



Cardiac metastases and tumor embolization: A rare sequelae of primary undifferentiated liver sarcoma



Monica M. Dua^{a,*}, Jordan M. Cloyd^a, Francois Haddad^b, Ramin E. Beygui^c, Jeffrey A. Norton^a, Brendan C. Visser^a

^a Department of Surgery, Division of Surgical Oncology, Stanford University School of Medicine, 300 Pasteur Drive, H3591, Stanford, CA 94305, United States¹

^b Department of Medicine, Division of Cardiovascular Medicine, Stanford University School of Medicine, Falk Cardiovascular Research Center, 870 Quarry Road, Stanford, CA 94305, United States

^c Department of Surgery, Division of Cardiothoracic Surgery, Stanford University School of Medicine, Falk Cardiovascular Research Center, 870 Quarry Road, Stanford, CA 94305, United States

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ABSTRACT

INTRODUCTION: Primary hepatic sarcomas are uncommon malignant neoplasms; prognostic features, natural history, and optimal management of these tumors are not well characterized.

PRESENTATION OF CASE: This report describes the management of a 51-year-old patient that underwent a right trisectionectomy for a large hepatic mass found to be a liver sarcoma on pathology. He subsequently developed tumor emboli to his lungs and was discovered to have cardiac intracavitary metastases from his primary tumor. The patient underwent cardiopulmonary bypass and resection of the right-sided heart metastases to prevent further pulmonary sequela of tumor embolization.

DISCUSSION: The lack of distinguishing symptoms or imaging characteristics that clearly define hepatic sarcomas makes it challenging to achieve a diagnosis prior to pathologic examination. Metastatic spread is frequently to the lung or pleura, but very rarely seen within the heart. Failure to recognize cardiac metastatic disease will ultimately lead to progressive tumor embolization and cardiac failure if left untreated.

CONCLUSION: The most effective therapy for primary liver sarcomas is surgery; radical resection should be performed if possible given the aggressive nature of these tumors to progress and metastasize.

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1. Introduction

Primary hepatic sarcomas are extremely rare tumors that comprise a heterogeneous group of histological subtypes including angiosarcoma, leiomyosarcoma, undifferentiated (embryonal) sarcoma (UES), epithelioid hemangioendothelioma, and fibrosarcoma. In the adult population, these sarcomas, as a group, represent less than 1% of liver malignancies^{1,2}; the various histological compositions, in addition to vague symptoms, lack of common tumor markers, and inconsistent imaging findings often make diagnosis difficult with delays in subsequent treatment.

Abbreviations: CT, computed tomography; IVC, inferior vena cava; PE, pulmonary emboli; UES, undifferentiated (embryonal) sarcoma; TVE, total vascular exclusion.

* Corresponding author. Tel.: +1 650 736 1355; fax: +1 650 724 9806.

E-mail addresses: mdua@stanford.edu (M.M. Dua), jclloyd@stanford.edu (J.M. Cloyd), fhaddad@stanford.edu (F. Haddad), rbeygui@stanford.edu (R.E. Beygui), janorton@stanford.edu (J.A. Norton), bvisser@stanford.edu (B.C. Visser).

¹ Tel.: +1 650 736 1355; fax: +1 650 724 9806.

2. Presentation of case

A 51-year-old male patient developed progressive right upper quadrant abdominal pain over several weeks. He presented to a local hospital with acute pain; computed tomography (CT) imaging demonstrated a 28 cm complex cystic tumor with septal enhancement, nodularity, and inferior vena cava (IVC) compression (Fig. 1). Aspiration of the tumor was noted to be initially hemorrhagic; this was followed by percutaneous drainage and removal of 4L serosanguinous fluid for symptom relief. The fluid quickly re-accumulated and he was transferred to our hepatobiliary surgical service for further management.

Due to mass effect of the large tumor and resultant anatomic stretch of the bile ducts, the patient was mildly jaundiced with an elevated bilirubin level of 3.7 mg/dL and alkaline phosphatase level of 509U/L. A percutaneous transhepatic biliary drain was placed into the left lateral segment of the liver for preoperative drainage and his jaundice improved. The tumor had imaging features concerning for malignancy, but minimal overall solid component; therefore, the differential diagnosis included biliary cystadenoma, cystadenocarcinoma, or less likely an intrahepatic sarcoma. There

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Fig. 1. CT scan of primary liver sarcoma. Axial CT scan slice of a 28 cm complex, multiloculated cystic mass with enhancing mural nodularity and septations predominantly in the right lobe of the liver and extending into the left medial section. There is mass effect from the liver displacing the IVC and left portal vein.

was a strong probability that the tumor had bled both into itself and into the peritoneum adjacent to it (causing his acute onset of symptoms); however, the cytology from the aspiration done at the local hospital was negative for malignancy. He underwent a right trisectionectomy with caudate lobectomy via a thoracoabdominal approach (Fig. 2A) given the large tumor size (Fig. 2B). Despite division of the right liver inflow, the weight of the tumor against the IVC produced a very high physiologic central venous pressure. This did not permit an anterior approach to parenchymal division; we encountered brisk venous back-bleeding during the initial attempt at transection. The right liver was mobilized and the short hepatic veins and right hepatic vein were divided. Total hepatic vascular exclusion was obtained by placing one Rummel tourniquet around the left liver inflow (for Pringle maneuver) and another tourniquet around the common middle and left hepatic vein outflow. Two periods of vascular clamping were used to divide the liver parenchyma; total occlusion time was 33 min. During the operation, anesthesia had placed a transesophageal echocardiogram probe for routine continuous monitoring which suggested a vegetation on the tricuspid valve – though the significance of this finding was uncertain so further evaluation was planned for after surgery. The liver specimen weighed 4650 g and demonstrated a heterogeneous mass with areas of hemorrhage and necrosis (Fig. 3). Histological sections demonstrated atypical spindled cells with



Fig. 3. Gross architecture of liver sarcoma. The specimen is bivalved to demonstrate a heterogeneous mass of solid and cystic components with areas of hemorrhage and necrosis.

hyperchromatic nuclei and multiple areas of necrosis consistent with an undifferentiated liver sarcoma of intermediate-grade.

On post-operative day one, the patient developed hypoxia and a CT angiogram of the chest demonstrated small, right-sided segmental pulmonary emboli (PE). A transthoracic echocardiogram confirmed a mobile mass on the tricuspid chordal apparatus. The patient was anticoagulated and subsequent blood cultures grew *staphylococcus*. The combination of events seemed odd, but he was presumptively diagnosed with endocarditis (believed to have been present preoperatively) and placed on a 6-week regimen of antibiotics. He recovered without further sequela was discharged 11 days after his initial operation. A repeat echocardiogram at 8 weeks postoperatively demonstrated a second mass originating from the right atrium and resultant pulmonary hypertension. Interval CT angiogram of the chest also showed progressive pulmonary emboli, despite being on therapeutic Lovenox. Finally at 10 weeks postoperatively, repeat imaging showed an increased size of the mass attached to the tricuspid chordal apparatus with extension into the main pulmonary artery (Fig. 4A) as well as a second mobile mass within the IVC originating from the left hepatic vein and extending into the right atrium (Fig. 4B). The bilateral pulmonary emboli had increased in size and number, suggestive of truly being tumor emboli from the cardiac mass.

Given such rapid progression and risk of further embolization, he was referred to cardiothoracic surgery for resection of the cardiac mass. A median sternotomy was performed and after initiation of cardiopulmonary bypass, umbilical tapes were placed around the superior and inferior vena cava. The right atrium was opened

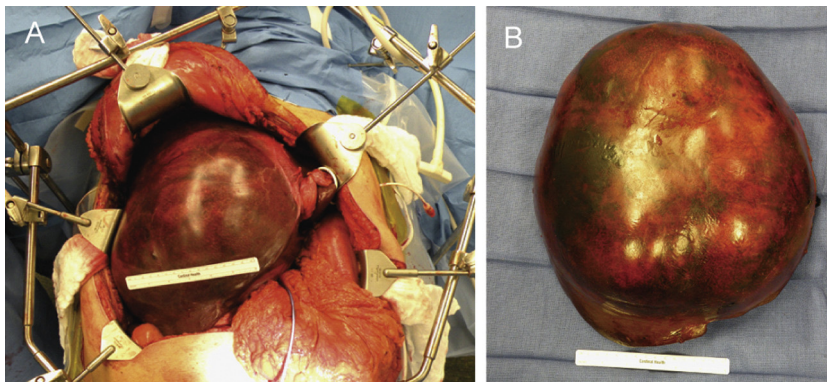


Fig. 2. Resection technique and specimen. Operative photographs illustrating (A) the thoracoabdominal extension used to split the costal margin and diaphragm for improved exposure of the massive tumor; and (B) the specimen after right trisectionectomy.

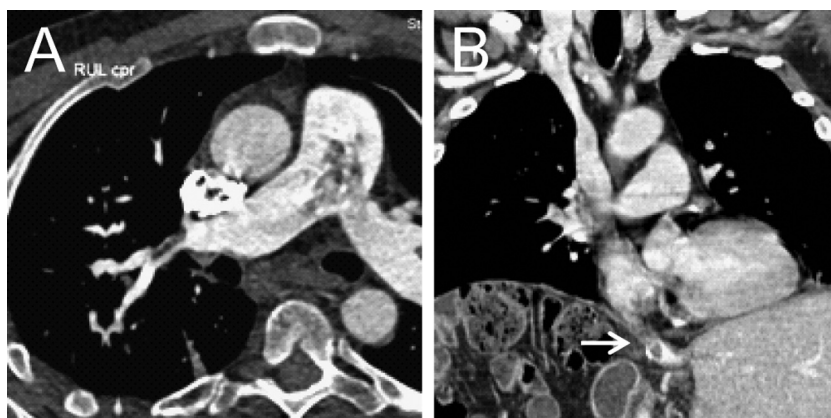


Fig. 4. CT scan of cardiac metastases. CT scan of the chest demonstrates (A) the presence of tumor in the main pulmonary artery on axial section (via extension of the right ventricular mass through the pulmonic valve); and (B) tumor extension into the IVC and right atrium on coronal section. White arrow indicates tumor originating from the left hepatic vein (only remaining hepatic vein after right trisectionectomy).

and demonstrated the right ventricular mass below the tricuspid valve and a right atrial mass with extension from the IVC. The mass did not incorporate the valve or the myocardium and had the appearance of multiple rubbery cystic clusters pedunculated on a stalk emanating from the hepatic vein (Fig. 5). As the patient had undergone a right trisectionectomy, there was only one remaining hepatic vein entering the IVC. Fogarty embolectomy was done through the left hepatic vein with no further tumor retrieved. A transverse arteriotomy was made in the main pulmonary artery for antegrade embolectomy and no additional masses or thrombus was removed. The right atriotomy was closed and total aortic cross-clamp time was 45 min. The patient recovered uneventfully and the pathology of the cardiac tumors was consistent with the liver sarcoma primary.

An echocardiogram at one month postoperatively demonstrated normal systolic function, improvement in right ventricular systolic pressures, and no residual masses. As the etiology of his pulmonary emboli was more likely to have been fragments of friable tumor as opposed to true thrombus, the need for anticoagulation was debatable; it was decided to maintain anticoagulation for 3 months postoperatively from his second surgery – until he had recanalization of his pulmonary artery and therefore, lower risk of thrombosis. A surveillance CT angiogram of the chest was done after completion of anticoagulation therapy and this showed no filling defects within the pulmonary arteries or the heart (Fig. 6). He was referred to medical oncology for adjuvant chemotherapy with 6 cycles of Ifosfamide and Doxorubicin.



Fig. 5. Gross architecture of atrial mass. Fragments of the intracavitary cardiac tumor consist of multiple grape-like clusters of soft tissue pedunculated on a stalk. The histological sections demonstrated variable cellular myxoid proliferation and spindled cells similar to the primary liver sarcoma.

3. Discussion

As a result of its infrequency, treatment approaches for primary hepatic sarcomas have not been standardized. Complete tumor

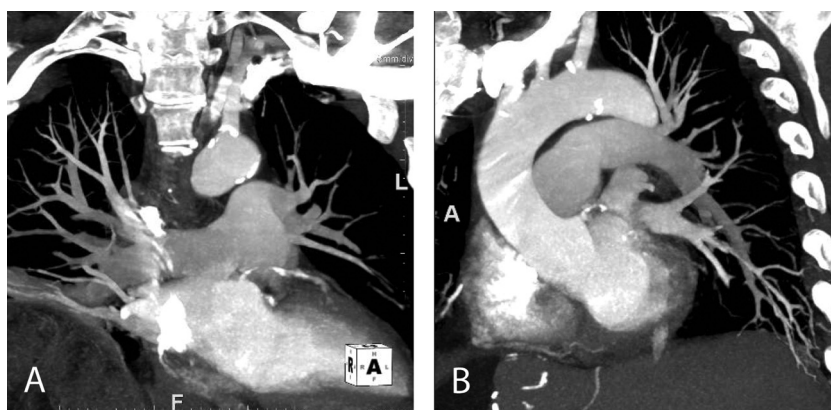


Fig. 6. Postoperative CT angiogram. CT angiogram of the chest performed at three months postoperatively (from intracavitary resection) and after completion of anticoagulation therapy. There are no residual cardiac masses (A) and no pulmonary emboli or abnormal filling defects noted within the cardio-pulmonary vasculature (B).

resection has been demonstrated to be the most effective therapy at present.^{1–3} The survival in most patients with unresectable tumors is poor, frequently surviving only a few months due to local tumor progression or early metastatic spread.^{4,5} Small series of adult patients undergoing surgery suggest that tumor histology,⁶ tumor grade,^{1,2} and completeness of resection are the most important predictors of survival.^{1,2,5,6} The 5-year survival after primary surgical treatment was reported between 64 and 77% in patients who underwent R0 resection; however, all patients in whom an R1 resection was performed died within three years. Local recurrence is frequent despite complete resection, with two of the studies reporting an intrahepatic recurrence rate of approximately 30% within the first three years.^{1,5} The presence of distant metastases was the predominant reason for treatment failure with the lung, pleural, and peritoneal surfaces being the most common sites of disease.^{1,7,8}

The frequency of cardiac metastases varies from 12 to 25% of post-mortem patients who have died of malignancies.^{9,10} In one series of 407 cases in which the heart or pericardium was secondarily involved with a malignant tumor, 4.2% of these tumors were from a sarcoma primary.¹¹ Cardiac metastases mostly appear in patients with advanced tumor disease; at this stage of disease, many patients have undergone some type of treatment for the primary tumor. The most common tumors with cardiac metastatic potential include carcinomas of the lung, breast and esophagus, malignant lymphoma, leukemia and malignant melanoma.⁹

There are four pathways by which metastases may reach the heart – through lymphatic or hematogenous spread and by direct or transvenous extension. Cardiac intracavitary metastases are infrequent, with the atrium being more commonly involved than the ventricle.¹⁰ These metastases are usually secondary to transvenous extension into the right atrium as a result of embolization or propagation along the vena cava. Our patient had no evidence of tumor in the hepatic veins or IVC on preoperative imaging; therefore, thrombectomy at the time of primary resection was not indicated. Pathology confirmed the mass to be confined to the liver with no vascular invasion and all margins negative. Operations for primary hepatic tumor with thrombus extending to the hepatocaval confluence are feasible, but remain challenging from a technical and hemodynamic standpoint given the need for total vascular exclusion (TVE) to control hemorrhage.¹² The majority of these high risk cases with TVE are done for retrohepatic or suprahepatic caval thrombus by direct extension; concurrent hepatectomy with cardiopulmonary bypass and removal of tumor thrombus extending to the right atrium has also been described.^{12,13} Although not diagnosed at the time of liver resection, our patient already had demonstrated propensity for tumor embolization (rather than direct extension of thrombus) with the presence of his isolated intracavitary cardiac metastasis. Mechanical factors during blunt mobilization and rotation of the liver are unavoidable when dissecting a large tumor and can be responsible for further tumor dislodgement or microembolization into the venous circulation with subsequent intracaval involvement.¹⁴

Several case reports of endometrial stromal sarcoma with intracardiac metastasis have been described, with the majority also having intracaval involvement.^{15,16} One such case that underwent surgical treatment reported a thin and string-like rubbery mass (a description similar to our findings) which was easily removed from the right ventricular outflow tract.¹⁶ As cardiac metastases usually remain clinically silent, most intracavitary tumors are found on autopsy with less than 10% presenting with symptoms indicative of cardiac dysfunction.⁹ Lack and colleagues examined the post-mortem pathologic features of 16 children with UES of the liver and found two cases of hepatic vein invasion with extension up the IVC into the right atrium and ventricle. Both children died of progressive dyspnea and massive tumor embolization to the lungs.¹⁷

Right-sided metastases can lead to pulmonary tumor emboli with progressive cor pulmonale over weeks to months.^{18,19} Establishing the diagnosis of pulmonary tumor embolism can be difficult as dyspnea in a patient with cancer may have several common causes including infection, thromboembolism, metastatic disease, or as a result of side effects from chemotherapy. Occlusion of the pulmonary vasculature with tumor cells and associated thrombus can present a subacute and progressive clinical scenario that resembles thromboembolic disease. Even in symptomatic patients, identifying a true diagnosis of microscopic tumor embolism is challenging as the diagnosis is under-recognized and radiographic findings are nonspecific. Upon complaint of dyspnea, initial CT angiogram of the chest in our patient demonstrated the presence of small filling defects in the segmental branches of the right upper and middle lobe pulmonary arteries suggestive of pulmonary emboli. The cardiac mass was initially believed to represent endocarditis and he was therefore treated with anticoagulation and antibiotics. His treatment failure (evidenced by increased size of the right heart mass and progressive pulmonary emboli on follow-up exams) prompted re-evaluation of the diagnosis and surgical intervention for the ongoing nature of his embolization.

Only a few adult cases of UES have been reported; however, this particular variety of hepatic sarcoma accounts for up to 13% of pediatric hepatic malignancies, commonly occurring in patients under the age of 10 years.^{4,8} Although a supportive role of neoadjuvant/adjuvant chemotherapy is not confirmed in all primary hepatic sarcomas, experience in the pediatric population with adjuvant chemotherapy after complete resection of UES has demonstrated improved survival compared with patients who undergo surgical resection alone in this chemosensitive subtype.^{3,20,21} More recently, aggressive multimodal therapy including neoadjuvant therapy and liver transplantation have been supported as a surgical option for patients whose tumors are initially unresectable or recur.⁴

4. Conclusion

The most effective therapy for primary liver sarcomas is surgery; radical resection should be performed if possible given the aggressive nature of these tumors to progress and metastasize. The histologic subtype UES is uncommon in adults and therefore, frequently gets misdiagnosed as benign disease due to its predominantly cystic appearance and mucoid composition on CT imaging. Operations are often technically difficult because of the large size (10–30 cm) of these tumors but offer the best chance of survival in combination with adjuvant chemotherapy. Local recurrences and metastatic disease to lung, pleura and peritoneum are common; metastases to the heart should also be considered in the differential of cardiac lesions detected by echocardiography. Failure to recognize cardiac metastatic disease will ultimately lead to progressive tumor embolization and cardiac failure if left untreated.

Conflict of interest

The authors declare that they have no competing interests.

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None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A

copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Authors' contributions

MD, RB, BV performed surgery; MD, FH, RB, JN, BV participated in preoperative and postoperative management, analysis and interpretation of data; MD, JN, BV conception and design; MD, JC acquisition of data; MD, BV drafting of manuscript; MD, JC, JN, BV critical review of manuscript. All authors have read and approved the final manuscript.

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