A Case of Right Atrial Obliteration Caused by Intracardiac Extension of Hepatocellular Carcinoma

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Abstract
As the fifth most common malignancy worldwide, hepatocellular carcinoma (HCC) is a frequently encountered clinical entity. Symptomatology associated with the diagnosis includes hepatic dysfunction and pain from capsular spread. Additionally, due to its propensity for vascular spread, extrahepatic intravascular involvement can also be seen. We present a unique case of intracardiac involvement of HCC. Originally diagnosed as acute on chronic heart failure, echocardiography revealed the symptom source – tumor obliteration of the right atrium. Clinical case presentation and management, along with radiographic images are presented. A review of the current literature highlights this uncommon presentation and the
need for clinical suspicion of cardiac involvement in patients with a history of HCC presenting with heart failure.

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common malignancy and the third most common cause of cancer death worldwide [1]. It is often a rapidly progressive tumor, with only 30–40% of patients amenable to surgery at the time of diagnosis [2]. A hallmark of HCC is its propensity for both direct and distant vascular spread. However, despite the high incidence of venous involvement and close proximity to the heart, reports of intracardiac metastasis are rare [3]. We present an interesting case presentation highlighting cardiac metastasis in HCC, followed by a brief review of cardiac metastasis, endocardial presentation of HCC, and potential treatment modalities.

Case Presentation

A 78-year-old male with hemochromatosis complicated by locally advanced HCC was admitted to our hospital from a skilled nursing facility with new-onset bilateral lower extremity edema. His comorbidities included atrial fibrillation and hypertension, but he had never suffered from significant edema or symptoms of congestive heart failure previously. He was at the skilled nursing facility for rehabilitation after a prolonged hospitalization during which he suffered from postembolization syndrome after his fourth round of transarterial chemoembolization (TACE).

On questioning, he complained primarily of discomfort in his legs related to edema but also endorsed fatigue and progressive dyspnea on exertion. On presentation, his vital signs were within the normal limits. Physical exam was notable for moderate jugular venous distension and an expected irregularly irregular cardiac rhythm without audible murmurs. His lungs were clear to auscultation, and his extremities had 4+ pitting edema to the sacrum. Laboratory evaluation revealed a mildly elevated BNP of 236 pg/mL, a slightly low serum sodium of 133 mmol/L, and normal kidney function. Small bilateral effusions were seen on chest X-ray.

The patient underwent transthoracic echocardiography, which revealed a 6.4 × 4.3 cm mass occupying nearly the entire right atrium, and extending to the inferior vena cava (IVC) (Fig. 1). Angiography was then pursued and showed subtotal occlusion of the IVC by a mass extending from the hepatic veins into the right atrium (Fig. 2). Biopsy of the cardiac mass confirmed poorly differentiated HCC. Unfortunately, the patient was not a candidate for surgical resection or chemotherapy due to his comorbidities. Palliative radiation was considered, but the patient’s symptoms progressed to the point of dyspnea at rest and anasarca before it could be initiated. Given his rapid decompensation, the patient elected to pursue hospice care. He was transitioned to a local hospice care facility and died 12 days later.
Discussion

With an incidence in North America of 2.1 cases per 100,000 people and 80 cases per 100,000 people in some Asian countries, HCC is a common malignancy [1]. Its high affinity for vascular spread results in only 30–40% of patients being candidates for curative therapy on presentation [2]. Reports of IVC thrombosis in HCC range widely, citing an incidence of 6.5–44% [2]. Despite the high propensity for intravascular dissemination and close proximity to the heart, clinically relevant cardiac metastases are a presumed rare occurrence. This is particularly true in western countries where the HCC population burden is less pronounced. Despite its rare nature, the presence of cardiac metastases should be considered in the differential of patients with known malignancies, specifically those with a high disease burden.

Cardiac Metastasis and HCC

Primary cardiac tumors are exceedingly rare, with postmortem studies reporting an incidence of 0.001–0.03% [4]. Metastatic cardiac tumors are much more common, with some authors reporting >10% incidence on autopsy review [5, 6]. Tumor spread occurs via 1 of 4 mechanisms: hematologic, lymphatic, intravascular, or direct invasion. The pericardium is the primary site in >60% of tumors, with the endocardium comprising a minority of cases [3]. Lung, breast, and hematologic cancers are the 3 most common malignancies associated with cardiac metastasis, but pleural mesothelioma and melanoma have a higher propensity for metastatic cardiac spread. In a large postmortem autopsy study, 48.4% of mesothelioma patients and 27.8% of melanoma patients were found to have a cardiac metastasis [3].

The reported incidence of cardiac involvement in HCC ranges from 1.2 to 4% [2, 3]. HCC’s propensity for intravascular spread is the primary mechanism by which cardiac metastasis is thought to occur. As in our case, direct invasion of the hepatic veins and IVC can result in eventual tumor growth into the right atrium. The life expectancy of HCC patients with cardiac involvement is less than 3 months after diagnosis. Given this dismal prognosis, timely diagnosis coupled with early initiation of various treatments is being actively investigated.

Signs and Symptoms of Atrial Involvement of HCC

Based on the results of postmortem studies in which a majority of patients were without cardiac symptoms at time of death, it appears most cardiac metastases are clinically silent [3]. For those who do have tumor-associated symptoms, the presentation is quite heterogeneous – a reflection of the variability in both size and location of these metastases. For patients with endocardial involvement, as in our case, signs and symptoms of heart failure secondary to inflow obstruction and impaired cardiac contractility are common [3]. Cardiac arrhythmias may also be seen at presentation, secondary to tumor invasion infiltrating the cardiac conduction pathway. Pulmonary embolism has also been reported as the primary presentation [7]. Presumed mechanisms include tumor dislodgement secondary to necrosis or as a result of flow stasis at the site of the tumor [8].

Treatment Modalities

As mentioned previously, current prognosis of HCC with cardiac involvement is very poor, due in part to aggressive tumor biology and also limited treatment options. As in other malignancies, treatment modalities include surgery, chemotherapy, and radiation, but given the widespread nature of disease in many patients at presentation, these therapies are often performed with a palliative as opposed to curative intent.
Surgery

Many consider HCC with cardiac metastasis a contraindication for surgery; this practice, combined with the rare incidence of such tumors limits the data available on surgical intervention. Thus, there is no consensus for the role of surgical intervention. Studies of hepatectomy and portal vein thrombectomy, without mention of cardiac involvement, suggest survival benefit and improved quality of life compared to chemotherapy [9]. With regard to right atrial involvement, case reports on resection validate surgical feasibility, but the survival benefit is less clear. Wang et al. [10] performed a retrospective review of surgical intervention versus TACE in patients with tumor extending into the IVC and right atrium. In their patient cohort, median survival after surgical resection was 19 months compared to only 4.5 months in the TACE group. The retrospective nature of the study and selection bias obviously limit conclusions, but suggest that for the patient with appropriate liver reserve, surgical resection may be a viable option.

Chemotherapy

For those who are not candidates for surgery, both systemic and local chemotherapies have been attempted. Unfortunately for most patients with HCC, including those with or without cardiac metastasis, chemotherapeutic response is modest. Cisplatin-, gemcitabine- and oxaliplatin-based treatment regimens are currently utilized with no clear optimal therapy. Newer molecular-based treatments – including sorafenib – are promising. Case reports on the use of systemic therapy with atrial tumor involvement suggest potential survival benefit. In 3 patients with intra-atrial tumor thrombus treated with oral thalidomide, Chang et al. [11] reported an overall survival of greater than a year. Additionally, in a case report by Vallakati et al. [12], the patient experienced significant atrial tumor regression and symptom improvement after only 4 weeks of sorafenib treatment.

Local chemotherapy delivery has also been attempted in atrial tumor involvement. As mentioned above in the study by Wang et al. [10], TACE resulted in a smaller survival benefit compared to surgical resection, but was superior to no intervention. In a case report by Kamal et al. [2], a patient experienced complete atrial tumor resolution after targeted TACE delivery. Yet again, the small patient population limits the ability to provide treatment recommendations.

Radiation

High-dose, external beam radiation therapy is not a commonly considered treatment of widespread HCC secondary to the susceptibility of the liver to radiation-induced liver disease (RILD). RILD is seen approximately 3 weeks after radiation therapy with as little as 30–40 Gy, well under the 60 Gy suggested for treatment [13]. Symptoms include anicteric ascites and painful hepatomegaly along with markedly elevated alkaline phosphatase levels. Normally reversible with supportive care, this can lead to permanent pain and liver dysfunction. Given that 80–90% of those diagnosed with HCC have cirrhosis, therapy which could induce further liver damage is avoided by many practitioners [14]. Despite the concerns for adverse events with curative radiation doses, palliative treatment and targeting of metastases has shown some success. Lower dose radiation can help alleviate the signs and symptoms of cardiac tumor thrombus [8, 15]. Giuliani et al. [8] describe use of such palliative radiation in targeting intracardiac thrombus in a patient with severe dyspnea. In this patient, after only 5 sessions of radiation his symptoms resolved and his cardiac tumor burden decreased by 30%. Despite no obvious survival benefit, the patient was without symptoms for the re-
mainder of his life. Such positive outcomes without significant risk of RILD suggest yet another potential therapeutic modality for this rare and challenging presentation.

**Conclusion**

Cardiac metastases are a rare clinical entity associated with multiple different malignancies, including HCC. Despite their uncommon nature, clinical suspicion should be high in any patient with HCC who presents with new-onset symptoms of cardiac failure or arrhythmia. Despite a poor prognosis, high clinical suspicion may allow for earlier detection and initiation of treatment, rapid palliation to improve quality of life, or avoidance of futile treatments. Further investigation into clinical and tumor-specific risk factors that increase the likelihood of cardiac metastasis (i.e., 3 or more hepatic tumors, single tumor greater than 6 cm, extension into the IVC) may help with identifying these individuals. For those patients deemed high risk, a one-time transthoracic echocardiography could allow for earlier recognition of cardiac involvement and increase treatment options. Beyond HCC, such screening algorithms could be developed for other cancers with a propensity for cardiac involvement, such as renal cell or adrenal cortical carcinoma, as well.

**Statement of Ethics**

The authors have no ethical conflicts to disclose.

**Disclosure Statement**

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Fig. 1. Initial transthoracic echocardiography (apical 4-chamber view). Arrows denote hyperechoic mass occupying right atrium.
Fig. 2. CT angiography with reconstruction showing tumor invasion into right atrium. a Axial view. b Sagittal view. c Coronal view; arrow noting transcardiac hepatic feeding vessel. d Coronal 3-D reconstruction; red denotes tumor mass.