Composite Hodgkin and Non-Hodgkin Lymphoma of the Mitral and Aortic Valves

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A 58-year-old man with a remote history of diffuse large B-cell lymphoma (DLBCL), status post chemotherapy, radiation, and peripheral blood stem cell transplantation, presented with splenic nodular sclerosis classical Hodgkin lymphoma. He was found to have aortic and mitral valve mass lesions. The mitral valve mass showed typical histologic and immunophenotypic features of nodular sclerosis classical Hodgkin lymphoma, whereas the aortic valve mass and aortic mitral curtain tissue showed DLBCL with necrosis. Both tumors were Epstein-Barr virus positive and were clonally related; however, they were not related to his DLBCL from 14 years prior. This is the first case report of a patient with a composite lymphoma affecting two cardiac valves. (J Am Soc Echocardiogr 2010;23:1113.e5-1113.e7.)

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Patients with histories lymphoma are at lifelong risk for developing both recurrences and different forms of lymphoma; however, involvement of the cardiac valves is very rare. Composite lymphomas, in which there are two types of lymphoma in a single anatomic site, are also remarkably rare. We present a patient with a history of diffuse large B-cell lymphoma (DLBCL), status post chemotherapy, radiation, and peripheral blood stem cell transplantation (PBSCT), who developed clonally related Hodgkin and non-Hodgkin lymphoma involving his aortic and mitral valves 12 years after PBSCT.

CASE PRESENTATION

In 1995, our patient was diagnosed with DLBCL on a tonsillar biopsy. He was treated with 8 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone and radiation to the tonsillar region. In 1996, he was diagnosed with a recurrence in the left upper arm. He received dexamethasone, cytarabine, and cisplatin salvage chemotherapy, achieving a partial response, and proceeded to carmustine, etoposide, dexamethasone, cytarabine, and cisplatin salvage chemotherapy, and PBSCT. After transplantation, he received adjuvant radiation therapy to the left upper extremity. He then did well for many years.

In December of 2008, a positron emission tomographic/computed tomographic scan performed for systemic symptoms showed lesions within the spleen and splenic hilar adenopathy. The patient underwent laparoscopic splenectomy. Pathology of the spleen and a peripancreatic lymph node demonstrated nodular sclerosis classical Hodgkin lymphoma (CHL). The tumor was positive for Epstein-Barr virus (EBV).

As part of a prechemotherapy evaluation, the patient underwent transthoracic echocardiography. It revealed a 2.2 × 1.6 cm mass attached to the atrial aspect of the anterior mitral leaflet. There was associated mild to moderate mitral regurgitation and mild stenosis. A 1.1 × 0.3 cm lesion was attached to the ventricular aspect of the non-coronary aortic valve cusp. There was mild to moderate aortic regurgitation. The ejection fraction was normal at 59%, without regional wall motion abnormalities. The estimated right ventricular systolic pressure was 48 mm Hg. The patient was hospitalized for further evaluation of the cardiac masses.

The patient denied fever, chills, rigors, vision changes, neurologic, and cardiovascular symptoms. He appeared well and had no stigmata of endocarditis. The cardiac apex was palpated at the sixth intercostal space and midclavicular line. The first heart sound was increased, and the second heart sound was normal. A grade II/VI systolic murmur was noted at the apex, which radiated to the axilla. There was no adenopathy.

Transesophageal echocardiography (Figure 1, Videos 1 and 2) confirmed the transthoracic echocardiographic findings of an echo-dense, broad-based mass attached to the anterior mitral valve leaflet. There was minimal mitral inflow obstruction, with a mean gradient of 3 mm Hg at a heart rate of 76 beats/min and mild mitral valve regurgitation. The differential diagnosis for the mitral valve mass included infection, metastatic tumor to the heart, primary cardiac tumor, marantic endocarditis, and thrombus. A linear echo-dense structure was identified on the noncoronary cusp of the thickened aortic valve. The differential diagnosis of the aortic valve lesion included infection, metastatic tumor to the heart, primary cardiac tumor, marantic endocarditis, fibroelastoma, and degenerative change. Blood cultures and serologic studies were performed and were negative. For tissue diagnosis and concern for embolism, the patient was referred for cardiac surgery.

Two-dimensional and three-dimensional intraoperative transesophageal echocardiography was done. The prebypass images showed...
a mass attached to the middle scallop (A2 segment) of the anterior mitral valve leaflet (Figure 2, Video 3). A primary median sternotomy was performed, and the patient was placed on cardiopulmonary bypass. A large tumor was noted on the anterior leaflet of the mitral valve (Figure 3). It covered almost the entire anterior leaflet and extended up into the anterior lateral trigone. The tumor was resected except for a thin layer on top of the mitral valve. On the aortic valve, there were multiple necrotic-appearing masses along the edges of all 3 cusps. There were also 2 pea-shaped masses on the aortomitral curtain below the left aortic valve cusp. They were debrided and debulked. Postbypass transesophageal echocardiographic imaging showed moderate mitral valve regurgitation and mild to moderate aortic valve regurgitation. Because of the degree of regurgitation after resection of the mass, and the frozen-section pathologic results of suspected lymphoma, valve replacement was deferred.

Pathologic examination of the mitral valve–derived mass showed typical histologic and immunophenotypic features of nodular sclerosing CHL, whereas the aortic valve mass and aortic mitral curtain tissue showed DLBCL with necrosis. Both tumors were Epstein-Barr Virus positive. Genomic deoxyribonucleic acid was extracted from both tumors, as well as the 1995 tonsillar biopsy. Polymerase chain reaction–based assays were performed using primers for the immunoglobulin heavy and κ light chain genes.11 The CHL and DLBCL from the heart had the same pattern of clonal gene rearrangements, suggesting that they were clonally related; however, this pattern was distinct from that obtained from the 1995 DLBCL specimen.

The patient's postoperative course was uneventful, and he was discharged on the fifth day. Six weeks after cardiac surgery, he started chemotherapy consisting of rituximab combined with cyclophosphamide, doxorubicin, vincristine, prednisone, etoposide, bleomycin, methotrexate, and cytarabine. He has since completed 6 cycles, and repeat positron emission tomography/computed tomography dem-

**Abbreviations**

CHL = Classical Hodgkin lymphoma  
DLBCL = Diffuse large B-cell lymphoma  
PBSCT = Peripheral blood stem cell transplantation

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Figure 1 Transesophageal images of 2.2 × 1.6 cm nodular sclerosis CHL (thick arrow) attached to mitral valve (A) and DLBCL (thin arrow) attached to the aortic valve (B). Ao, Aorta; LA, left atrium; LV, left ventricle.

Figure 2 Three-dimensional transesophageal images of the mitral valve mass (arrows) viewed from the left ventricle (A) and from the left atrium (surgeon’s view) (B). AL, Anterior leaflet.
onstrated complete remission. His mitral valve regurgitation progressed to severe, associated with left ventricular enlargement and symptoms. The valve was successfully repaired 7 months after his initial operation.

DISCUSSION

This case represents several unique features. Cardiac involvement is not uncommon in lymphoma, however, valvular involvement is exceedingly rare. In 2 autopsy studies with a total of 346 patients with lymphoma, 61 patients (18%) had metastases to the heart, but only 1 had valvular involvement. There have been other isolated case reports of primary lymphoma affecting prosthetic valves, and 1 case report of primary lymphoma affecting native valves.

Although patients with one type of lymphoma are at lifelong risk for developing both recurrences and different types of lymphoma, it is very unusual to develop two types of lymphoma in a single anatomic site, a so-called composite lymphoma. This is the first report documenting a composite lymphoma affecting the heart. Further evaluation of this patient suggested that the CHL and DLBCL components were clonally related to each other, and both were EBV positive. The comparative molecular data in this patient suggest that the composite lymphoma in the heart was clonally unrelated to his original DLBCL. Despite the 12-year interval following PBSCT, it is likely that immunosuppression contributed to the Epstein-Barr Virus-associated composite lymphoma in this patient.

Transthoracic and transesophageal echocardiographic imaging demonstrated an incidental finding of a large sessile mitral and smaller, less well defined aortic valve masses. Real-time three-dimensional transesophageal echocardiographic imaging provided additional characterization of the masses and demonstrated extension on to the left atrial wall toward the mitral aortic intervalvular fibrosa. These features were highly suspicious for recurrent lymphoma.

CONCLUSION

Because of increasing rates of immunosuppression, either human immunodeficiency virus related or iatrogenic, cardiac lymphomas are increasing in frequency. It is important for cardiologists and cardiothoracic surgeons to maintain a high level of suspicion of malignancy when masses are discovered in the heart, as they potentially respond to chemotherapy.

REFERENCES