Primary Cardiac Lymphoma Patients Presenting With Heart Failure

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INTRODUCTION

Diffuse large B cell lymphoma (DLBCL) is the most common histologic type of non-Hodgkin lymphomas, accounting for 24% of new cases.[1] Typically, DLBCL manifests as a symptomatic enlarged mass, most commonly a lymphatic nodule, located in the neck, abdomen, or mediastinum. Constitutional symptoms, such as fever, night sweats, and weight loss, are observed in 30% of patients.[1] Approximately 30% of the patients will have disease originating from extralymphatic organs, which is associated with poorer prognosis.[1] We present 3 unique patients diagnosed with DLBCL who presented with heart failure symptoms and a mass involving the right atrium and ventricle (RA and RV).

CASE PRESENTATION 1

A 77-year-old woman with a medical history of hypertension and type 2 diabetes mellitus was diagnosed 5 years prior to the current admission with right breast human epidermal growth factor receptor 2–(HER2-) positive adenocarcinoma. The patient underwent neoadjuvant chemotherapy (including doxorubicin and cyclophosphamide), followed by lumpectomy, adjuvant radiation, and trastuzumab plus pertuzumab therapy. The patient attained complete response without recurrence.

The patient was admitted to the hospital due to exacerbating dyspnea, development of bilateral lower extremity edema, and gradual worsening fatigue and abdominal distension for the prior 3 months. Physical examination was notable for dyspnea, desaturation of 88% on room air, elevated jugular venous pressure (JVP), and bilateral lower extremity edema. The lung examination revealed findings consistent with bilateral pleural effusion, which was confirmed on chest x-ray. Transthoracic echocardiography (TTE) showed a dilated RV (mid-RV diameter of 5.1 cm and RV base to apex of 8.2 cm), with a large mass located on and protruding from the RV free wall into the RV. Another small, noninferior vena cava–involving mass was observed in the RA (Figure 1, Videos 1 and 2). To further evaluate the cardiac masses, the patient underwent a cardiac computed tomography (CCT) scan, which revealed the presence of large intracardiac masses involving both the RA and RV (Figure 2). The primary differential diagnosis (DD) included sarcoma, breast carcinoma, or lymphoma. Following a multidisciplinary team discussion, the patient underwent right pleural tap, which yielded large, atypical cells upon analysis. Flow cytometry conducted on the pleural fluid indicated the presence of a clonal population of B cells, confirming the diagnosis of DLBCL.

VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, apical 4-chamber view, demonstrates the right ventricular (RV) mass measuring 3.3 × 5.5 cm (*arrow*) within the dilated (mid diameter, 5.1 cm; RV length, 8.2 cm) and dysfunctional (tricuspid annular plane systolic excursion, 1.4 cm; S′ wave, 6.0 cm/sec) RV in patient 1.

Video 2: Two-dimensional TTE, zoomed 4-chamber view, demonstrates the RA mass (*arrow*) in patient 1.

Video 3: Two-dimensional TTE, apical 4-chamber view, demonstrates the resolution of the masses in both the RV and RA in patient 1 after successful treatment.

Video 4: Two-dimensional TTE, apical 4-chamber, RV-focused view, demonstrates the RV mass (*upper arrow*; 2.3 × 4.4 cm) and RA mass (*lower arrow*; 2.3 × 3.0 cm) and a small pericardial effusion in patient 2. The mid-RV diameter is dilated at 3.2 cm, and the RV systolic function was reduced (tricuspid annular plane systolic excursion, 1.3 cm; S′ wave, 8.0 cm/sec).

Video 5: Two-dimensional TTE, apical 4-chamber view, demonstrates resolution of RV and RA masses after treatment in patient 2.

Video 6: Two-dimensional TTE, parasternal long-axis view, demonstrates a large (>3.0 cm) pericardial effusion (*arrow*) with evidence of cardiac tamponade based on diastolic RV free-wall motion in patient 3.

Video 7: Two-dimensional TTE, subcostal view, demonstrates the RA mass (5.3 × 3.3 cm; *arrow*) in patient 3.

Video 8: Two-dimensional TTE, subcostal view, demonstrates resolution of the RA mass in patient 3 after treatment.

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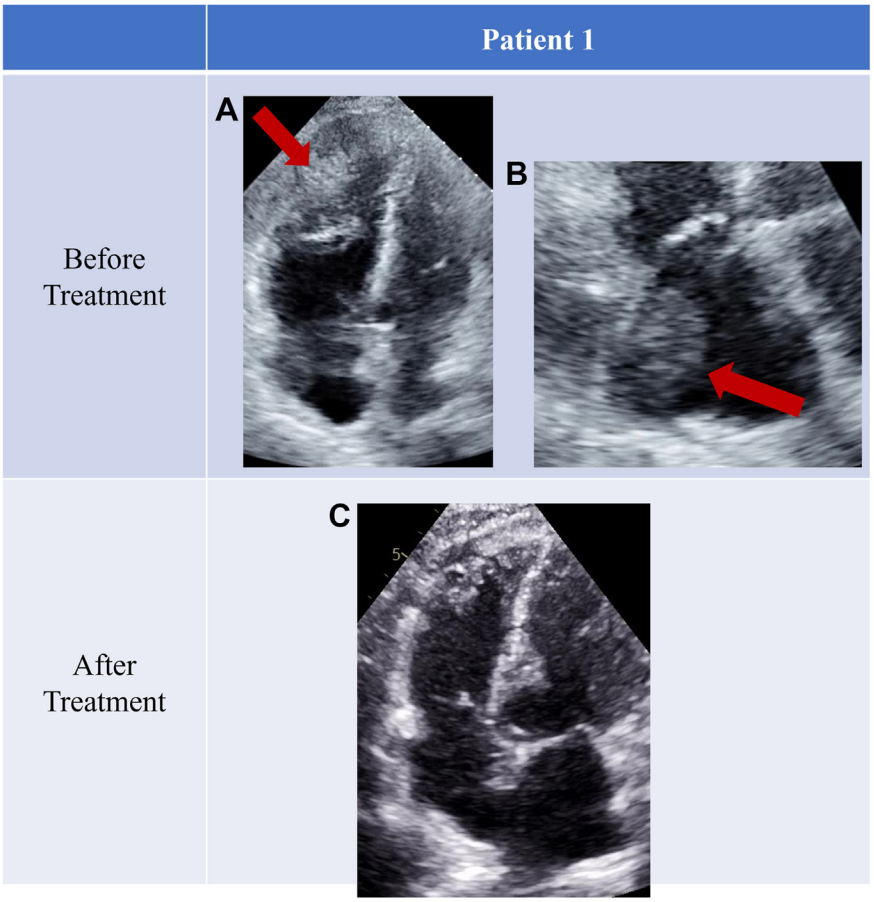

Figure 1 Transthoracic echocardiogram of patient 1 before (*top row*) and after treatment (*bottom row*). **(A)** Apical 4-chamber view, mid diastolic phase, demonstrates the RV mass measuring 3.3 × 5.5 cm (*arrow*). **(B)** Apical 4-chamber zoomed view, systolic phase, demonstrates the RA mass measuring 2.3 × 3.3 cm (*arrow*). **(C)** Apical 4-chamber view, mid diastolic phase, demonstrates the regression of the masses in both the RV and RA after treatment.

CASE PRESENTATION 2

A 73-year-old woman with a history of dyslipidemia was admitted due to 6 weeks of exertional dyspnea and bilateral lower extremity edema. No fever, chest pain, weight loss, or night sweats were reported. Vital signs were normal; however, physical examination was notable for increased JVP, diminished heart sounds, and bilateral lower extremity edema. Labs were significant for elevated brain natriuretic peptide levels (216 pg/mL). The initial point-of-care ultrasound showed large pericardial effusion, followed by TTE examination revealing a large mass in the RA and RV (Figure 3, Video 4). The DD considered the possibility of both primary and secondary cardiac tumors. Total-body computed tomography identified 2 large masses in the RA and RV (Figure 4) and 2 enlarged lymph nodes in the mediastinum, with the largest measuring up to 1.3 cm. Pericardial tap was nondiagnostic.

A multidisciplinary team composed of an interventional cardiologist, hematologist, radiologist, and pulmonary specialist determined that a cardiac mass biopsy would be the most optimal and secure method for diagnosis. Consequently, a transcutaneous biopsy of the RV mass led to a tissue diagnosis of DLBCL.

CASE PRESENTATION 3

A 76-year-old woman with a history of localized left breast intraductal carcinoma, treated with lumpectomy and radiation therapy 1 year prior to the current admission, presented to the hospital with complaints of fatigue and exertional dyspnea. Vital signs were normal, except for a sinus tachycardia of 100 beats per minute. Physical examination was notable for tachypnea, elevated JVP, and diminished heart sounds. Lab tests were significant for elevated brain natriuretic peptide

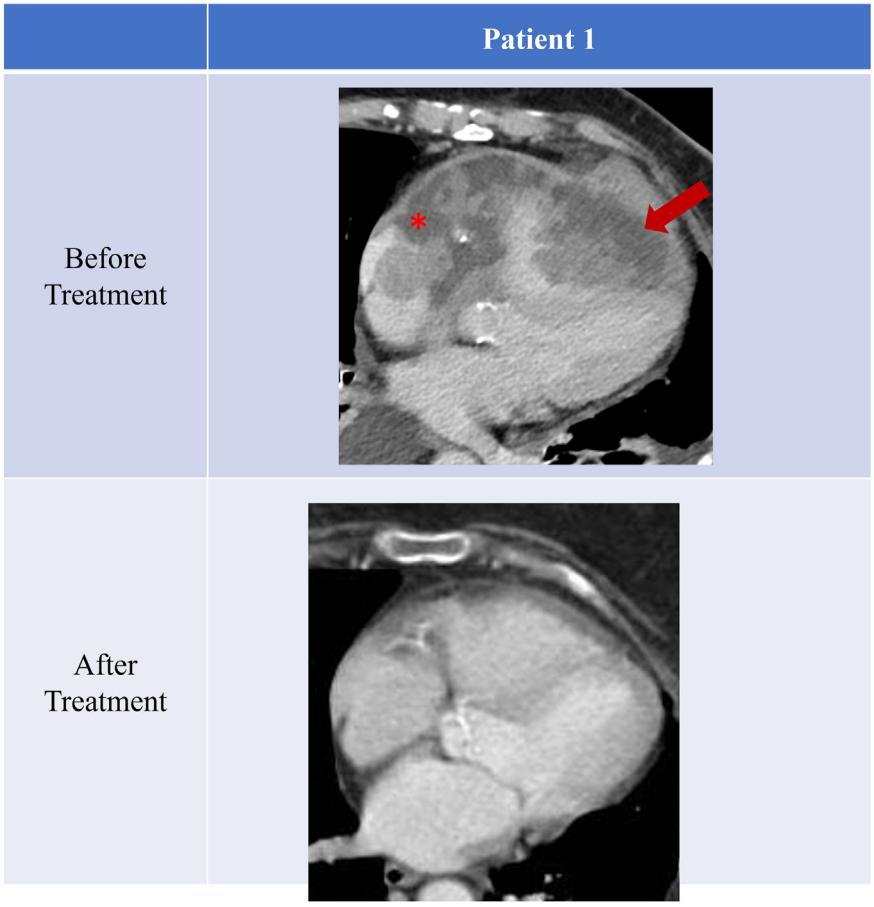

Figure 2 Cardiac computed tomography images of patient 1 before (*top*) and after (*bottom*) treatment. Axial view at the midlevel of the heart (*top*) demonstrates the RA (*asterisk*) and RV (*arrow*) masses, measuring 3.0 × 3.2 cm and 4.0 × 5.5 cm, respectively. After treatment, mass regression is demonstrated at a similar level of the heart for direct comparison (*bottom*).

levels of 1,202 pg/mL. Transthoracic echocardiogram revealed a large pericardial effusion (maximal diameter of the pericardial effusion space measured 3.7 cm) and a large mass in the RA, along with a smaller mass detected in the other 3 heart chambers (Figure 5, Videos 6 and 7).

After a multidisciplinary team discussion and consideration of the patient's medical history, the major DD included angiosarcoma, lymphoma, or relapse of breast carcinoma. Given the patient's pretamponade state, a therapeutic pericardiocentesis was performed, which drained 1 L of fluid. Cytological analysis of the fluid excluded the presence of sarcoma and carcinoma cells but revealed atypical lymphoid cells, which were consistent with lymphoma. Subsequently, the patient underwent CCT imaging (Figure 6) and laboratory workup, which excluded involvement of other organs. Histological and immunohistochemical analyses of the fluid were consistent with the diagnosis of DLBCL.

Following a comprehensive hematological workup for staging, all 3 patients were treated with 6 courses of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP protocol, first cycle given in reduced dosage with cyclophosphamide pro-phase). It is noteworthy that the third patient required a pacemaker implantation before the treatment due to symptomatic complete atrioventricular block. Following discharge, they were closely monitored with frequent imaging assessments. A significant improvement in heart failure symptoms was observed shortly after the second treatment in all 3 cases, along with a significant decrease in the size of the masses. All patients achieved complete response.

DISCUSSION

Lymphoma affecting the heart and pericardium is typically secondary to disseminated disease and rarely seen as primary malignancy.

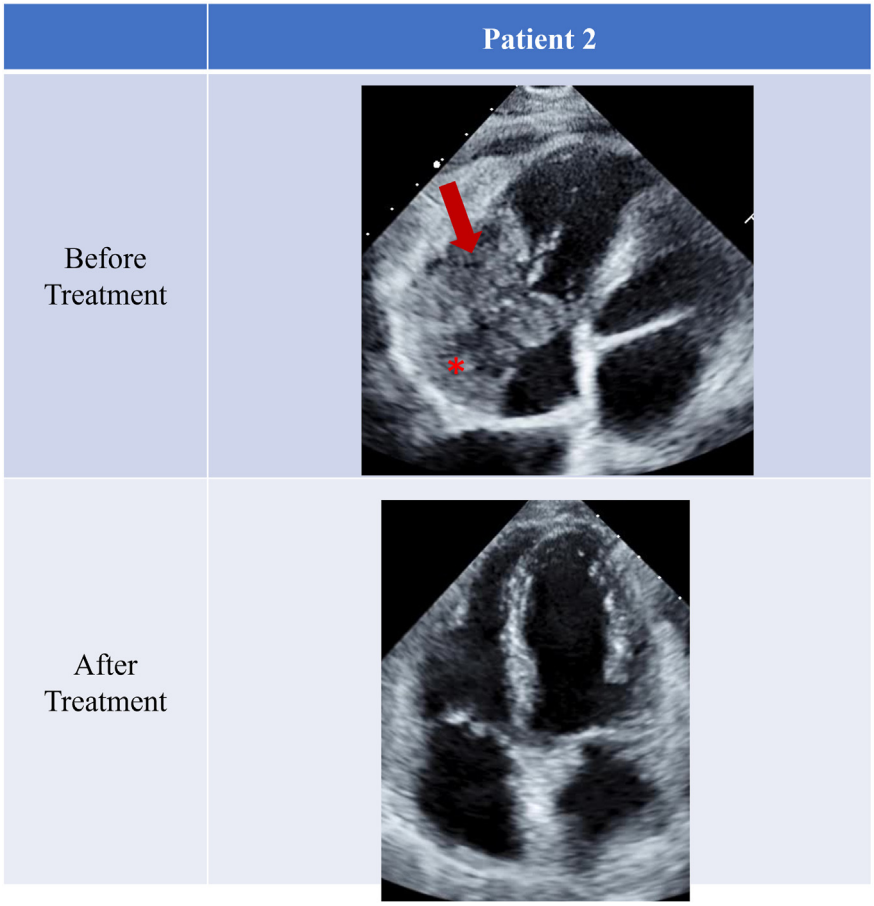

Figure 3 Transthoracic echocardiogram of patient 2 before (*top*) and after treatment (*bottom*). Apical 4-chamber, RV-focused view, systolic phase (*top*), demonstrates the RA (*asterisk*) and RV (*arrow*) masses measuring 2.3 × 4.4 cm and 2.3 × 3 cm, respectively. The RV cavity is dilated (mid-RV diameter = 3.2 cm). Apical 4-chamber view, systolic phase (*bottom*), demonstrates the resolution of the masses in both the RV and RA after treatment.

Among primary cardiac tumors, lymphomas represent only 1.3%, and among extranodal lymphomas, the incidence is 0.5%. However, up to 20% of secondary cardiac involvement has been reported.[2,3] Diffuse large B cell lymphoma is considered the most common type of lymphoma involving the heart. The diagnostic criteria for primary cardiac lymphoma (PCL) have evolved since its initial description in the 1930s, leading to various definitions.[4] According to the 2015 World Health Organization classification, PCL is defined as lymphoma that exclusively involves the heart or when the primary burden of the tumor is located in the cardiac chambers, myocardium, or pericardium, even if a limited extracardiac lymphoma is present.[5]

Primary cardiac lymphoma is most commonly found in the right-sided cardiac chambers, particularly the RA,[5] and is almost exclusively classified as DLBCL.[2] Symptoms of heart failure are typically the initial presenting symptoms of PCL, with dyspnea being the most common. The complications of cardiac lymphoma reflect the location of the tumor and can include conduction abnormalities, pericardial effusion (including tamponade), congestive heart failure, angina, and superior vena cava syndrome.[4] Our patients demonstrated clinical and imaging findings consistent with existing literature. All 3 patients presented with symptoms indicative of heart failure, while 2 patients exhibited an additional complication of pericardial effusion, requiring drainage. Notably, all patients presented with masses affecting the right heart chambers.

Echocardiographic imaging allows a noninvasive assessment of lymphoma cases involving the heart, with TTE identifying approximately 55% of intracardiac masses and transesophageal echocardiography raising the sensitivity to nearly 100%.[2,6,7] Cross-sectional imaging plays an important role in further characterizing the cases, with both CCT and cardiovascular magnetic resonance imaging

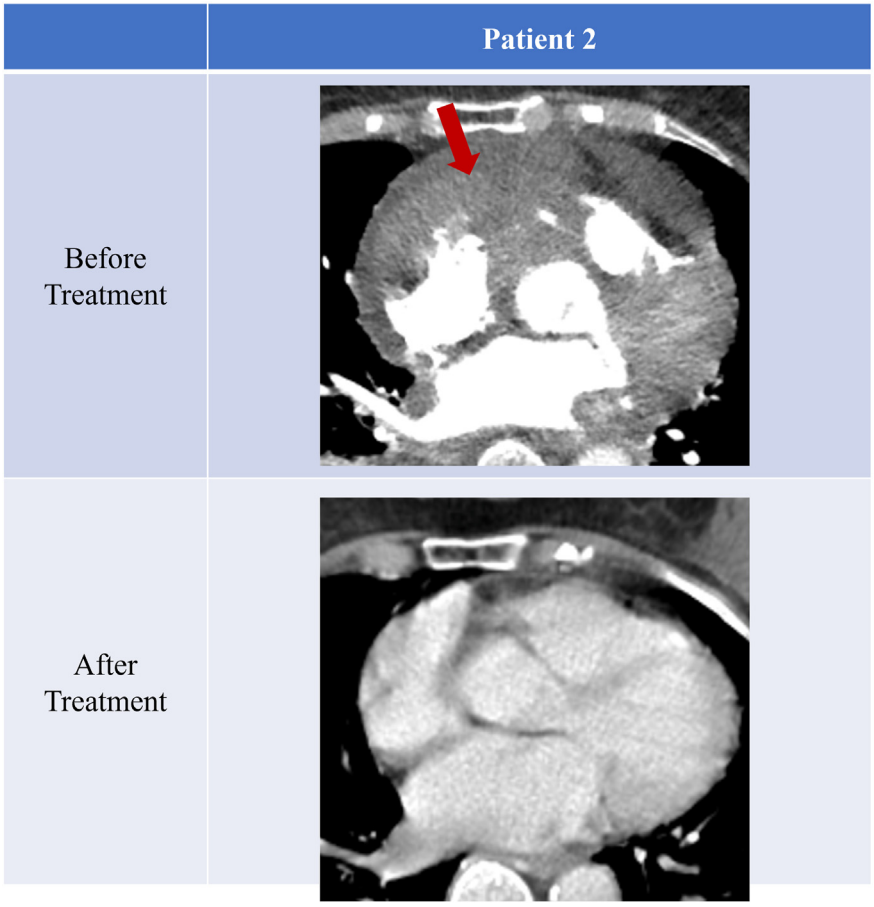

Figure 4 Cardiac computed tomography images of patient 2 before (*top*) and after (*bottom*) treatment. Axial view at the midlevel of the heart demonstrates the continuous, contrast-enhanced mass from the RA through the tricuspid valve to the RV (*arrow*) measuring 6.0 × 5.0 cm. After treatment, mass regression is demonstrated at a similar level of the heart for direct comparison (*bottom*).

providing enhanced evaluation of heart involvement and ruling out other diagnoses.[2,8] Histologic examination is necessary for the final diagnosis of lymphoma. Obtaining a tissue diagnosis for heart masses may be challenging due to the mass mobility and suboptimal three-dimensional visuality. As demonstrated in our cases, starting with a safe procedure for tissue diagnosis may suffice and prove effective.

All 3 of our patients underwent a total-body computed tomography scan. The imaging modality was selected due to its wide availability, capacity to identify other affected sites, and routine use as part of the standard lymphoma protocol before commencing treatment.

The standard therapy protocol for DLBCL involves the administration of the R-CHOP chemotherapy protocol. Although radiation and surgery have been employed as treatment options, they are usually reserved for palliative care or when chemotherapy cannot be tolerated by the patient.[9]

The prognosis for PCL or secondary cardiac lymphoma is generally poor, with a median overall survival rate of 2.2 years.[10]

CONCLUSION

In this paper, we describe 3 cases of PCL that were presented with symptoms of heart failure. All 3 patients demonstrated significant improvement in quality of life and complete response to standard protocol.

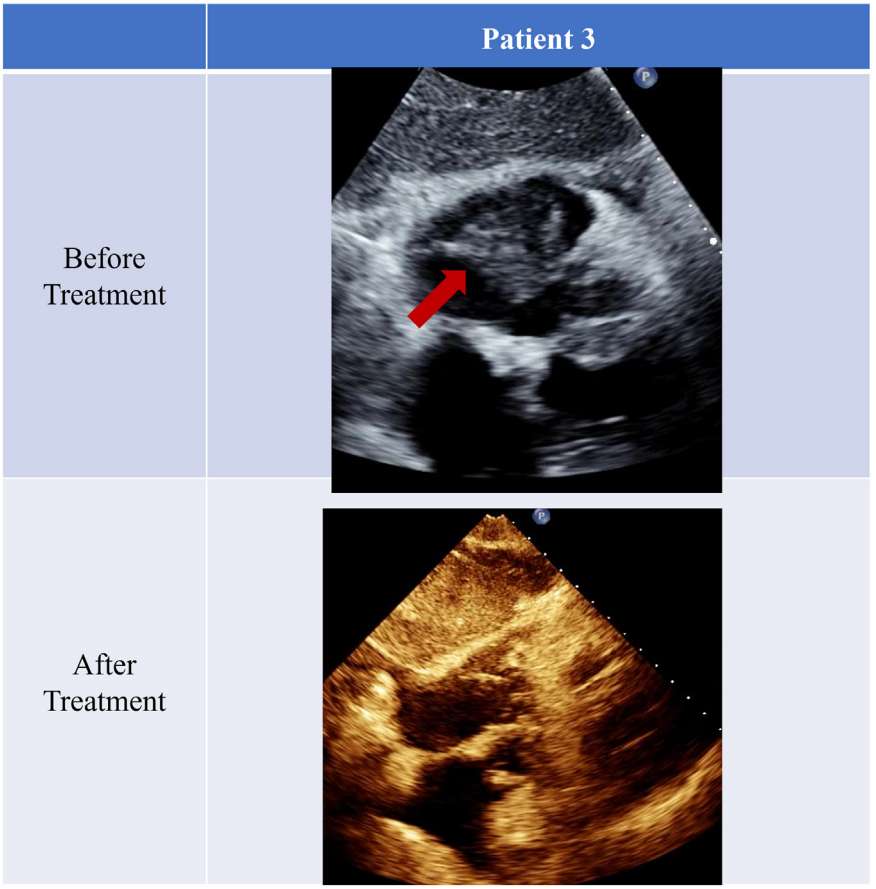

Figure 5 Transthoracic echocardiogram of patient 3 before (*top*) and after treatment (*bottom*). Subcostal 4-chamber view, systolic phase (*top*), demonstrates the RA mass (*arrow*) measuring 5.3 × 3.3 cm. Subcostal 4-chamber view, diastolic phase (*bottom*), demonstrates the regression of the RA mass after successful treatment.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing deidentified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

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DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

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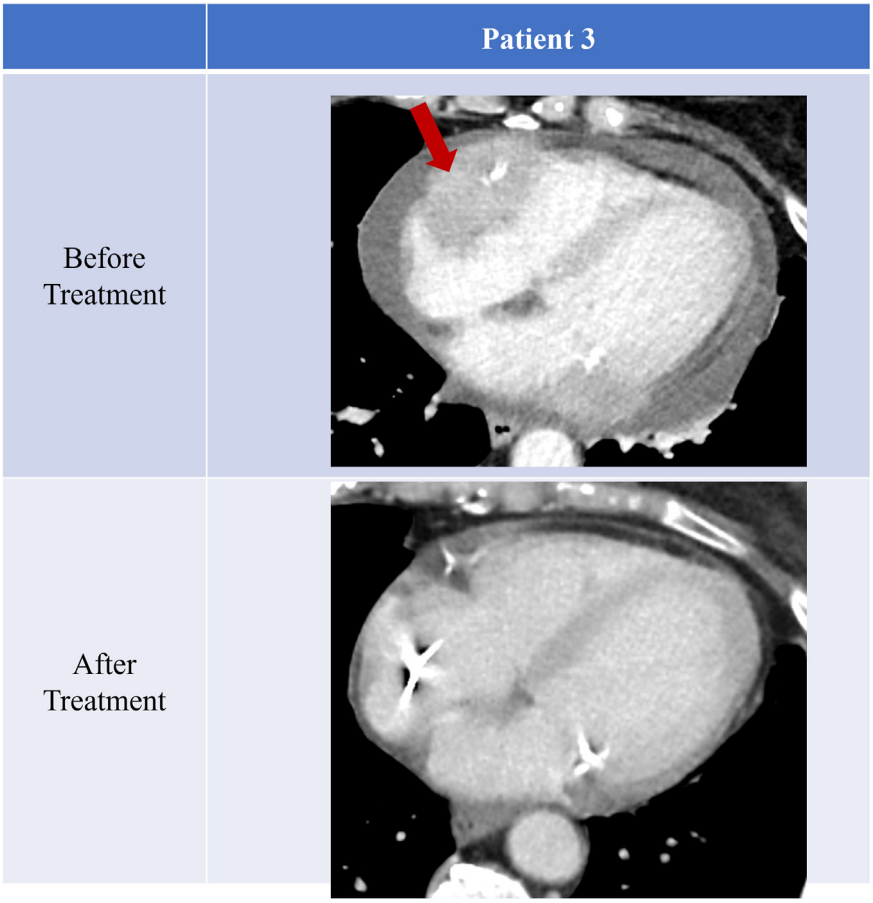

Figure 6 Cardiac computed tomography images of patient 3 before (*top*) and after (*bottom*) treatment. Axial view at the midlevel of the heart demonstrates the contrast-enhanced mass protruding from the right atrioventricular groove into the RA cavity continuous toward the RV (*arrow*) measuring 6.0 × 4.0 cm. After treatment, mass regression is demonstrated at a similar level of the heart for direct comparison. Multiple "star" artifacts are seen from the pacemaker wires.

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