Inoperable Primary Ovarian Carcinoid Led to the Progression of Carcinoid Heart Disease From Right-Sided to Both-Sided Involvement

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A 73-year-old woman presented with diarrhea, leg edema, and exertional dyspnea. Six years before admission, she had been hospitalized for heart failure with moderate-to-severe tricuspid regurgitation because of incomplete leaflet coaptation (Figure 1A; Movie I in the Data Supplement). She was treated with furosemide and has remained on this therapy since then. In the same period of time, an ovarian tumor was detected after total hysterectomy and unilateral salpingo-oophorectomy for uterine myoma. Although the surgeons tried to resect the tumor, it was inoperable and could not be diagnosed definitively at that time because of postoperative adhesion.

On admission, physical examination revealed jugular venous distention, hepatomegaly, and ascites. Compared with the echocardiogram at the previous hospitalization (Figure 1A), the tricuspid valve leaflets were further retracted with severe regurgitation (Figure 1B; Movie II in the Data Supplement). The pulmonary valve was also retracted with moderate regurgitation (Figure 1C and 1D; Movies III and IV in the Data Supplement). It was noteworthy that the aortic and mitral valves became thickened and moderately regurgitant (Figure 2A through 2D; Movies V and VI in the Data Supplement). The positive contrast echocardiography suggested an intracardiac right-to-left shunt through patent foramen ovale (Movie VII in the Data Supplement). Urinary 5-hydroxyindoleacetic acid was markedly increased (197.2 mg/d, normal range <6.0 mg/d), and serum 5-hydroxytryptamine levels were increased in both venous and arterial blood (1.18 and 1.07 μg/mL, respectively; normal range <0.35 μg/mL). Pelvic T2-weighted magnetic resonance imaging showed low-intensity solid components with cystic mass, which was consistent with the fibrosis of carcinoid induced by serotonin (Figure 3). Sequential blood sampling from a peripheral catheter system showed a step-up of serotonin levels between right atrium and right common iliac vein and between right atrium and superior vena cava (1.06, 0.67, and 0.73 μg/dL in right atrium, right common iliac vein, and superior vena cava, respectively; normal range <0.35 μg/dL). The step-up suggested the drainage of serotonin from ovarian vein to inferior vena cava. Systemic computed tomography and gastrointestinal endoscopy did not show any tumors in any other organs, such as gut, liver, and lung. These findings were consistent with carcinoid heart disease arising from a suspected primary ovarian carcinoid (OC) tumor. She underwent surgical replacement of the tricuspid, pulmonary, and aortic valves with bioprosthetic valves and a direct suture of the interatrial septum. As preoperative 3-dimensional echocardiograms showed, thickening of the chordae and papillary muscle of the retracted tricuspid valve was observed (Figure 4A and 4B), and all the aortic valve leaflets were thickened intraoperatively (Figure 4C and 4D). As a coronal view of cardiac magnetic resonance imaging showed, the mildly stenotic pulmonary valve was observed from pulmonary artery side (Figure 4E and 4F). Glistening white and yellow deposits were macroscopically found in the excised valves (Figure 5A through 5C). Pathological analysis showed the fibrosis over proper valve tissue not only in the tricuspid valve (Figure 5D) but also in the aortic valve (Figure 5E). The valve tissue was replaced with edematous tissue in the pulmonary valve (Figure 5F). These pathological findings established the diagnosis of carcinoid heart disease on both sides of the heart. Her postoperative course was uneventful. When last seen 16 months later, she was asymptomatic on a somatostatin analog, octreotide.

Carcinoid heart disease can lead to heart failure and remains a major cause of morbidity and mortality in patients with carcinoid syndrome. A mean life expectancy of carcinoid heart disease is reported to be <2 years. The vasoreactive substances from the carcinoid tumor cause valvular lesion development. Left-sided lesions occur in <10% of the patients because the substances are mostly inactivated in the lung.[1] Resumption of patent foramen ovale is one of the causes of the involvement of left-sided valves. The left-sided carcinoid heart disease can cause hemodynamic instability that necessitates surgical intervention. Although the optimal timing of surgical intervention has not been identified, the onset of the symptoms may be one of the timings

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in consideration of poor prognosis in symptomatic carcinoid heart disease.[2] Therefore, early diagnosis and subsequent follow-up are indispensable.

OC is a rare neuroendocrine neoplasm in elderly female patients, accounting for only 0.3% to 1.0% of all carcinoid tumors.[3] In OC, the direct venous drainage of vasoreactive substances into the systemic circulation results in the cardiac involvement without hepatic metastasis. There are few published reports about OC-related carcinoid heart disease. To the best of our knowledge, only one necropsy study reported both-sided carcinoid heart disease possibly caused by OC.[4] Here, we demonstrated for the first time by a series of 2-dimensional echocardiograms the time-dependent progression from right-sided to both-sided involvement of the heart in OC-related carcinoid heart disease. Preoperative 3-dimensional echocardiogram and cardiac magnetic resonance imaging could provide detailed anatomic information of its long-term degenerative changes. The unexpectedly long-term progression over the course of 6 years could be seen due mainly to the inoperable state of the undiagnosed OC. OC-related carcinoid heart disease should be considered as a differential diagnosis in the case of an elderly female patient with isolated right-sided valve disease and ovarian tumor. Furthermore, the follow-up of heart disease is more important especially when a primary tumor is inoperable because there is still a possibility of the disease progression as seen in this case.

Disclosures

None.

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KEY WORDS: carcinoid heart disease ■ echocardiography ■ heart failure ■ magnetic resonance imaging ■ valve replacement

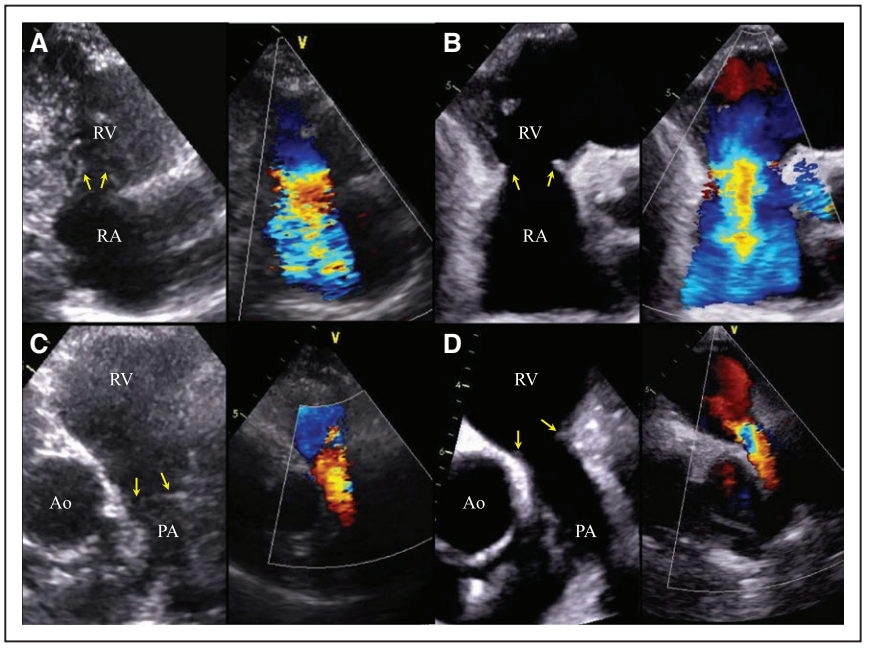

Figure 1. The time-course of changes in the echocardiograms of the right-sided heart valves. **A** and **C**, Tricuspid and pulmonary valves recorded 6 years earlier (arrows). **B** and **D**, Tricuspid and pulmonary valves recorded on admission (arrows). **Left**, The B-mode image; and **right**, the color Doppler image. Ao indicates aorta; PA, pulmonary artery; RA, right atrium; and RV, right ventricle.

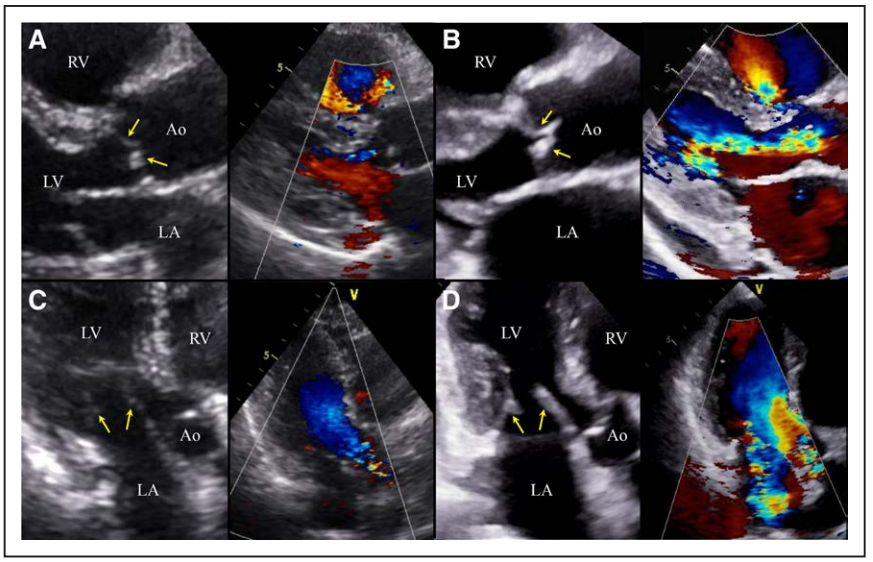

Figure 2. The time-course of changes in the echocardiograms of the left-sided heart valves. **A** and **C**, Aortic and mitral valves recorded 6 years earlier (arrows). **B** and **D**, Aortic and mitral valves recorded on admission (arrows). **Left**, The B-mode image; and **right**, the color Doppler image. Ao indicates aorta; LA, left atrium; LV, left ventricle; and RV, right ventricle.

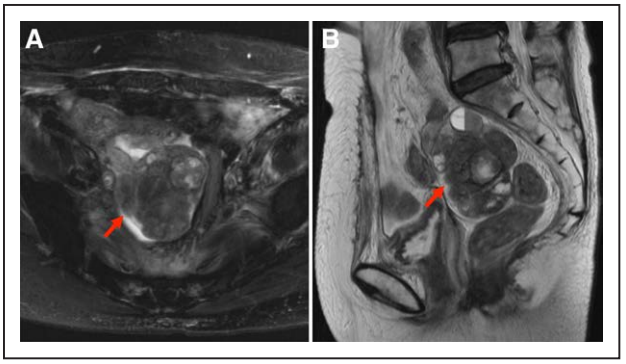

Figure 3. Pelvic magnetic resonance image of the ovarian carcinoid. An axial fat-saturated T2-weighted image (**A**) and a sagittal T2-weighted image (**B**) of the ovarian carcinoid. Arrow indicates the ovarian carcinoid.

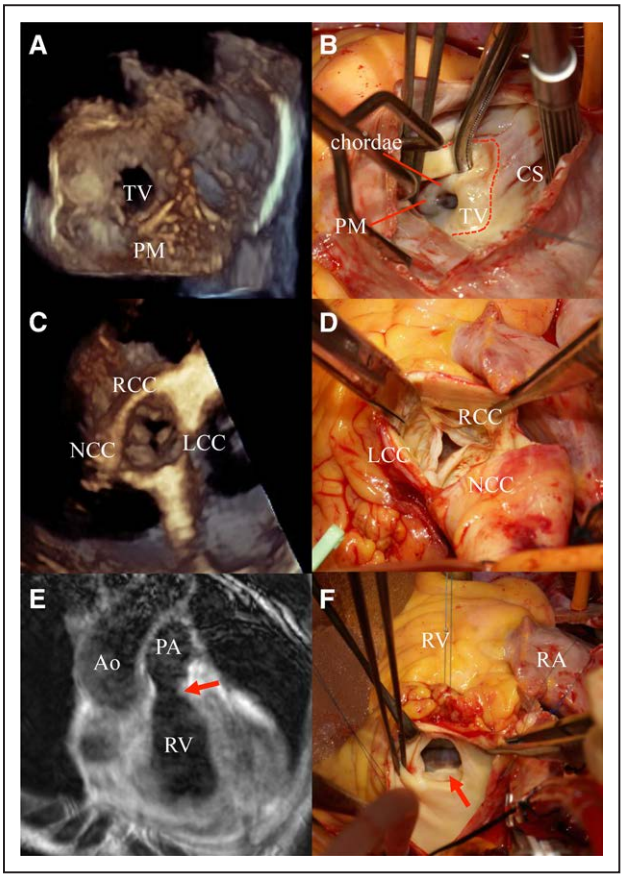

Figure 4. The 3-dimensional echocardiograms, cardiac magnetic resonance image (MRI), and intraoperative view of the heart valves. **A** and **B**, Three-dimensional echocardiogram (**A**) and intraoperative view (**B**) of the tricuspid valve with thickening of the chordae and papillary muscle. Red dotted line indicates tricuspid annulus. **C** and **D**, Three-dimensional echocardiogram (**C**) and intraoperative view (**D**) of the aortic valve. **E** and **F**, Cardiac MRI (**E**) and intraoperative view (**F**) of the pulmonary valve (arrow). Ao indicates aorta; CS, coronary sinus; LCC, left coronary cusp; NCC, noncoronary cusp; PA, pulmonary artery; PM, papillary muscle; RA, right atrium; RCC, right coronary cusp; RV, right ventricle; and TV, tricuspid valve.

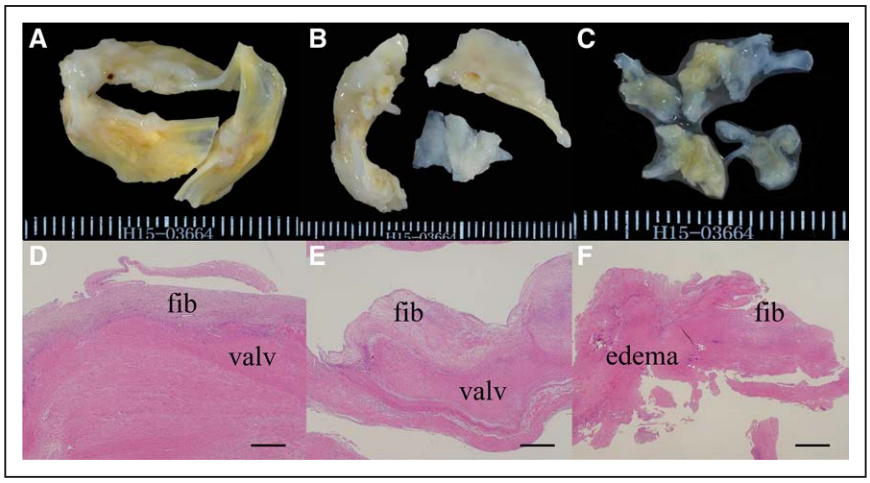

Figure 5. Operatively excised specimens and pathological analysis of the valve leaflets. **A**–**C**, Operatively excised tricuspid (**A**), aortic (**B**), and pulmonary valve leaflets (**C**). **D**–**F**, Pathological analysis of the tricuspid (**D**), aortic (**E**), and pulmonary valve leaflets (**F**). edema indicates edematous tissue; fib, fibrosis; and valv, valve tissue. Bars in Figure 5D, 5E, and 5F indicate 500 μm.

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