Carcinoid heart disease and the utility of 3D trans-thoracic and trans-esophageal echocardiography: Two clinical cases

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Carcinoid tumors are rare neuroendocrine malignancies. We present two cases of metastatic carcinoid tumors, complicated by carcinoid syndrome and by cardiac valve involvement. Carcinoid syndrome is characterized by secretory diarrhea, episodic flushing, and bronchospasm. Cardiac involvement occurs in up to 50% of patients with metastatic carcinoid tumors which commonly causes abnormalities of the right sided valves. Echocardiography is the best available and non invasive technique for diagnosis. Characteristic features of carcinoid heart disease are thickened, shortened, retracted, and fixed or partially fixed valve leaflets. Three-dimensional (3D) echocardiography provided an en face view of pulmonary and tricuspid valve, not obtainable by two-dimensional echocardiography, and improved delineation of the relationship between these structures and cardiac chambers.

Keywords: Carcinoid heart disease, Echocardiography, Pulmonary, Three-dimensional, Tricuspid, Valve

Introduction

Carcinoid tumors first described by Lubarsh in 1888 have been reported in a number of organs, most commonly including the gastrointestinal (GI) tract, respiratory tract and ovaries [1,2]. This tumor is often associated with a syndrome characterized by secretory diarrhea, episodic flushing, and bronchospasm [3,4]. Carcinoid syndrome is thought to occur after liver metastases which allows high levels of 5-hydroxytryptamine (5-HT) in systemic circulation [3,5]. Cardiac involvement
occurs in up to 50% of patients and predominantly affects the endocardium and right cardiac valves [3,5,6]. Left side cardiac involvement is less common (7%) as the lung parenchyma inactivates tumor substrates [2,4]. Left side valvular involvement is due to the presence of patent foramen ovale (PFO), or less commonly as a consequence of high circulatory levels of serotonin, or pulmonary metastasis [5]. We present two cases of metastatic carcinoid tumors, complicated by carcinoid syndrome and demonstrate the utility of 3D TTE and TEE in assessment of cardiac valve involvement.

Case 1
A 43-year-old man presented with four-year history of unprovoked cutaneous flashing. He also complained of an intermittent watery diarrhea, unrelated to meals, and an exacerbating exertional dyspnea over the last two years. Peripheral edema accompanied these symptoms during this month before presentation. He was referred to Ghaem hospital with right-sided heart failure symptoms. On clinical examination, he was wasted, had an elevated jugular venous pressure with CV wave, pan-systolic murmur (3/6) over the left lower sternal border, as well as mid-systolic murmur (2/6) and early to mid-diastolic murmur over the left upper sternal border. On abdominal examination, the liver span was enlarged.

Twenty-four hour urinary 5-hydroxyindolacetic acid (5-HIAA) was elevated at 780 µmol/24 h. Upper gastrointestinal endoscopy was normal. Colonoscopy showed a mass in the cecum with

![Figure 1. Two-dimensional trans-thoracic echocardiogram: Four-chamber view showing RV and RA enlargement. The color Doppler demonstrating severe free tricuspid regurgitation.](image)

![Figure 2. Real-Time three-dimensional capture: Anterior enface view of mitral and tricuspid valves showing the thickened and retracted tricuspid leaflet without coaptation.](image)
histological compatibility for well differentiated neuroendocrine carcinoid tumor. Hepatomegaly with multiple metastases was confirmed using abdominal computed tomography (CT) scan. Spiral lung CT-scan was normal.

Two- and three-dimensional (2D, 3D) transthoracic echocardiography (TTE) and trans-esophageal echocardiography (TEE) was performed using Philips iE33 equipped with a matrix array TTE and TEE transducer (Philips medical system, Andover, MA). 2D and 3D TTE revealed severe right ventricular enlargement and dysfunction, and septal flattening in diastole consistent with volume overload. Tricuspid valve (TV) leaflets were retracted, thickened, and fixed in mid position without systolic coaptation causing severe free tricuspid regurgitation (TR) and mildly increased trans-valvular gradient up to 5mmHg (Figs. 1 and 2). Sub-valvular apparatus was also visualized. Chordae tendineae were thickened and partially fused. Pulmonary valve leaflets were also severely retracted, thickened and shortened causing severe pulmonary regurgitation (PR). The main pulmonary trunk was narrowed (Fig. 3). However, mitral and aortic valve functions, left ventricle (LV) and atrium (LA) dimensions were within normal limits. After a suitable control of the systemic disease, the patient underwent replacement of the pulmonary and tricuspid valves with biologic valves. Histological
examination of the excised valves confirmed the diagnosis of carcinoid heart disease. Patient survived surgery and was discharged in good condition.

Case 2

A 48-year-old man with carcinoid syndrome presented with worsening dyspnea on minimal exertion (class III to IV, New York Heart Association). He had presented peripheral edema a few weeks ago. His symptoms of carcinoid syndrome were episodic facial flushing and diarrhea being well controlled with somatostatin analogue. Clinical examination showed an elevated jugular venous pressure. Heart auscultation demonstrated pan-systolic murmur over the left lower sternal border which increased with inspiration and diastolic murmur over the left second intercostal space. In abdominal examination, his liver was massively enlarged. He had mild pedal edema. The primary source of carcinoid tumor was in the small intestine which had previously undergone surgery due to obstructive symptoms. Multiple hyponodular masses were reported in abdominal CT-scan being consistent with liver metastases. Urinary 5-HIAA level was 975 μmol/24 h. Liver function tests were normal.

The patient underwent 2D and 3D TTE and TEE using Philips iE33 equipped with a matrix array TTE and TEE transducer (Philips medical system, Andover, MA). 2D TTE and Doppler echocardiography revealed RV and RA enlargement with mild RV dysfunction and severe TR (Fig. 4). TV was markedly thickened, fixed and shortened associated with thickening of chordae tendinea (Fig. 5). The pulmonary valve was thickened and poorly mobile, resulting in severe pulmonary regurgitation. The pulmonary valve annulus was also restricted. Real time 3D TEE provided more anatomical information on all three cusps of the pulmonary valve, as well as allowing assessment of the main pulmonary artery and annulus of pulmonary valve and visualization of the right ventricle outflow. Valve replacement surgery was recommended, but due to patient’s refusal for surgery, medical therapy for right heart failure symptoms was continued.

Discussion

Carcinoid heart disease is a rare cause of valvular heart disease [6,7]. It often affects right side valves resulting in unique morphology and echocardiographic characteristics [3,6]. Patients with carcinoid heart disease typically present with symptoms of right-sided heart failure (hepaticomegaly, edema, ascites, fatigue, and low cardiac output), and when symptoms are advanced (NYHA class 3 or 4), outlook is poor [3]. The involvement of left side heart valves and foramen ovale is also seen in carcinoid heart disease. 2D echocardiography is usually the first available tool for diagnosis; however, 3D TEE and TTE have attained incremental value for better visualization of PV and TV.

Abnormality of TV includes straightened, immobile and thickened valve leaflets and subvalvular apparatus. In most severe cases, leaflets become fixed and non-coaptated causing regurgitation or stenosis of the tricuspid with a characteristic “dagger-shaped” profile. Chordae tendinea and papillary muscles may be thickened, fused and shortened [2,5,8]. Moreover, the right ventricle becomes dilated and the right atrium is also

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Figure 5. Real-time three-dimensional capture: Ventricular view of tricuspid valve revealed severely retracted, fixed and non-coapted leaflets.
enlarged. The present report showed that the 3D TEE and TTE visualized all the leaflets of TV from either atrial or ventricular side. The technique improved the evaluation of coaptation zone and delineation of sub-valvular structures, and enabled us to compare the leaflets simultaneously.

Abnormality of pulmonary valve is less common than TV involvement. The changes are similar to TV deformity including thickened and straightened valve with retraction and reduction in excursion of valve leaflets in severe cases [9]. In these cases, the 3D TEE and TTE produced an en-face view of the all three pulmonary leaflets simultaneously [10].

**Conclusion**

The present medical cases, where the tricuspid and pulmonary valves are involved, are considered as a minority of carcinoid valve disease cases. The combination of echocardiographic imaging and 5-HIAA level provided useful insights, leading to the accurate and undoubted diagnosis, which was subsequently verified by the histological study. Echocardiography is vitally important in the evaluation of patients with carcinoid syndrome and suspected carcinoid heart involvement. Advanced techniques such as 3D TEE and TTE proved to be helpful in assessing the cardiac involvement particularly the pulmonary valve which cannot be entirely evaluated by 2D echocardiogram.

**References**


