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# Intracardiac Thrombosis and Heart Failure in a Patient with Hepatocellular Carcinoma and Cardiac Amyloidosis and an Implanted Cardiac Resynchronization Therapy Device

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**Conflict of interest:** None declared

**Patient:** Female, 68  
**Final Diagnosis:** Hepatocellular carcinoma  
**Symptoms:** Shortness of breath  
**Medication:** —  
**Clinical Procedure:** Cardiac resynchronization therapy  
**Specialty:** Cardiology

**Objective:** Diagnostic/therapeutic accidents





**Background:** Intracardiac thrombosis has been known to be associated with not only hepatocellular carcinoma but also with amyloidosis and use of a cardiac implantable electronic device. We report a case of a continuous tumor thrombus with hepatocellular carcinoma from the portal vein and hepatic vein to the right atrium via the inferior vena cava in a patient with a cardiac amyloidosis and an implanted cardiac resynchronization therapy (CRT) device.

**Case Report:** A 68-year-old female first admitted to our hospital because of heart failure with an AL type primary cardiac amyloidosis. After 3 years, she underwent an implantation of a CRT device for biventricular pacing following repeated episodes of heart failure and low left ventricular ejection fraction of 34% with NYHA class III. Again, she presented with symptoms of heart failure and cardiomegaly on chest x-ray at 7 years after the CRT device implantation. The echocardiography showed a huge echogenic mass occupying the right atrium, and 64 multi-detector computed tomography showed a lobulated heterogeneously enhancing mass of hepatocellular carcinoma in the right upper lobe of her liver and a continuous tumor thrombus from the portal vein and hepatic vein to the right atrium via the inferior vena cava.

**Conclusions:** Intracardiac thrombosis and heart failure occurred in a patient with hepatocellular carcinoma and cardiac amyloidosis, who had an implanted CRT device, which resulted not only in hypercoagulability by the hepatocellular carcinoma itself and the accumulation of various risk factors, but also the progression of myocardial damage with the development of amyloidosis.

**MeSH Keywords:** Amyloidosis • Carcinoma, Hepatocellular • Cardiac Resynchronization Therapy • Heart Failure • Thromboembolism

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## Background

Hepatocellular carcinoma (HCC) is a highly aggressive malignancy in which tumor thrombus is known to invade portal and hepatic veins in late stages [1]. Because the prognosis of HCC with intracavitary cardiac involvement is poor, with median survival ranging from 1 to 4 months [2], direct cardiac invasion with thrombus have been mainly reported at the time of autopsy in previous studies [3]. Possible cardiopulmonary and vascular complications of intracardiac thrombus with HCC are heart failure, tricuspid stenosis or insufficiency, ventricular outflow tract obstruction, ball-valve thrombus syndrome, sudden cardiac death, secondary Budd-Chiari syndrome, and pulmonary embolism [4].

On the other hand, primary amyloidosis is considered an uncommon disease, and the primary systemic type, AL, is due to monoclonal immunoglobulin free light chains [5]. The heart is affected in close to 50% of AL type cardiac amyloidosis, and congestive heart failure is the presenting clinical manifestation in about half of these patients. Once heart failure occurs, the median survival is <6 months in untreated patients, and death in more than one-half these patients is due to heart failure or arrhythmia. Previous random trials in the United States have shown that cardiac resynchronization therapy (CRT) device with biventricular pacing in these patients with repeated heart failure by severely reduced function improves cardiac function, quality of life, and survival [6].

Intracardiac thrombosis has been known to be associated with not only HCC [4] but also amyloidosis [7] and CRT devices [8,9].

We report a case of a continuous tumor thrombus with HCC from the portal vein and hepatic vein to the right atrium via the inferior vena cava in patient with cardiac amyloidosis and an implanted CRT device.

## Case Report

A 68-year-old female first admitted to our hospital because of heart failure, and was finally diagnosed as an AL type of primary cardiac amyloidosis including the endomyocardial biopsy (Figure 1A). After 3 years followed-up, she underwent a CRT device implantation for biventricular pacing following the repeated episodes of heart failure (NYHA class III) with reduced left ventricular ejection fraction of 34% and wide QRS with complete left bundle branch block of 143 ms. She kept a silent condition for 7 years after a CRT device implantation. A shortness of breath, symptoms of heart failure on physical examination, and remarkable cardiomegaly with extended cardiothoracic ratio of 74% on chest x-ray (Figure 1B) were again presented when she was 78 years old. The echocardiography

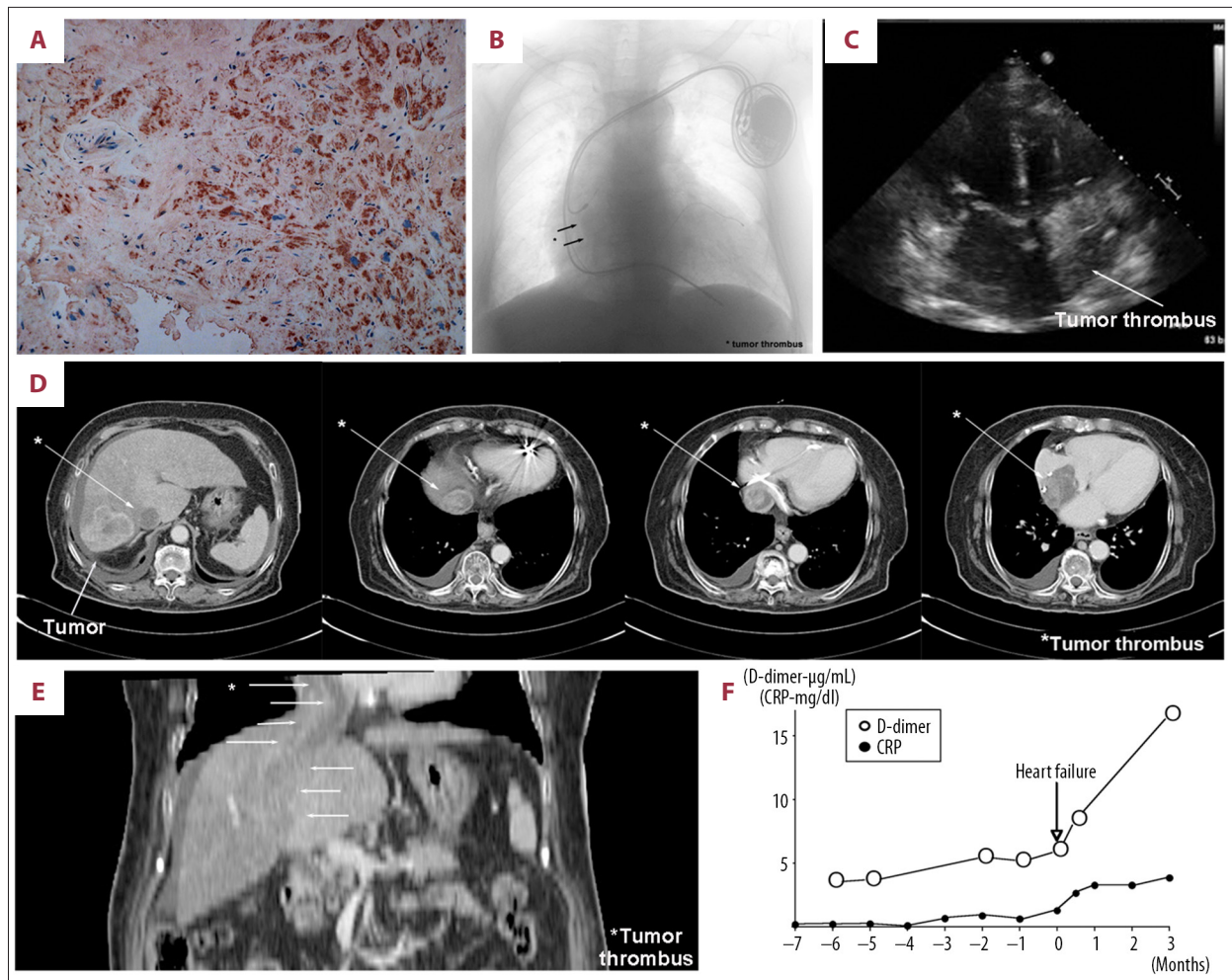
showed a huge echogenic mass occupying the right atrium (Figure 1C). Sixty-four multi-detector computed tomography (CT) showed a lobulated heterogeneously enhancing mass in the right upper lobe of liver, and a continuous tumor thrombus from the portal vein and hepatic vein to the right atrium via the inferior vena cava (Figure 1D, 1E). Alpha-fetoprotein level was >20 000 ng/mL (reference range: 0.0 to 10.0 ng/mL), and HCC was diagnosed by a contrast enhanced CT. The continuous hypercoagulability was shown more than 6 months before the last occurrence of heart failure despite of anticoagulant therapy (Figure 1F). She improved the symptoms of heart failure by the diuretics as a standard medical therapy. An extensive tumor thrombus with HCC was considered to have caused a hemodynamic complication in this case.

## Discussion

Kojiro et al. found that 4.1% of patients with HCC had thrombi that extended into and invaded the right atrium at the time of autopsy [3], but premortem diagnosis of HCC with intra-atrial invasion is very rare. We found that a continuous direct invasion of HCC with thrombus from the portal vein and hepatic vein to the right atrium via the inferior vena cava caused heart failure with amyloidosis, and an implanted CRT device. Generally, HCC is a consequence of liver cirrhosis, which causes the hypercoagulability [10]. Development of venous thromboembolic complications with HCC results from an increased fibrinogen concentration/polymerization, thrombocytosis, and a release of tissue factor-expressing extracellular vesicles [11]. Interestingly, this case had the other risk factors that accelerated thromboembolism.

Previous studies have identified a high prevalence of intracardiac thrombosis in these patients at autopsy, especially in AL cardiac amyloidosis [12,13]. In our case, advanced age, heart failure, left ventricular dysfunction, and hypertension were complications, which have also been reported as risk factors for thromboembolism [14]. Endomyocardial damage and endothelial dysfunction from amyloid depositions may be responsible for the occurrence of thrombosis [15]. Hypercoagulability may also contribute [16]. The combination of systolic and diastolic ventricular dysfunction, chronic amyloid infiltrate in the atria, and a direct toxic effect on myocardium [17] could lead to atrial mechanical dysfunction, atrial enlargement, and blood stasis [18]. Thus, atrial electrical-mechanical dissociation may explain the development of atrial thrombosis [19].

Thrombus formation is also a recognized complication of any type of cardiac implantable electronic device [9]. Endothelial trauma, blood turbulence, and blood stasis with depressed ventricular function may increase the risk of thrombosis. The pacemaker leads may themselves produce inflammation and fibrosis



**Figure 1.** (A) On endomyocardial biopsy, the deposition of amyloid fibrils especially in interstitial tissue surrounding capillary was demonstrated by the pink reticular pattern of the Congo-Red stain (100×). (B) A patient showed remarkable cardiomegaly with the inter-cardiac mass on chest x-ray. (C) Echocardiography showed a huge echogenic mass occupied a right atrium. (D, E) Sixty-four multi-detector computed tomography showed a lobulated heterogeneously enhancing mass in the right upper lobe, and a continuous tumor thrombus from portal vein, hepatic vein and inferior vena cava to right atrium. (F) The d-dimer and c-reactive protein (CRP) of serum concentrations continued a high level more than 6 months before the occurrence of heart failure.

along the course of the wire [20]. Moreover, a higher incidence of venous thrombosis has been found in patients who had a previous transvenous temporary pacemaker lead [21].

In our patient case, the intracavitary cardiac involvement of HCC was a direct trigger for the occurrence of heart failure, but the process may have been influenced by the progression of myocardial damage with amyloidosis and the acceleration of thromboembolism due to the accumulation of various risk factors.

## Conclusions

Intracardiac thrombosis and heart failure occurred in a patient with HCC and cardiac amyloidosis, who had an implanted CRT device, which resulted in not only hypercoagulability by the HCC itself and the accumulation of various risk factors, but also the progression of myocardial damage with the development of amyloidosis.

## References:

1. Okuda K: Hepatocellular carcinoma: Clinicopathological aspects. *J Gastroenterol Hepatol*, 1997; 12(9–10): S314–18
2. Chang JY, Ka WS, Chao TY et al: Hepatocellular carcinoma with intra-atrial tumor thrombi. A report of three cases responsive to thalidomide treatment and literature review. *Oncology*, 2004; 67: 320–26
3. Kojiro M, Nakahara H, Sugihara S et al: Hepatocellular carcinoma with intra-atrial tumor growth. A clinicopathologic study of 18 autopsy cases. *Arch Pathol Lab Med*, 1984; 108(12): 989–92
4. Sung AD, Cheng S, Moselehi J et al: Hepatocellular carcinoma with intracavitary cardiac involvement: A case report and review of the literature. *Am J Cardiol*, 2008; 102: 643–45
5. Selvanayagam JB, Hawkins PN, Paul B et al: Evaluation and management of the cardiac amyloidosis. *J Am Coll Cardiol*, 2007; 50(22): 2101–10
6. Fonarow GC, Albert NM, Curtis AB et al: Improving evidence-based care for heart failure in outpatient cardiology practices: Primary results of the Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting (IMPROVE HF). *Circulation*, 2010; 122: 585–96
7. Feng D, Edwards WD, Oh JK et al: Intracardiac thrombosis and embolism in patients with cardiac amyloidosis. *Circulation*, 2007; 116: 2420–26
8. Buttigieg J, Asciak R, Azzopardi CM: Pacemaker lead-associated thrombosis in cardiac resynchronisation therapy. *BMJ Case Rep*, 2015; 2015: pii: bcr2015210314
9. Novak M, Dvorak P, Kamaryt P et al: Autopsy and clinical context in deceased patients with implantable pacemakers and defibrillators: Intracardiac findings near their leads and electrodes. *Europace*, 2009; 11: 1510–16
10. Heimbach JK, Kulik LM, Finn RS et al: AASLD guidelines for the treatment of hepatocellular carcinoma. *Hepatology*, 2018; 67: 358–80
11. Zanetto A, Campello E, Spiezia L et al: Cancer-associated thrombosis in cirrhotic patients with hepatocellular carcinoma. *Cancers (Basel)*, 2018; 10(450): 1–19
12. Roberts WC, Waller BF: Cardiac amyloidosis causing cardiac dysfunction: Analysis of 54 necropsy patients. *Am J Cardiol*, 1983; 52: 137–46
13. Feng D, Syed IS, Martinez M et al: Intracardiac thrombosis and anticoagulation therapy in cardiac amyloidosis. *Circulation*, 2009; 119(18): 2490–97
14. Predictors of thromboembolism in atrial fibrillation, I: Clinical features of patients at risk. The Stroke Prevention in Atrial Fibrillation Investigators. *Ann Intern Med*, 1992; 116: 1–5
15. Berghoff M, Kathpal M, Khan F et al: Endothelial dysfunction precedes C-fiber abnormalities in primary (AL) amyloidosis. *Ann Neurol*, 2003; 53: 725–30
16. Yood RA, Skinner M, Rubinow A et al: Bleeding manifestations in 100 patients with amyloidosis. *JAMA*, 1983; 249: 1322–24
17. Liao R, Jain M, Teller P et al: Infusion of light chains from patients with cardiac amyloidosis causes diastolic dysfunction in isolated mouse hearts. *Circulation*, 2001; 104: 1594–97
18. Murphy L, Falk RH: Left atrial kinetic energy in AL amyloidosis: Can it detect early dysfunction? *Am J Cardiol*, 2000; 86: 244–46
19. Dubrey S, Pollak A, Skinner M, Falk RH: Atrial thrombi occurring during sinus rhythm in cardiac amyloidosis: Evidence for atrial electromechanical dissociation. *Br Heart J*, 1995; 74(5): 541–44
20. Fabijanić D, Giunio L, Vujičić M et al: Right atrial pacemaker lead thrombosis incidentally detected by transesophageal echocardiography. *Coll Antropol*, 2005; 29(1): 159–61
21. Da Costa SS, Scalabrini Neto A, Costa R et al: Incidence and risk factors of upper extremity deep vein lesions after permanent transvenous pacemaker implant: A 6-month follow-up prospective study. *Pacing Clin Electrophysiol*, 2002; 25: 1301–6