Best Practice & Research Clinical Endocrinology & Metabolism 30 (2016) 149–158

Contents lists available at ScienceDirect

Best Practice & Research Clinical Endocrinology & Metabolism

journal homepage: www.elsevier.com/locate/beem

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Carcinoid heart disease: Diagnosis and management

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ARTICLE INFO

Article history:
Available online 9 October 2015

Keywords:
carcinoid
valves
Hedinger syndrome
echocardiography

Hedinger syndrome refers to carcinoid valvular heart disease. The disease is believed to be triggered by vasoactive substances that result in valvular fibrosis. It classically occurs in patients with metastatic carcinoid and preferentially involves the right sided cardiac valves. Affected valves become thickened and retracted, exhibiting regurgitation and sometimes, stenosis. Echocardiography is recommended in patients with carcinoid syndrome and a follow up study is advisable in those who develop a murmur or other symptoms or signs of valvular heart disease. For appropriately selected patients, valve replacement surgery appears to improve outcomes.

Carcinoid tumors typically arise from derivatives of the embryological gastrointestinal tract, with the majority of such tumors arising from the small intestine, particularly the ileum and appendix. Tumors may, however, also arise from the lung, and more rarely from ovary or kidneys. Carcinoid tumors secrete a multitude of vasoactive substances, the most important of which include serotonin, histamine, tachykinins, kallikrein and prostaglandins. In the presence of small intestinal carcinoid, such vasoactive substances are filtered from the portal circulation by the liver prior to entering the systemic circulation. The development of hepatic metastases allows secretion of such substances into the systemic circulation with resulting carcinoid syndrome.

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http://dx.doi.org/10.1016/j.beem.2015.09.005
1521-690X/

Carcinoid heart disease, also known as Hedinger syndrome, is reported to affect at least 20% of patients with carcinoid syndrome [1]. It is thought to be the result of cardiac exposure to high systemic levels of circulating hormones, predominantly serotonin. The disease process most commonly results in valvular fibrosis as a result of the paraneoplastic effects of circulating serotonin. Myocardial metastases are rare, occurring in less than 5% of patients, and appear as non-infiltrating, well-circumscribed intramyocardial masses [2]. The onset of carcinoid heart disease is associated with a significantly worse prognosis when compared to carcinoid patients without cardiac involvement [2].

The disease process primarily affects right sided heart valves, particularly involving the tricuspid valve. Left sided valvular involvement may occur albeit rarely, with increased risk in those patients with an inter-atrial shunt or prolonged high levels of 5-hydroxyindoleacetic acid (5-HIAA) [2]. It has been hypothesized that the lower incidence of left sided valvular heart disease may be related to pulmonary deactivation of circulating serotonin resulting in reduced left heart serotonin concentrations. Recent work, however, has demonstrated no significant difference in serotonin levels between right and left sided cardiac chambers in carcinoid heart disease patients, suggesting that the development of valvular disease is not purely the result of circulating serotonin levels [3]. The echocardiographic and macroscopic pathological valvular appearance in this disease process bears similarities to those found in chronic rheumatic valvular heart disease with leaflet thickening and retraction, mild focal commissural fusion, and chordal thickening (Fig. 1) [4]. Microscopically, plaques appear along the valvular or endocardial surface and consist of myofibroblasts, collagen, a myxoid matrix and elastin [4]. Plaques typically appear to have a “stuck-on” appearance and do not result in destruction of the underlying valvular architecture (Fig. 2) [4].

Carcinoid heart disease most frequently affects the tricuspid valve, with a lesser frequency of pulmonary valve involvement. The left sided valves are significantly less frequently affected with mitral valve disease occurring slightly more frequently than aortic valve disease [2]. The pattern of functional valvular abnormality varies depending on the valve affected. The tricuspid valve is most commonly affected by isolated regurgitation, with a smaller percentage suffering from mixed stenosis and regurgitation [4]. In contrast, the pulmonary valve most commonly presents with mixed regurgitation and stenosis, with isolated regurgitation or stenosis occurring slightly less frequently (Fig. 3) [4]. The increased observation of stenosis with this valve is likely due to its smaller annulus compared to the tricuspid valve. Left sided carcinoid valvular disease most frequently results in isolated regurgitant lesions [4]. In addition to rheumatic valvular heart disease, valvular heart disease related to the use of either diet drugs [5] or ergot alkaloids [6] has an appearance similar to that of carcinoid valvular heart disease, but without the right-sided predilection.

Fig. 1. Surgical specimen from a patient with carcinoid heart disease demonstrating a markedly thickened tricuspid valve with chordal thickening. [Reprinted from Mayo Clinic Proceedings, Volume 77, Simula et al., Surgical Pathology of Carcinoid Heart Disease: A Study of 139 Valves From 75 Patients Spanning 20 Years, pages 139–147, 2002, with permission from Elsevier].