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【 CASE REPORT 】

Successful Transcatheter Aortic Valve Implantation in a Patient with Radiation-induced Aortic Stenosis for Mediastinal Hodgkin Lymphoma

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Abstract:

Aortic stenosis (AS), a late complication of thoracic radiation therapy for chest lesions, is often coincident with porcelain aorta or hostile thorax. We herein report a 59-year-old man with a history of mediastinal Hodgkin lymphoma treated with radiation therapy but later presenting with heart failure caused by severe AS. Severe calcification in the mediastinum and around the ascending aorta made it difficult to perform surgical aortic valve replacement. The patient therefore underwent transcatheter aortic valve implantation (TAVI). It is important to recognize radiation-induced AS early, now that TAVI is a well-established treatment required by increasing numbers of successfully treated cancer patients.

Key words: aortic stenosis, TAVI, radiation, Hodgkin lymphoma, calcification

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Introduction

With increasingly effective treatments for Hodgkin lymphoma available, more survivors are at risk of developing radiation-induced valvular disease, such as aortic stenosis (AS), very late after therapy cessation (1, 2). The safety and effectiveness of transcatheter aortic valve implantation (TAVI) for patients who are at high risk due to the challenge of surgery is now well established; in addition, TAVI has good outcomes in patients with a history of radiation therapy (3, 4).

We herein report a patient who had been treated with both radiation therapy and surgery for mediastinal Hodgkin lymphoma who then successfully underwent transfemoral TAVI 25 years later.

Case Report

A 59-year-old man presented with dyspnea on exertion over the previous 4 months. He was being regularly followed up with echocardiography for moderate AS and aortic regurgitation. He had a history of mediastinal Hodgkin lymphoma 25 years earlier for which he had been treated with radiation therapy and surgery. He had received percutaneous coronary intervention (PCI) for the left-main branch 12 years earlier and had had alveolar hemorrhaging of unknown cause.

On admission, his blood pressure was 128/56 mmHg, pulse rate 86 beats/min, and oxygen saturation 98% (ambient air). Grade II/VI systolic murmur and grade I/VI diastolic murmur were audible at the second right sternal border, and respiratory sounds were clear. Laboratory findings were as follows: hemoglobin, 8.9 g/dL; serum creatinine, 1.0 mg/dL; white blood cell count, 6,350/μL; C-reactive pro-

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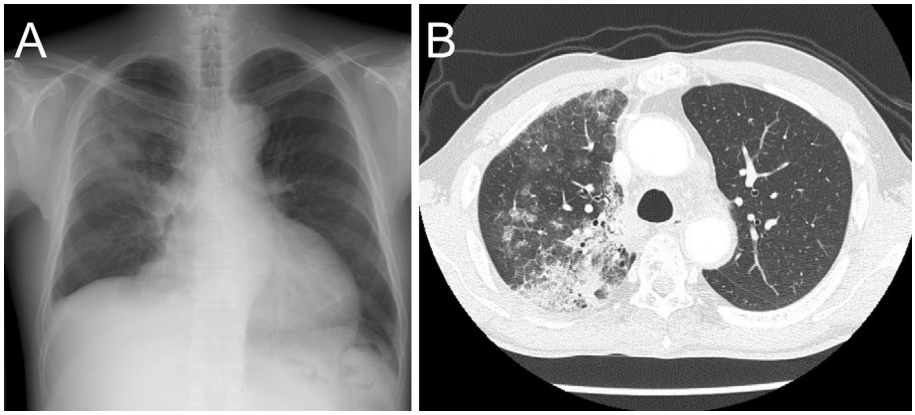

Figure 1. **(A) Chest radiography on admission showing infiltrative shadows in the right lung field. The cardiothoracic ratio (55.7%) is high, and the right cardiopulmonary angle is slightly dull. (B) Chest computed tomography (lung window) showing ground-glass opacity and patchy shadows in the right upper lung field, suggesting pulmonary hemorrhaging. There is pleural effusion in the right thorax.**

tein, 0.27 mg/dL; and brain natriuretic peptide, 866.8 pg/mL.

An electrocardiogram showed left ventricular hypertrophy with strain pattern. Chest radiography and computed tomography (CT) showed infiltrative shadows in the right middle lung field (Fig. 1). A transthoracic echocardiogram showed severe AS (peak aortic valve velocity, 4.0 m/s mean pressure gradient, 40 mmHg, and aortic valve area, 0.78 cm^2) and moderate aortic regurgitation with a mildly decreased left ventricular ejection fraction of 49.2%. The mean pulmonary capillary wedge pressure by right heart catheterization was 7 mmHg at rest with a normal cardiac index of 3.18 L/min/m^2; however, it increased significantly to 32 mmHg with isometric handgrip exercising. This suggested that his dyspnea was due not to alveolar hemorrhaging but to severe AS-related congestive heart failure.

The patient's surgical risk scores were low [European System for Cardiac Operative Risk Evaluation (Euro SCORE) II of 2.15%; Society of Thoracic Surgeons (STS) score of 2.79%]. However, chest CT showed severe calcification in the mediastinum and around the ascending aorta, indicating that it would likely be difficult to divide the adhesions surgically and clamp the aorta (Fig. 2A-C). In addition, high-dose heparin for cardiopulmonary bypass might have exacerbated the alveolar hemorrhaging. Surgical aortic valve replacement (SAVR) was therefore considered to be too high risk for both anatomical and clinical reasons. After discussion in a heart-team conference, transfemoral aortic valve implantation was performed. An Evolut R valve (Medtronic, Minneapolis, USA) was selected to avoid annulus rupture due to severe calcification of the left ventricular outflow tract (Fig. 2E).

A 29-mm Evolut R valve was successfully implanted (Fig. 3), after which post-dilation with 20- and 22-mm VACS III balloons (Osypka, Berlin, Germany) was performed. The procedure was completed without any complications, except for residual mild aortic regurgitation caused by the calcification. The patient's post-operative course was uneventful, including the absence of recurrent alveolar hemorrhaging despite starting dual antiplatelet therapy. He was discharged nine days after the operation.

Discussion

This case emphasizes the importance of recognizing the occurrence of valvular disease very late after radiation therapy and the usefulness of TAVI for patients at high surgical risk for anatomical reasons. Recent improvements in treatment for Hodgkin lymphoma mean that increasing numbers of survivors may be at a risk of developing valvular heart disease (1).

Radiation therapy to the mediastinum for a number of different cancers, including Hodgkin lymphoma and breast cancer, can result in severe valvular heart disease as long as several decades later. The pathophysiology of radiation-induced valvular disease is not fully understood. However, radiation exposure causes interstitial cells to activate transforming growth factor (TGF) β1, which leads to fibroblast proliferation and collagen synthesis. This process results in the thickening of the valve. Radiation exposure also increases the production of osteogenic factors, such as bone morphogenetic protein 2, osteopontin, alkaline phosphatase, and the transcription factor Runx2, promoting osteogenesis. A similar mechanism activated in bone formation results in valve calcification (2).

Radiation therapy is associated with different cardiac diseases, including coronary artery disease and vascular disease, as well as valvular disease. It induces inflammation, resulting in atherosclerosis with both micro- and macrovascular lesions. Radiation-induced coronary artery disease typically affects the proximal parts of the coronary arteries. Symptomatic radiation-induced coronary artery disease usually precedes radiation-induced valvular disease (5). These characteristics were evident in this patient, who had a his-

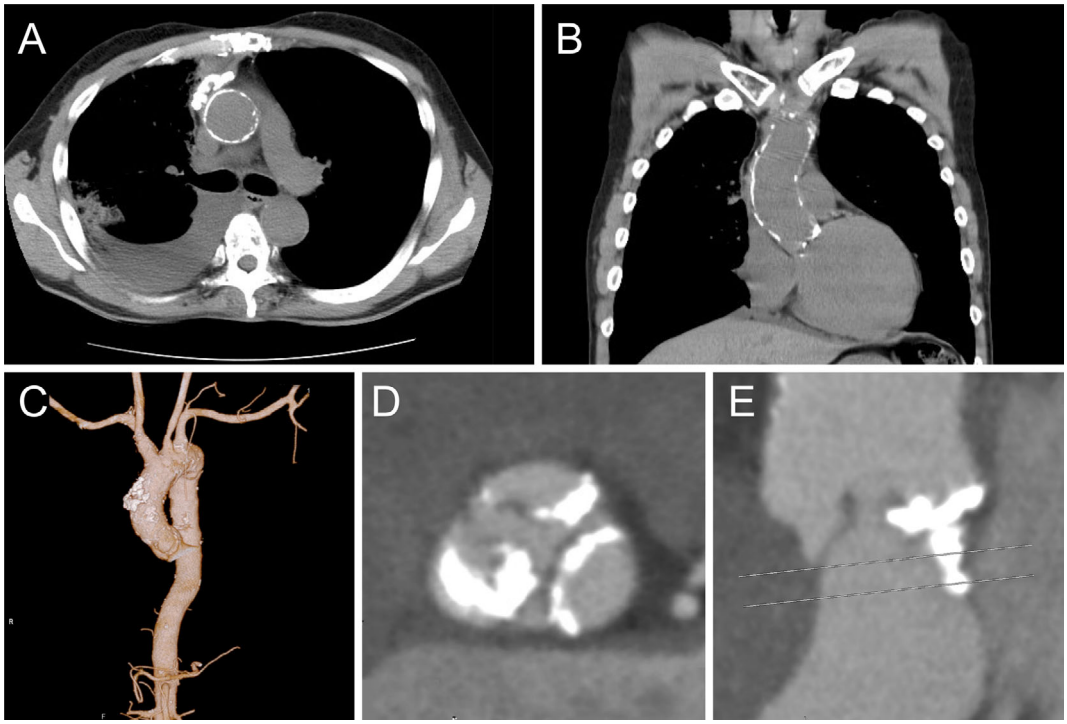

Figure 2. **Chest CT [mediastinal window, axial view (A), coronal view (B)] showing porcelain aorta and hostile thorax caused by radiation therapy. (C) 3D image of the aorta showing heavy calcification in the ascending aorta. (D) Short-axis view of the aortic valve. All three cusps are severely calcified, especially in the non-coronary cusp. (E) A self-expandable valve is suitable for the icicle calcification in the left ventricular outflow tract. Residual aortic regurgitation is also attributable to the calcification.**

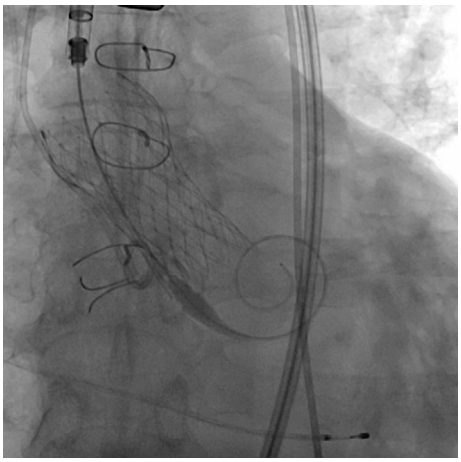

Figure 3. **An Evolut R valve (29 mm) was successfully expanded, and post-dilation was performed for residual prosthetic valve regurgitation.**

tory of PCI for the left-main branch before AS became symptomatic. Porcelain aorta (extensive circumferential calcification of the thoracic aorta) is another important complication after radiation therapy. It increases the risk of stroke when manipulating the aorta during surgical procedures. Sequelae of chest radiation and porcelain aorta are already considered important factors favoring the performance of TAVI rather than SAVR, according to current guidelines (6), although these anatomical factors are not reflected in surgical risk scores, such as the Euro SCORE II and STS score. The prevalence of porcelain aorta is reported to be 13% in radiation-induced cardiac disease and approximately 20% in patients undergoing TAVI (7).

Dijos et al. reported that patients undergoing TAVI after chest radiation therapy had a significantly higher prevalence of porcelain aorta and hostile thorax (52.6% vs. 28.5%, $p< 0.05$), were younger (68.3 vs. 82.5 years, $p<0.05$), had a lower surgical risk score (Euroscore: 7.1% vs. 21.8%, $p< 0.05$), and lower 6-month mortality rate (0% vs. 18%, $p= 0.048$) than those with degenerative AS (3). Using an inverse propensity weighting analysis, Zhang et al. reported lower 30-day and 1-year all-cause mortality rates in patients with a history of chest radiation therapy undergoing TAVI than in those with SAVR (4).

Although the durability of transcatheter aortic valves (TAVs) is of crucial concern in younger patients, severe structural valve deterioration occurs very rarely even 5 to 10 years after implantation, and the rate of such deterioration is acceptable (8). Furthermore, repeating TAVI, so-called "TAV-in-TAV", is reportedly a feasible and safe alternative in patients with degeneration of their first TAV (9).

In conclusion, this case illustrates the importance of being aware of severe AS as a late complication of radiation therapy for Hodgkin lymphoma. TAVI is an appropriate treatment for patients who are relatively young but at high surgi-

cal risk.

The authors state that they have no Conflict of Interest (COI).

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