Carcinoid heart disease: An immense challenge despite medical and surgical advances

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In their recently published clinical vignette, Waligóra et al. [1] reported an interesting case of symptomatic carcinoid heart disease (CHD) in a 49-year-old male, after successful treatment of severe tricuspid regurgitation with implantation of a bioprosthesis followed by resection of the primary tumor localized in the ileum. The authors also reported tricuspid valve deterioration throughout the follow-up period, which they linked to the interval between the abdomen and cardiac surgery and the exposure of the prosthetic valve to high levels of serotonin metabolites before initial tumor resection [1]. As CHD is the most serious consequence of carcinoid syndrome [2] and serotonin activity appears to be crucial in the development of valvular CHD [3], we would like to write a short comment.

CHD development is linked to increased morbidity and mortality. It generally results in increasing malfunction of the valves involved (mainly tricuspid and pulmonary) and patient disability. CHD has a poor prognosis if not treated, with 3-year survival as low as 31%. However, the prognosis for individuals with diagnosed CHD has improved in recent decades, possibly as a result of advances in cardiac imaging techniques, anticancer treatments, perioperative care, and cardiac surgery.

Transthoracic echocardiography assessed by a clinician familiar with typical CHD valve morphology is still the method of choice for diagnosis of CHD. Several biomarkers for the prevalence and severity of CHD have been found in studies. The most relevant biomarker to date is N-terminal pro-B-type natriuretic peptide (NT-proBNP), which has been demonstrated to be both diagnostic of and prognostic for cardiac involvement. Other essential biomarkers used in disease diagnosis and monitoring include urinary 5-hydroxyindoleacetic acid (u5-HIAA), chromogranin A, and activin A [2]. Accordingly, we wonder whether the patient [1] had other biomarkers tested before the final diagnosis of carcinoid syndrome and CHD.

There are several serotonergic 5-HT1 and 5-HT2 receptor subtypes found in cardiac valve tissues, with subtype 5-HT2B receptors being the most prevalent and having a significant role in valve disease [4]. Treatment with somatostatin analogs, which are meant to lower circulating tumor metabolites (including 5-HT), has been demonstrated to generate a biochemical and clinical response in 60% to 70% of patients and an antiangiogenetic/antitumoral response in 5% to 10% [2].

As was done in the reported case [2], cardiac catheterization provides a direct method of assessing the degree of valve insufficiency by invasive hemodynamic pressure measurement [3]. In individuals with significant cardiac involvement and well-controlled carcinoid syndrome, valve replacement surgery is an effective therapy method that can reduce persistent symptoms and contribute to better outcomes. However, the appropriate time for valve replacement surgery in relation to severity of valve dysfunction and symptoms has not been determined. According to guidelines, patients referred for cardiac surgery should present with symptoms of right heart failure and at least 12 months of expected post-operative survival from their neuroendocrine tumor condition [2]. Early investigations of valve surgery found 30-day perioperative mortality to be as high as 63%, but with increased expertise and surgical procedures, 30-day perioperative mortality has recently been reported to be as low as

3.7% [3]. It is also worth noting that even in the context of advanced valve disease, patients with normal natriuretic peptide levels had a favorable prognosis [3]. Unfortunately, CHD can progress rapidly [2].

In all patients with neuroendocrine neoplasms of the small intestine (with and without CHD), primary tumor resection with metastatic disease (resectable and unresectable) has been found to increase survival. This might be due to decreased production of vasoactive substances and a reduction in potentially fatal consequences such as intestinal obstruction generated by tumor progression and occlusion [5]. Accordingly, we wonder if the authors of the presented case [1] could provide more information on tumor characteristics, echocardiographic findings, as well as on levels of 5-HIAA and chromogranin A after primary tumor resection.

CHD treatment is complicated since both the systemic malignant disease and cardiac involvement should be managed at the same time [2]. However, it is not always as simple as in the guidelines. The reported case by Waligóra et al. [1] emphasized that patient management requires involvement of a multidisciplinary team to adequately select patients for valve or primary tumor surgeries, and plan preoperative and perioperative treatment procedures. It should be highlighted that the authors took up this extremely difficult challenge and that the cardiac surgery and primary tumor resection were successful without any complications [2].

In conclusion, all of these facts prove that nowadays, it is crucial to concentrate on precise patient diagnosis, treatment, and management, all under the guidance of a multidisciplinary team, to increase the overall survival of patients with CHD.

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