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## Case Report

# Unique association of cardiac amyloidosis and right atrial tumor thrombus in a patient with hepatocellular carcinoma

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## ABSTRACT

Tumor thrombus is a very rare complication observed in patients with hepatocellular carcinoma. We report a unique case of hepatocellular carcinoma with extension of tumor along the inferior vein cava into the right atrium, in a patient with cardiac amyloidosis and without any cardio respiratory distress or typical clinical findings suggestive of cardiovascular involvement from cardiac amyloidosis. Cardiac magnetic resonance imaging is a useful tool to assess intracardiac tumor extension as well as to provide myocardial tissue characterization.

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## Case report

A 73-year-old man, Hepatitis C Virus (HCV) positive came to our Institution for a syncopal episode; past medical history included 2 previous myocardial infarcts, chronic lower limb arteriopathy, carotid atherosclerosis, arterial hypertension, and dyslipidaemia. On admission, the patient underwent an echo color doppler of the supra-aortic vessels which showed: thrombosis of the right common and internal carotid arteries and stenosis of 90% of the left internal carotid artery. Subsequently an echocardiography was performed, which showed

the presence of a large (30 × 20 mm) mobile tumor, with irregular margins, nearly obliterating the right atrial cavity extending to the level of the tricuspid valve. In order to further characterize this tumor, a Cardiac magnetic resonance (CMR) was performed. CMR confirmed the presence of the large solid lesion of 33 × 27 mm, fluctuating into the right atrium and in continuity with an expansive hepatic lesion. T1-weighted late gadolinium enhancement (LGE) sequences, acquired at 10, 15, and 20 minutes, allowed to identify altered postcontrast kinetics of the blood-pool consistent with cardiac amyloidosis (CA). In particular, a widespread LGE affecting both left and right ventricular walls was encountered (Fig. 1A and B). Subsequently, the patient underwent a contrast-enhanced CT scan of the abdomen to better characterize the hepatic lesion (Fig. 2A-D). A large mass of 10 cm involving the caudate lobe and the IV liver segment was identified showing inhomogeneous

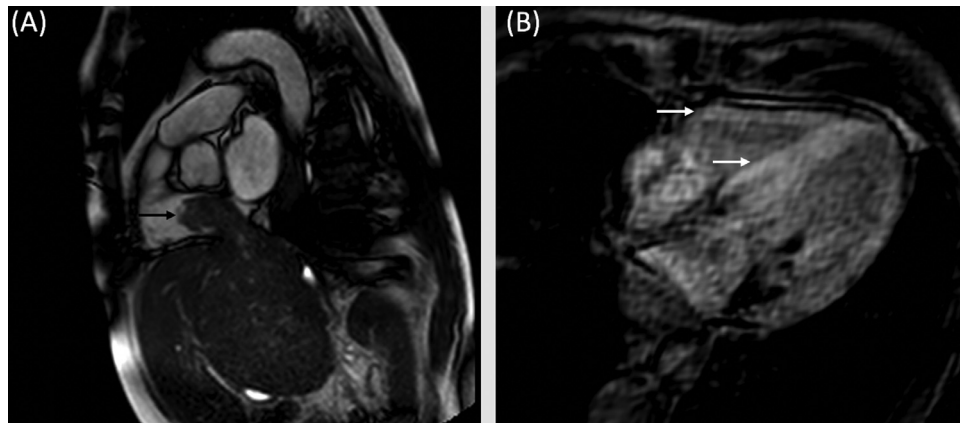
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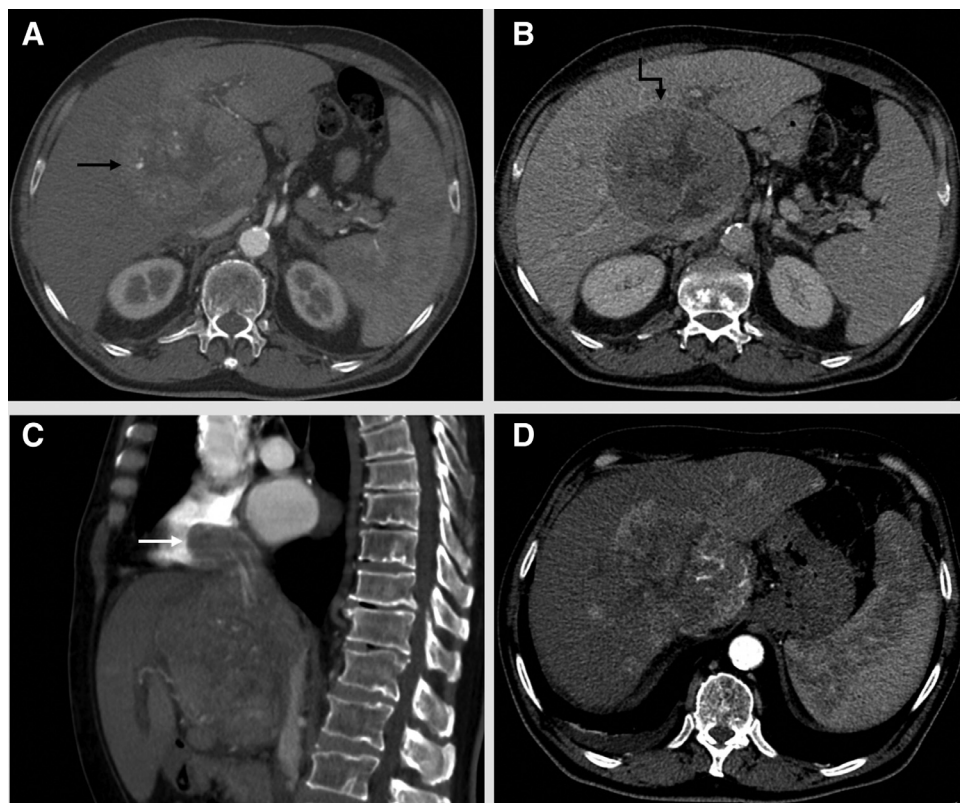
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**Fig. 1** – Cardiac magnetic resonance. Sagittal view showing a large hepatic mass directly extending into the right atrium (black arrow, A). Horizontal long axis 3D-T1 weighted late gadolinium enhancement (LGE) image showing widespread LGE affecting both LV and RV walls (white arrows, B).



**Fig. 2** – Computed tomography. Axial view showing a large mass involving the caudate liver lobe and the IV segment with inhomogeneous arterial enhancement (black arrow, A) and washout in the portal phase with evidence of a pseudocapsule (curved black arrow, B). Sagittal view showing the large tumor thrombus extending from the IVC into the right atrium (white arrow, C). Arterial phase axial view showing multiple hypervascular nodular lesions involving both hepatic lobes (D).

arterial enhancement and washout in portal phase, suggestive of hepatocellular carcinoma (HCC). In addition, the presence of a large tumor thrombus extending from the inferior vein cava (IVC) into the right atrium without infiltration of the portal vein was also confirmed. Furthermore, multiple additional nodular foci of HCC were appreciated in all remaining

hepatic segments. Finally, in order to confirm the diagnosis of CA, an abdominal fat pad excisional biopsy was performed, and final histopathological analysis showed a positive Congo red stain with apple-green birefringence under polarized light microscope. At laboratory examinations, Amyloid light-chain (AL) amyloidosis was confirmed with testing for serum free

light chains; in particular, there was a significant increase in serum free kappa light chains: 434 mg/dL (reference range: 6.7–22.4 mg/dL) with an abnormal kappa/lambda ratio and an increase in urinary kappa light chains (16.1 mg/L) (reference range: <10 mg/L). Moreover, the patient had high B-type natriuretic peptide (BNP): 587 pg/mL (reference range: 0–150 pg/mL). High BNP values are considered as a marker of cardiac involvement even before the onset of heart failure in patients with CA. Altered liver function tests were also observed with aspartate aminotransferase of 61 IU/L (reference range: 10–40 IU/L), gamma-glutamyl transpeptidase of 91 IU/L (reference range: 7–56 IU/L), and alpha fetoprotein of 33.6 ng/mL (reference range: 0–15 ng/mL). In particular, AFP is the standard serum tumor marker for the evaluation of suspected HCC even if high levels may be found in chronic hepatitis and liver cirrhosis, as well as in other tumor types.

The patient was treated with low molecular weight heparin and is currently under treatment with Sorafenib.

## Discussion

Worldwide, more than 780,000 cases of new primary liver cancer arise yearly and about 70%–90% of them are due to HCC [1]. More than 80% of HCC is attributable to the combined effects of chronic hepatitis B and C infections [2,3]. Yet advanced HCC with an invasion of IVC is an uncommon way for the disease to progress and it is rare to see an extension of tumor thrombus into the right atrium [4–6]. According to Kim et al, only 0.53% of HCC patients have invasion to the IVC [7]. Our patient presented with a huge tumor thrombus extending from the IVC into the right atrium. Such an extensive thrombus on presentation is extremely rare. Extension of the tumor thrombus to the IVC and/or the right atrium is usually first disclosed at autopsy; there are only a few reported cases in which the intra-atrial growth could have been diagnosed by noninvasive radiology and echocardiography prior to death [4,5].

To the best of our knowledge, there is only 1 reported case in the English literature of a patient presenting HCC associated with systemic amyloidosis, demonstrated at autopsy [8]. Our patient was admitted to the hospital because of a syncopal episode, but he had no cardiorespiratory symptoms despite having such a large thrombus. Syncope is a serious prognostic sign in AL amyloidosis and is often a precursor of sudden cardiac death, most likely due to electromechanical dissociation [9]. In a recent study, Lippman et al described a case of a patient who presented with the primary concern of syncope secondary to CA (AL-type) but it wasn't associated with HCC. They reported that AL amyloidosis must be suspected in patients presenting with syncope in the setting of autonomic neuropathy, proteinuria, cardiomyopathy, chronic diarrhoea, and purpura [10].

The literature also states that right atrial thrombus may not cause any symptoms but can sometimes lead to shock from ball valve obstruction of the tricuspid valve, right heart failure, pulmonary emboli, and sudden death [11,12]. The tu-

mor thrombus and its extension were diagnosed on echocardiography and confirmed by CMR in the reported case. In addition, CMR was able to incidentally discover the association with CA, subsequently confirmed by positive abdominal fat pad excisional biopsy. Biopsy with histopathology remains the gold standard showing deposition of amorphous deposits of amyloid fibrils, having a sensitivity of approximately 75% and specificity of 92%. Moreover, the subtype AL amyloidosis was identified with testing for serum free light chains.

Our patient also showed increased BNP. According to Bhogal et al, if seen along with amyloidosis, elevated BNP levels are considered as a marker of cardiac involvement even before the onset of heart failure [13]. Primary systemic or AL amyloidosis is characterized by the presence of monoclonal plasma cells and deposition of immunoglobulin light chain-derived amyloid deposits in various organs. The outcome of patients with AL amyloidosis is highly dependent on the spectrum and severity of organ involvement, especially cardiac involvement [14,15]. Mortality is high when cardiac involvement is present, and prognosis remains poor [13]. In fact, CA is a progressive but under-diagnosed and under-appreciated cause of right sided heart failure. Infiltration of amyloid fibrils results in stiffening and thickening of ventricles causing decreased compliance and increased pressure altering the mechanics of ventricular function manifesting as diastolic dysfunction [13]. Involvement of cardiac conduction system causes first degree, second degree, or advanced heart block or arrhythmias that can be symptomatic secondary to direct amyloid deposits in conduction system or due to ischemia. Syncope can be due to heart block or arrhythmias and could be an indicator for poor survival outcome [9]. In the last few years, CMR has become the gold standard for noninvasive diagnosis of CA with the characteristic widespread LGE, allowing accurate differentiation from other cardiomyopathies [16–20]. Echocardiography has been shown to be a useful additional diagnostic step for detection of cardiac metastasis and other complications like thrombosis. Echocardiography can provide information not only about the size and extension of the thrombus, but also regarding the mobility of the tumor thrombus and its relationship with the valve and the cardiac muscle. Moreover, echocardiography is very useful to diagnose such rare complications in the early stages of the disease and also for follow-up after treatment [21]. Surgical resection, liver transplantation, nonsurgical procedures such as, radio frequency ablation, intraarterial chemoembolization, and drugs such as thalidomide and sorafenib (multikinase inhibitor) have been shown to be effective for relieving symptoms and prolonging life in HCC patients with multiple or extensive metastasis. However, very high mortality rates are observed for advanced HCC with IVC and intra-atrial tumor extension. Mean survival time reported is 3–4 months whether the patient is treated or not [7].

In conclusion, our case illustrates the unusual and incidental association of advanced HCC with intracardiac involvement and CA. CMR should be performed for a better assessment of intracardiac tumor extension and to provide tissue characterization, allowing to identify the presence of pathological myocardial LGE.

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