Case Report

Journal Of Clinical & Medical Images Case Reports

Open Access, Volume - 1

Severe tricuspid regurgitation as first manifestation of a primary ovarian carcinoid tumor

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Received Date : Nov 14, 2021
Accepted Date : Dec 10, 2021
Published Date : Dec 17, 2021
Archived : www.jcmimagescasereports.org

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Abstract

A 52-year-old woman presented with a 1 year-history of reduced exercise tolerance and fatigue. Physical examination revealed a grade II/VI systolic murmur at the left sternal border. Transthoracic echocardiography showed thickened tricuspid leaflets with retraction and restricted movement, resulting in a severe tricuspid regurgitation. The characteristic pattern aroused the suspicion of a systemic or hormonal etiology. 24-Hour urine analysis revealed an increased level of 5hydroxyindoleacetic acid and abdominal computed tomography (CT) showed a large tumor in the pelvis; however, without the presence of liver metastasis. During uncomplicated trans-abdominal surgery a large mass in the ovary was removed, and pathology showed a primary ovarian carcinoid tumor. One year after the diagnosis, patient remains clinically stable without signs of right heart failure and an excellent exercise tolerance. This case report shows that isolated tricuspid valve pathology in the absence of left valvular disease may raise the suspicion for an atypical cause of valvular dysfunction, in which carcinoid tumor is included.

Background

Carcinoid tumors are neuroendocrine malignancies that can release serotonin and other vasoactive peptides into the systemic circulation. These substances are thought to cause the carcinoid syndrome, which is characterized by episodes of vasomotor changes (flushing, hypo-or hypertension), diarrhea, bronchospasm or carcinoid heart disease [1]. The overall incidence of these tumors is 2.5-5.0 cases per 100.000 of the population per year, most frequently arising from the gastrointestinal tract or bronchopulmonary system. Approximately 50% of the patients develop symptoms of carcinoid syndrome in the course of the disease. Primary ovarian carcinoid tumors are rare, only accounting for 0.5% of all carcinoid tumors [2, 3]. They are considered unique in the development of carcinoid heart disease in the absence of liver metastasis, as the venous drainage of the ovaries bypasses the portal system [4]. Cardiac manifestations, initiated by the circulating vasoactive substances, are caused by a process of endocardial fibrosis that leads to the formation of carcinoid plaques classically on the right-sided heart valves. This often causes valvular thickening, retraction and fixation of the leaflets of the tricuspid and pulmonary valves leading to multiple patterns of severe valve dysfunction [5]. We report the case of a patient who presented with a severe tricuspid insufficiency as first manifestation of a primary ovarian carcinoid tumor.

Case Presentation

A 52-year-old woman was referred to our outpatient clinic for a secondary consultation. For one year the patient experienced declining exercise tolerance and fatigue. She had no specific cardiovascular risk factors. Her medical history revealed a vitamin B –deficiency without a clear cause, and colonoscopy, upper endoscopy and abdomen ultrasound, performed because of complaints of nausea and weight loss, showed no abnormalities. On physical examination, heart sounds were regular and a grade II/VI systolic murmur at the left sternal border was heard. In addition, there was very mild pitting edema of the ankles.

Investigations

TOn the initial electrocardiogram a sinus rhythm with normal repolarization was seen and with laboratory examination an increased level of natriuretic peptide, T-pro BNP (390 pg/ml) was found. Transthoracic echocardiography showed a left ventricle with normal dimensions and function, with a left ventricular ejection fraction of 55% and a normal aortic and mitral valve. In contrast, on rightsided heart evaluation there was an abnormal aspect of the tricuspid valve. The leaflets and subvalvular apparatus were thickened and echogenic, with retraction of both leaflets, restricted movement and caused

Citation: AL Duijnhouwer, ML Leijssen, APJ van Dijk. Severe tricuspid regurgitation as first manifestation of a primary ovarian carcinoid tumor. J Clin Med Img Case Rep. 2021; 1(1): 1047.

malcoaptation. Consequently, severe tricuspid regurgitation was noted on color Doppler imaging, showing an increased regurgitation velocity of 2.3 m/s with an early peak pressure and rapid decline. At pulsed-wave Doppler the hepatic vein showed marked systolic flow reversal. In addition, there was also tricuspid stenosis (**Figure 1**).

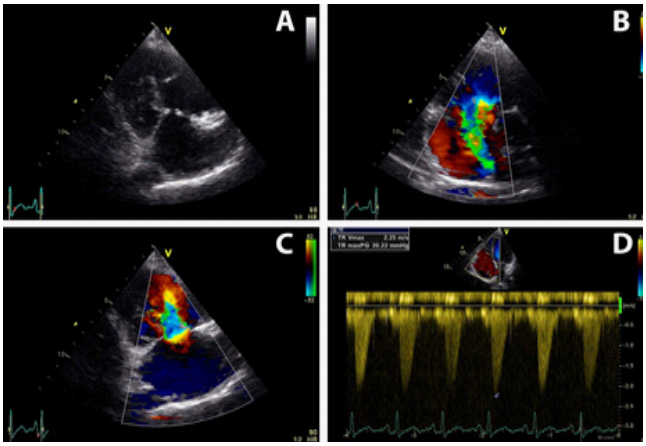

Figure 1: *Echocardiographic findings of carcinoid involvement of tricuspid valve (TV).*
A. Right ventricular inflow view showing thickened and retracted tricuspid valve leaflets failing to coapt and resulting in constant "semi-open" position.
B. Color Doppler of the tricuspid valve demonstrating severe regurgitation.
C. Color Doppler demonstrating turbulent RV inflow during systole.
D. Continuous-wave Doppler showing dagger-shaped profile of tricuspid regurgitation (TR).

Differential diagnosis

Primary diseases of the tricuspid valve are uncommon, with an incidence of approximately 8–10%. The aetiology includes congenital abnormalities, systemic rheumatic disease such as Libman- Sacks endocarditis, hypereosinophilic syndromes, infective endocarditis, myxomatous degeneration, trauma, radiation therapy, drugs and fibrosis due to pacemaker and defibrillator leads. However, the echocardiographic findings seen in this case are almost pathognomonic for carcinoid heart disease.

Outcome and Follow-up

A 24-hour urinary assessment on levels of 5-hydoxyindoleatic acid (5-HIAA) was performed, a reliable diagnostic marker for the presence of a carcinoid tumor. An increased level was found of 58.5 micromol/mmol creatinine (reference 0.5-4.0 micromol/mmol creatinine). Plasma level of chromogranin A was also increased, 1234 ug/l (reference 0-120 ug/l). Additionally, an octreotide scan was performed which showed a somatostatin receptor positive mass in the lower pelvis, indicating neuroendocrine tumor. For further localization an abdominal computed tomography (CT) imaging was performed. On CT images, a large tumor of 9,6 x 7,2 cm in the pelvis was detected most likely originating from the right ovary (**Figure 2**) with a normal aspect of the liver without evidence of liver metastasis. The ovarian mass was removed during a uncomplicated transabdominal surgery. Pathological analysis of the resected tissue confirmed the diagnosis of a carcinoid tumor of the right ovary.During follow-up the echocardiography showed no improvement of the valve deformity or tricuspid regurgitation severity. The right ventricle showed no dilatation with a preserved systolic functionic function, and an unchanged mild dilated right atrium. Patient showed no clinical signs of right heart failure. Almost one year after the diagnosis, patient remains clinically stable with an excellent exercise tolerance in VO2max treadmill test. She will be regularly followed-up at our outpatient clinic.

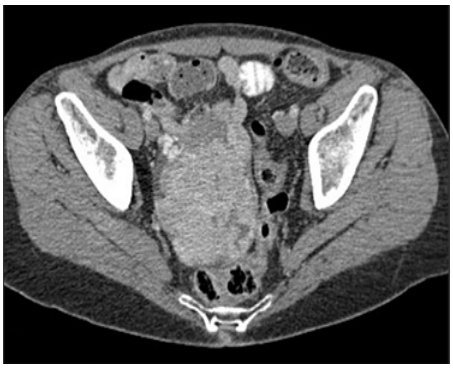

Figure 2: *Computed tomographic findings of carcinoid tumor. A large mass of 9.6 x 7.2 cm in the pelvis with heterogenous density and some calcifications, most likely originating from the right ovary. No evidence of liver metastases.*

Discussion

In patients with a carcinoid tumor, approximately 50% develop carcinoid syndrome. Once the carcinoid syndrome has developed, about half of the patients develop carcinoid heart disease which typically causes abnormalities of the right side of the heart. Carcinoid heart disease is associated with an increased risk of morbity and mortality. Three-year mortality data shows a 31% survival rate, whereas carcinoid patients without cardiac involvement have approximately twice the survival rate. Advanced NYHA class and right ventricular size are identified as important predictors of outcome [6]. The cardiac manifestations in carcinoid syndrome are related to the paraneoplastic effects of serotonin and other vasoactive substances that are released by the tumor. Normally once released, the active serotonin is metabolized in the liver, lungs and brain to metabolically inactive 5hydroxyindoleacetic (5-HIAA) which has renal clearance. However, the presence of hepatic metastasis may allow that a large proportion of these vasoactive substances reach the right side of the heart [7]. This is related to higher concentrations of 5-HIAA in patients with carcinoid heart disease than in carcinoid patients with no cardiac involvement. However, the development of carcinoid heart disease is not completely understood, because development and progression of cardiac lesions may occur despite aggressive therapy to attenuate serotonin release.

Therefore, in most instances, arcinoid tumors have to metastasize to the liver to result in symptoms of carcinoid syndrome. However, primary ovarian carcinoid tumors are unique in this regard; because these tumors release vasoactive substances directly into the inferior vena cava (right ovary) or renal vein

(left ovary) entering the systemic circulation.

Transthoracic echocardiography plays an important role in the diagnosis and prognostic evaluation of carcinoid heart disease. It shows a typical pattern of thickened, shortened and retracted leaflets of the tricuspid and pulmonary valve with poor systolic coaptation, leading to the valve remaining in a semi-open position, with a moderate or severe tricuspid and pulmonary valve regurgitation as result. In addition, there may be a coexistent tricuspid and/or pulmonary stenosis. As a consequence of the right sided valve disease, dilatation of the right atrium and ventricle is a common finding and paradoxical motion of the interventricular septum occurs in almost half of the cases due to volume overload. Left sided heart disease, myocardial metastases and pericardial effusion are other, less frequent, manifestations of the disease [6]. In the absence of metastatic disease, surgical removal of the primary tumor seems to be the only effective treatment; two-year survival with surgical removal has been reported to be 40%, whereas that of medical treatment without surgery is only 8% [8]. However, treatment resulting in decreased 5-HIAA excretion does not result in regression of cardiac manifestations. The most effective treatment option for carcinoid valve disease is cardiovalvular surgery. Indications for valve replacement surgery include progressive fatigue, significant impaired exercise capacity, symptomatic right heart failure and progression of right ventricular failure. Cardiac surgery should be considered in patients with controlled disease with a reasonable life expectancy [10]. In the case of a carcinoid related to a primary ovarian carcinoid, the early detection and surgical removal of the tumor may result in an excellent outcome [8]. Normally patients with carcinoid heart disease often present with symptoms of right sided heart failure (hepatomegaly, edema, ascites, fatigue and low cardiac output). In the case we report, although severe tricuspid regurgitation was present, there were no signs of heart failure. However, the typical pattern found with transthoracic echocardiography raised the suspicion of a rare condition such as carcinoid heart disease, together with weight loss and fatigue.

Learning points

• Isolated combined tricuspid valve pathology in absence of left valvular disease should raise the suspicion of carcinoid heart disease as the cause of right-sided valvular disease.

• Transthoracic echocardiography in carcinoid heart disease shows a typical pattern of thickened, shortened and retracted leaflets of the tricuspid and pulmonary valve with poor systolic coaptation, resulting in moderate or severe tricuspid and pulmonary valve regurgitation.

• Carcinoid heart disease due to primary ovarian tumor is unique because it can develop in the absence of liver metastasis.

References

1. Kulke MH, Mayer RJ. Carcinoid tumors. New England Journal of Medicine. 1999; 340:858-868.

2. Modlin IM, Sandor A. An analysis of 8305 cases of carcinoid tumors. Cancer. 1997; 79:813-29.

3. Modlin IM, Lye KD, Kidd M. A 5-decade analysis of 13,715 carcinoid tumors. Cancer 2003; 97:934959.

4. Chaowalit N, Connolly HM, Schaff HV, Webb MJ, Pellikka PA. Carcinoid Heart Disease Associated With Primary Ovarian Carcinoid Tumor. Am J Cardiol. 2004; 93:1314-1315.

5. Lundin L, Norheim I, Landelius J, Oberg K, Theodorsson-Norheim E. Carcinoid heart disease: relationship of circulating vasoactive substances to ultrasound-detectable cardiac abnormalities. Circulation. 1988; 77:264-9.

6. 6 Pellikka PA, Tajik AJ, Khandheria BK, et al. Carcinoid heart disease. Clinical and echocardiographic spectrum in 74 patients. Circulation. 1993; 87(4):1188-96.

7. Fox DJ, Khattar RS. Carcinoid heart disease: presentation, diagnosis, and management. Heart. 2004; 90:1224-1228.

8. Møller JE, Pellikka PA, Bernheim AM, Schaff HV, Rubin J, Connolly HM. Prognosis of carcinoid heart disease: analysis of 200 cases over two decades. Circulation. 2005; 112:3320-7.

9. Davis KP, Hartmann LK, Keeney GL, Shapiro H. Primary ovarian carcinoid tumors. Gynecol Oncol. 1996; 61:259-265.

10. Wells Askew J, Connolly HM. Carcinoid valve disease. Current treatment Options in Cardiovascular Medicine. 2013; 15:544-555.