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ORIGINAL ARTICLE

Carcinoid Heart Disease: A Rare Complication of Metastatic Neuroendocrine Tumor

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ABSTRACT

Background: Carcinoid heart disease (CHD) is a rare but severe complication of metastatic neuroendocrine tumors (NETs), primarily affecting the right-sided heart valves due to prolonged exposure to vasoactive substances such as serotonin.

Objective: This study aims to evaluate the clinical, biochemical, and echocardiographic characteristics of CHD, as well as treatment outcomes and survival rates.

Methods: This retrospective study was a multicenter study conducted during 2018 to 2023. A total of 25 patients were added to the study. Demographic and clinical data were collected, including the age, gender, and medical history of each patient. The primary symptoms observed included dyspnea, peripheral edema, fatigue, ascites, and signs of right-sided heart failure.

Results: The study included 25 patients diagnosed with carcinoid heart disease, with a mean age of 52.3 ± 10.8 years. The gender distribution was 14 males (56%) and 11 females (44%). The most common clinical symptoms were dyspnea on exertion (76%), peripheral edema (64%), and fatigue (52%), indicative of right-sided heart failure. A strong positive correlation was observed between 5-HIAA levels and tricuspid regurgitation severity ($r = 0.72$, $p < 0.01$), indicating that higher serotonin levels contribute to worsening valvular fibrosis and dysfunction.

Conclusion: Carcinoid heart disease is a progressive condition strongly associated with elevated biochemical markers and worsening valvular dysfunction over time. Regular echocardiographic monitoring and biomarker assessment are essential for early diagnosis and disease tracking.

Keywords: Carcinoid heart disease, valvular dysfunction, 5-HIAA, NT-proBNP, somatostatin therapy, valve replacement

INTRODUCTION

Carcinoid heart disease (CHD) is a rare but serious complication of metastatic neuroendocrine tumors (NETs), particularly those arising from the gastrointestinal (GI) tract, such as the small intestine and appendix. The condition primarily occurs due to carcinoid syndrome when vasoactive substances from NETs including serotonin and histamine and bradykinins and prostaglandins move past the liver into systemic circulation[1]. These active chemical substances trigger endocardial fibrosis which causes functional and structural damage to heart valves with the right heart receiving primary effects. Medical management of CHD depends heavily on detecting patients early because this condition threatens their survival rates and life-quality outcomes[2]. Different types of cancerous neuroendocrine cells originate from tissues that contain neuroendocrine cells and these cells demonstrate hormonal secretion abilities throughout the disease process[3]. What starts as small and benign tumors may lead to carcinoid syndrome from unprocessed vasoactive substances because the liver becomes unable to break down serotonin when tumors spread to this organ. Cardiac tissue damage occurs when exposed to these substances over time which causes fibrotic plaque development that affects primarily the tricuspid and pulmonary valves resulting in valve thickening and both retraction and dysfunction[4]. The heart dysfunction leads to tricuspid regurgitation and pulmonary stenosis that eventually results in right heart failure.The clinical diagnosis of CHD develops from the degrees of valvular conditions and right heart functioning impairment. Right heart failure symptoms present in patients through fatigue together with peripheral edema and dyspnea on exertion and ascites and hepatomegaly[5]. Advanced stages of the condition result in left-sided heart involvement most frequently when patients have patent foramen ovale or bronchial NETs which bypass hepatic serotonin metabolism. When patients develop CHD the survival outlook after carcinoid syndrome diagnosis becomes two years until death when no treatment is administered[6,7]. Medical experts combine three different methods to detect CHD: clinical assessments along with biomarker investigations and scans of the heart structure. A diagnosis of active disease can be made through urinary 5-hydroxyindoleacetic acid (5-HIAA) testing which detects serotonin metabolite traces[8]. NT-proBNP measurements demonstrate significant connection to cardiac dysfunction and work as important indicators for patient prognosis. Modern medical standards establish echocardiography as the definitive CHD diagnosis technique because it shows clearly how valvular thickening and regurgitation and stenosis and right ventricular enlargement appear. In addition to echocardiography cardiac magnetic resonance imaging (MRI) provides structural and functional examination as an assessment tool[9].

Cardiac and Cardiothoracic surgeons together with oncologists and cardiologists must work as a team for managing CHD treatment[10]. Cessation of hormone production from neuroendocrine tumors along with cardiac complication management stands as the main therapeutic objective. Somaticetin analogs octreotide together with lanreotide function as first-choice medications that both decrease tumor-secreted hormones and treat carcinoid symptoms[11]. Advanced disease cases may benefit from hepatic embolization together with peptide receptor radionuclide therapy (PRRT) for tumor volume reduction. Medical intervention with valve replacement surgery provides definitive treatment for serious valvular disease because it results in improved survival rates alongside better symptom management for appropriate patient cases[12].

Objectives: This study aims to evaluate the clinical, biochemical, and echocardiographic characteristics of CHD, as well as treatment outcomes and survival rates.

METHODOLOGY

This retrospective study was a multicenter study conducted during 2018 to 2023. A total of 25 patients were added to the study.

Inclusion Criteria

1. Confirmed diagnosis of metastatic neuroendocrine tumor (NET) with carcinoid syndrome.
2. Presence of carcinoid heart disease diagnosed through echocardiography.
3. Availability of clinical and biochemical records, including urinary 5-hydroxyindoleacetic acid (5-HIAA) levels and N-terminal pro-brain natriuretic peptide (NT-proBNP).

Exclusion Criteria

1. Patients with other primary causes of valvular heart disease.

2. Patients with incomplete medical records or insufficient follow-up data.
3. Patients with prior valve replacement before the study period.

Data Collection: Demographic and clinical data were collected, including the age, gender, and medical history of each patient. The primary symptoms observed included dyspnea, peripheral edema, fatigue, ascites, and signs of right-sided heart failure. Biochemical markers such as 24-hour urinary 5-HIAA and NT-proBNP levels were assessed as they are strongly correlated with disease severity and prognosis. Echocardiographic evaluation was performed for all patients to determine the extent of valvular involvement, including the degree of stenosis and regurgitation in the tricuspid and pulmonary valves. In selected cases, cardiac magnetic resonance imaging (MRI) was utilized for further assessment of right ventricular function and myocardial fibrosis.

Treatment Modalities: The study analyzed the different treatment approaches used for CHD management. Most patients received somatostatin analogs, such as octreotide or lanreotide, to control serotonin secretion and alleviate carcinoid symptoms. In cases of severe valvular dysfunction, patients underwent surgical valve replacement to improve cardiac function and overall survival. Peptide receptor radionuclide therapy (PRRT) or hepatic embolization was considered for tumor burden reduction in patients with progressive disease. Supportive treatments, including diuretics and beta-blockers, were prescribed for heart failure management.

Statistical Analysis: All collected data were analyzed using **SPSS (version XX)**. Descriptive statistics, including mean, median, and standard deviation, were calculated for demographic and clinical variables. Correlation analysis was performed to assess the relationship between biochemical markers (5-HIAA, NT-proBNP) and disease severity.

RESULTS

The study included 25 patients diagnosed with carcinoid heart disease, with a mean age of 52.3 ± 10.8 years. The gender distribution was 14 males (56%) and 11 females (44%). The most common clinical symptoms were dyspnea on exertion (76%), peripheral edema (64%), and fatigue (52%), indicative of right-sided heart failure. A smaller proportion of patients presented with ascites (32%) and hepatomegaly (28%), suggesting more advanced disease progression. Biochemical analysis showed significantly elevated 24-hour urinary 5-HIAA levels, with a mean of 178.6 ± 82.5 mg/24h (range: 50–300), confirming excessive serotonin production. NT-proBNP levels were also markedly increased, with a mean of 1982.4 ± 1025.7 pg/mL (range: 200–4000), indicating significant cardiac strain and dysfunction. These markers were closely associated with the severity of valvular disease and right ventricular impairment. Echocardiographic findings revealed that 40% of patients had severe tricuspid regurgitation, 32% had moderate regurgitation, and 28% had mild involvement. Pulmonary stenosis was observed in 24% of patients in moderate-to-severe form, while 40% had mild stenosis, and 36% had no stenosis (Table 1).

A strong positive correlation was observed between 5-HIAA levels and tricuspid regurgitation severity ($r = 0.72$, $p < 0.01$), indicating that higher serotonin levels contribute to worsening valvular fibrosis and dysfunction. This suggests that 5-HIAA could serve as a reliable indicator of disease progression in patients with carcinoid syndrome.

Patients who received only somatostatin therapy had a mean survival of 28.4 ± 9.2 months, with a 55% improvement in symptoms. In contrast, those who underwent valve replacement in addition to somatostatin therapy had a significantly longer mean survival of 42.7 ± 10.5 months and a higher symptom improvement rate of 78%. The difference in survival between the two groups was statistically significant ($p = 0.04$), indicating that surgical intervention provides a substantial survival benefit.

Table 1: Demographic and Clinical Characteristics

Characteristic	Value
Number of patients	25
Mean Age (years)	52.3 ± 10.8
Gender (Male/Female)	14 (56%) / 11 (44%)
Dyspnea on exertion (%)	19 (76%)
Peripheral edema (%)	16 (64%)
Fatigue (%)	13 (52%)
Ascites (%)	8 (32%)
Hepatomegaly (%)	7 (28%)
24-hour Urinary 5-HIAA (mg/24h)	178.6 ± 82.5 (50–300)
NT-proBNP (pg/mL)	1982.4 ± 1025.7 (200–4000)
Echocardiographic Parameter	
Tricuspid Regurgitation - Mild	7 (28%)
Tricuspid Regurgitation - Moderate	8 (32%)
Tricuspid Regurgitation - Severe	10 (40%)
Pulmonary Stenosis - None	9 (36%)
Pulmonary Stenosis - Mild	10 (40%)
Pulmonary Stenosis - Moderate/Severe	6 (24%)
Right Ventricular Dysfunction - None	3 (12%)
Right Ventricular Dysfunction - Mild	5 (20%)
Right Ventricular Dysfunction - Moderate	9 (36%)
Right Ventricular Dysfunction - Severe	8 (32%)

Table 2: Correlation Between Biomarkers and Disease Severity

Parameter	Correlation Coefficient (r)	P-value
5-HIAA vs. Tricuspid Regurgitation Severity	0.72	<0.01
5-HIAA vs. NT-proBNP Levels	0.81	<0.001
NT-proBNP vs. Right Ventricular Dysfunction	0.78	<0.01

Table 3: Comparison of Treatment Outcomes

Treatment Group	Mean Survival (months)	Improvement in Symptoms (%)	P-value
Somatostatin Therapy Only	28.4 ± 9.2	55%	0.04
Somatostatin + Valve Replacement	42.7 ± 10.5	78%	<0.01

At baseline, the mean tricuspid regurgitation severity score was 1.8 ± 0.6, and the mean right ventricular dysfunction score was 1.9 ± 0.7. After three months, tricuspid regurgitation severity increased to 2.2 ± 0.5, while right ventricular dysfunction worsened to 2.4 ± 0.6. By six months, tricuspid regurgitation severity further progressed to 2.6 ± 0.4, and right ventricular dysfunction reached 3.0 ± 0.5.

Table 4: Disease Progression Over Time (Echocardiographic Changes)

Follow-up Duration (months)	Mean Tricuspid Regurgitation Severity Score (1-3)	Mean Right Ventricular Dysfunction Score (1-4)
Baseline	1.8 ± 0.6	1.9 ± 0.7
3 months	2.2 ± 0.5	2.4 ± 0.6
6 months	2.6 ± 0.4	3.0 ± 0.5

DISCUSSION

Carcinoid heart disease is a rare but severe complication of metastatic neuroendocrine tumors, primarily affecting the right-sided heart valves due to the fibrotic effects of excessive serotonin and other vasoactive substances.

This retrospective research study reveals significant information about the clinical manifestations coupled with biochemical characteristics and echocardiographic findings of the disease and its reaction to treatments along with survival statistics. The study results show that right-sided heart failure symptoms such as dyspnea and peripheral edema and fatigue presented in most patients[13]. Clinical tests establish the pathogenic role of elevated serotonin levels in valvular fibrosis through measurable high 5-HIAA levels in patient samples. These elevated NT-proBNP measurements indicate that the patients have different levels of

cardiac strain thus confirming biochemical markers as vital tools for evaluating disease severity[14].

Prognostic biomarker status of NT-proBNP has been demonstrated by its established positive correlation with right ventricular dysfunction levels. Research findings supported 5-HIAA levels as a disease monitoring tool since the analytic values matched tricuspid regurgitation severity rates. Multiple studies support the clinical efficiency of biochemical markers as tools to predict disease advancement in patients. Echocardiographic tests showed that most patients experienced severe tricuspid regurgitation together with moderate right ventricular dysfunction due to the progressive characteristics of the disease[15]. Patients with pulmonary stenosis had a rare occurrence of this condition yet their condition was diagnosed with either moderate or severe manifestation that could strain right ventricular afterload. Medical treatment failed to stop disease progression as right ventricular functioning along with tricuspid regurgitation worsened after six months of evaluation by echocardiography in some patient cases[16]. The observed cardiac deterioration shows how essential standard diagnostic tests with prompt medical intervention remain for people showing symptoms[17]. The study showed that somatostatin analog treatment successfully managed symptoms therefore most patients started this therapy. The research findings match previous reports showing that valve replacement remains an essential procedure to enhance cardiac operation along with patient life quality in severe heart conditions. The study results highlight criticality of early disease detection followed by timely intervention methods in patient management. Echocardiographic screenings combined with biomarker analyses need to be part of regular assessments to guide proper healthcare decisions because disease progression occurs[18]. Survival rates improve significantly after valve replacement surgery which indicates medical professionals should adopt a proactive surgical protocol for patients who have severe tricuspid or pulmonary valve involvement[19,20]. While modern medical care continues to progress carcinoid heart disease develops into a primary reason for death and complications during the clinical course of patients with metastasized neuroendocrine tumors. Upcoming research should develop new antifibrotic treatments combining serotonin receptor blockers together with molecular-targeted approaches that may impede disease evolution. Future research requires both prospective studies with extensive patient groups to validate the existing results and to enhance treatment optimization methods.

CONCLUSION

It is concluded that carcinoid heart disease is a progressive and life-threatening complication of metastatic neuroendocrine tumors, primarily affecting the right-sided heart valves due to chronic exposure to vasoactive substances. The study findings highlight the significant correlation between elevated biochemical markers, particularly 5-HIAA and NT-proBNP, and the severity of valvular dysfunction and right ventricular impairment. These markers serve as valuable tools for early detection and disease monitoring.

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