Occurrence of left-sided heart valve involvement before right-sided heart valve involvement in carcinoid heart disease

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Carcinoids are rare neuroendocrine tumours that occur primarily in the gastrointestinal tract. Carcinoid heart disease is characterized by fibrous plaque deposition on the endocardial surface of the cardiac valves and chambers. It affects the right heart valves in 85% of cases and the left heart valves in 15%. We present an unusual case of a patient with metastatic carcinoid heart disease in whom typical carcinoid aortic and mitral valve lesions developed 2 years prior to the development of severe right-sided carcinoid valvular heart disease.

Keywords Aortic valve insufficiency • Carcinoid heart disease • Mitral valve

Introduction

Carcinoids are rare neuroendocrine tumours, with an incidence in the general population of 1.2–2.1/100 000.1 About 55% of primary carcinoid tumours occur in the gastrointestinal tract, mostly in the small intestine.2 The next most common sites are the rectum (20%), appendix (16%), and colon (11%).3 Common sites of metastasis are the liver and regional lymph nodes, but the propensity of carcinoid tumours to metastasize correlates mainly with the primary tumour size and location.3

Carcinoid heart disease affects the right side of the heart in 85% of patients, but left-sided involvement has been reported in up to 15% of patients.2,4 We present a case of carcinoid heart disease that primarily involved the aortic and mitral valves 2 years before the development of right-sided valvular disease.

Case report

A 76-year-old woman with no prior exposure to anorexigens who had an established diagnosis of carcinoid disease from an external institution presented with liver metastasis. She originally sought treatment for diarrhoea and flushing and was found to have a caecal mass that ultimately resulted in a diagnosis of carcinoid disease. Subsequently, she underwent partial resection of the distal small bowel and the proximal large bowel. One year later, she had a total hysterectomy and bilateral salpingo-oophorectomy.

Over the next 10 years, her health was relatively good; then she began losing weight and had increasing symptoms of diarrhoea and fatigue. Further evaluation by computed tomography scans of the abdomen and pelvis and an octreotide nuclear scan of the patient revealed metastatic carcinoid tumours not only in the liver but also in the pelvis and the head of the pancreas; the concentration of urinary 5-hydroxyindoleacetic acid (5-HIAA) was 38 mg/24 h. An echocardiogram showed preserved left and right ventricular systolic function. However, the mitral valve was thickened, with restriction of the posterior mitral valve leaflet and minimal regurgitation but no stenosis (Figure 1A). The aortic valve was also thickened, with slight doming of the right coronary cusp during systole with mild regurgitation (Figure 1B and C, and see Supplementary data online, Movie 1). Although the pulmonary valve was not well visualized, Doppler imaging did not show any pulmonary valve stenosis or regurgitation (Figure 2). The tricuspid valve had minimal thickening without regurgitation (Figure 3 and see Supplementary data online, Movie 2). Echocardiographic imaging during agitated saline contrast injection confirmed the existence of a patent foramen ovale.

Over the next 2 years, the patient experienced progressive shortness of breath, ascites, and marked deterioration in functional capacity. Echocardiography showed normal left ventricular systolic function but moderate right ventricular systolic dysfunction and enlargement. The right atrium was found to be severely enlarged.
**Figure 1** (A) Initial echocardiogram shows thickened mitral valve leaflets as seen from the apical four-chamber view. Image also shows posterior leaflet (arrow) motion being restricted in diastole. (B) Parasternal long-axis view showing thickened aortic valve leaflets (arrow). (C) Doppler colour flow imaging from apical long-axis view showing aortic regurgitation. Ao indicates aorta; LA, left atrium; LV, left ventricle; RV, right ventricle.

**Figure 2** Initial echocardiogram shows Doppler velocity profile from the pulmonary valve and the absence of significant stenosis or regurgitation (peak velocity of only 1 m/s).
and the mitral valve was thickened, resulting in the restriction of the posterior mitral valve leaflet. The aortic valve was also thickened and had doming of the leaflets during systole, with mild regurgitation. Both the aortic valve and the mitral valve appeared to show progressive thickening since they had been last examined 2 years earlier (see Supplementary data online, Movie 3). Unlike its appearance on the previous echocardiogram, the tricuspid valve was markedly thickened, with nearly immobile tricuspid valve leaflets (Figure 4A and see Supplementary data online, Movie 4) and severe tricuspid valve regurgitation (Figure 4B and see Supplementary data online, Movie 4). The dagger-shaped tricuspid regurgitation signal was consistent with severely elevated right atrial pressure indicated by a large V-wave (Figure 4C). The pulmonary valve was thickened (Figure 5A), with significant regurgitation (Figure 5B), and the Doppler signal showed minimal stenosis of the pulmonary valve (Figure 5C and see Supplementary data online, Movie 4). Specifically, pulmonary valve regurgitation showed rapid deceleration, which indicated clinically significant pulmonary regurgitation and elevated right ventricular diastolic pressure. Urinary 5-HIAA increased to 49 mg/24 h, compared with 38 mg/24 h noted 2 years earlier. The patient subsequently underwent cardiac surgery that consisted of closure of the patent foramen ovale and replacement of both the tricuspid valve and the pulmonary valve with tissue valves. The explanted tricuspid valve was observed to be markedly thickened and fibrotic (Figure 6), as was the pulmonary valve.

Discussion

Carcinoid heart disease is characterized by plaque-like deposits of fibrous tissue that commonly occur on the endocardial surfaces of the valve cusps, leaflets, and cardiac chambers. The diagnosis is suspected when echocardiography shows thickening, shortening, and retraction of the tricuspid valve leaflets with severe tricuspid...
regurgitation with or without stenosis. The pulmonary valve is also thickened and retracted, resulting in regurgitation and/or stenosis. When there is left-sided valvular involvement, the mitral valve appears thickened, with a reduction in excursion of the leaflets, as was observed in our patient. The severity of the mitral regurgitation varies, depending on the extent of the valvular involvement. Observable aortic valve thickening and doming, like that seen in our patient, are the result of the deposition of carcinoid plaque on the aortic valve. Similar echocardiographic findings are also found in patients with drug-induced valvular heart disease, radiation-induced valve disease, and even rheumatic heart disease.3

In carcinoid heart disease, the presence of hepatic metastases plays a permissive role in allowing high quantities of tumour products, such as serotonin and other vasoactive amines, to be available and carried directly to the right heart.4,6 However, the left heart is less involved due to the protective mechanism of the lung. As blood passes through the lungs, serotonin is degraded to 5-HIAA, which substantially reduces serotonin levels capable of inducing left heart fibrosis.7 Nonetheless, the presence of primary bronchial carcinoid, high-circulating vasoactive substances, and an atrial right-to-left shunt such as a patent foramen ovale may facilitate involvement of the left heart.8 In the case of our patient, the presence of elevated vasoactive peptides and a patent foramen ovale paved the way for earlier involvement of the left-sided valves before the clinically significant right-sided valvular involvement.

This case illustrates the relatively less common manifestation of carcinoid heart disease in that aortic and mitral valve abnormalities due to carcinoid heart disease preceded the development of more common right-sided valvular heart disease. This finding underscores the need for close surveillance of patients with carcinoid tumours.9

**Supplementary data**

Supplementary data are available at *European Journal of Echocardiography* online.
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References