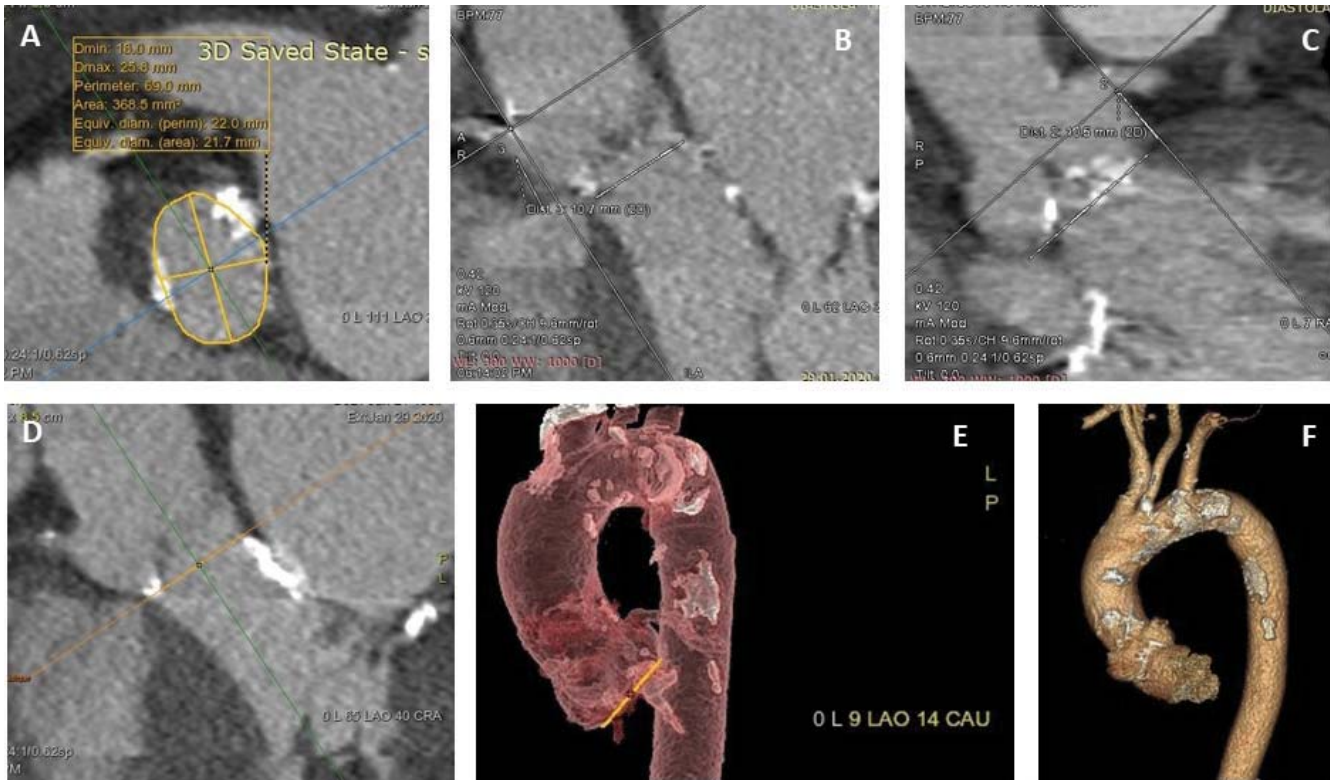

Figure 4. Computer tomography (CT) planning of the TAVI procedure. A. Systolic measurements of the longest and shortest annulus diameters, area and perimeter. Severe annulus calcification with nodules protruding into annular lumen can be seen. B and C. Right and left coronary ostium height measurements, which in this case, are permissive for TAVI procedure. D. Subannular calcification extending from the left coronary cusp into the LVOT up to mitro-aortic junction. E. Fluoroscopic planning- provision of optimal fluoroscopic projection angulations based on CT. F. Porcelain aorta.

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