Case Report

Hepatic angiosarcoma in an adult who had Wilms tumor treated in childhood: A case report

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Article history:
Received 21 October 2020
Revised 11 November 2020
Accepted 11 November 2020

Keywords:
Hepatic angiosarcoma
Liver failure
CT scan
Wilms tumor
Malignancy

Abstract

Hepatic angiosarcoma is a rare, highly aggressive mesenchymal liver malignancy with poor prognosis that stems from the endothelial cells that line the walls of blood or lymphatic vessels. It is the third most common primary liver malignancy and is most prevalent among older males. It is difficult to diagnose due to various clinical presentations from asymptomatic to abdominal pain, pleural effusion, and liver failure. The diagnosis of liver angiosarcoma is suspected on imaging features and confirmed by histopathological assessment. Primary management is determined based on the stage of tumor from surgery to palliative care such as chemotherapy or tumor transarterial embolization. We report a 51-year-old female who presented with stage 4 liver angiosarcoma and a history of childhood Wilms tumor. We focus on tumor management using radiological modalities and pathological analysis and discuss secondary liver tumors in survivors of childhood Wilms tumor.

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Introduction

Liver angiosarcoma is an extremely rare, aggressive vascular tumor with a high rate of recurrence, metastasis, and poor prognosis with a median survival of less than a year. It represents less than 2% of primary liver malignancies and predominantly appears in male patients older than 60 years of age. Risk factors for angiosarcoma include the use of oral contraceptives, polyvinyl chloride, arsenic, anabolic steroids, and exposure to radiation. However, approximately 75% of liver angiosarcomas are found in patients without any risk factors [1–3]. It is difficult to diagnose since patients are usually asymptomatic in the early stages of the disease and later may show nonspecific symptoms such as abdominal pain, fever, shortness of breath, and hemoptysis secondary to pulmonary metastasis. Since clinical manifestation and laboratory tests are not specific for the detection and diagnosis of hepatic angiosarcoma, the main focus for early diagnosis should be on radiological imaging and histopathology [4,5]. For single, small, and localized tumors, radical resection is the primary management approach but in the case of unresectable tumors, chemotherapy, immunotherapy, and transarterial chemoembolization have shown clinical efficacy and can prolong survival time [6–8].

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https://doi.org/10.1016/j.radcr.2020.11.021
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Case report

A 51-year-old female with a past medical history of Wilms tumor metastatic to the lung as a child at age 4 who was successfully treated with chemoradiation therapy including vincristine, dactinomycin, radiation to the right renal tumor and multiple lung lesions, and right nephrectomy presented with a 2-month history of right upper quadrant pain and dyspnea. A CT scan revealed a right posterior liver mass measuring 5.8 × 4.6 cm and loculated right-sided pleural effusion with enhancement of pleura and internal septations for which a chest tube was placed and 2 L of bloody pleural effusion was removed. Cytology of pleural effusion detected blood, fibrin with rare atypical cells. CT-guided biopsy of the liver mass showed a malignant spindle and epithelioid cell neoplasm. An immunoprofile of the cells was positive for CD31, ERG, and FLI-1 and negative for CK8/18, HepPar1, S100, HMB45, MART1, WT-1, and desmin, which supported the diagnosis of hepatic angiosarcoma. In the next step, pleural decortication was performed to prevent recurrent, symptomatic pleural effusion. Histopathologic analysis of the pleural biopsy showed clusters of malignant cells with positive immunostaining for CD31/34 and Factor VIII and negative for pancytokeratin and calretinin, which was consistent with metastatic angiosarcoma. The patient’s treatment was started with weekly paclitaxel. After 2 months, she came to the clinic for clinical trial assessment (pazopanib plus endothelial receptor antibody TRC 105) but was admitted for further evaluation of fever as well as tachycardia, and found to have leukocytosis, acute anemia, and atrial fibrillation with rapid ventricular response treated with metoprolol. A CT scan illustrated subsegmental acute pulmonary emboli in the posterior left lung base and an enlarging 6.3 cm heterogeneous ill-defined mass in the right hepatic lobe and other smaller low-attenuation lesions throughout the liver in keeping with intrahepatic metastatic angiosarcomas (Figs. 1,2). Heterogeneously attenuating located right pleural effusion and the hepatic subcapsular lesion were consistent with likely hemorrhagic metastatic lesions (Figs. 1,2). No active bleeding was seen. Cinematic rendering (CR) images well demonstrate the heterogeneous nature of the liver masses and hemorrhagic liver subcapsular and pleural metastatic lesions (Fig. 3). CR images also well demonstrate compressed right hemidiaphragm between the right pleural and liver subcapsular lesions (Fig. 3). Based on symptoms and positive sepsis workup, an empiric antibiotic was started. She was discharged with plans for outpatient gemcitabine/paclitaxel chemotherapy but readmitted a week later with low-grade fever, right subcostal pain, abdominal distension, and bilateral leg edema with hyponatremia. The initial goal was to get her to more chemotherapy. However, during the hospitalization, her liver function worsened and she declined. A decision was made with the patient, family, and her primary oncologist to move to hospice care. Regrettably, she passed away a few months later.

Fig. 1 – (a, b). Contrast-enhanced venous phase axial computed tomography images show a 6.3 cm heterogeneous ill-defined hypodense mass (black arrow) located in the posterior inferior right hepatic lobe with extension to the heterogeneous subcapsular fluid collection (black asterisk) and multiple scattered hypoattenuating lesions throughout the liver representing intrahepatic metastases. Some liver cysts are also present. Heterogeneous right pleural effusion (white asterisk) is partially seen in (a). In (b) (inferior to a), the right hepatic lobe is small relative to the left hepatic lobe. The right kidney is surgically absent. An incidental left renal cyst is partially seen. Note hypoplastic right hemiabdomen with thinner subcutaneous fat and abdominal wall musculature secondary to childhood radiation therapy to the right abdomen.

Discussion

Primary hepatic angiosarcoma is characterized as a rare, high-grade malignant tumor originating in endothelial cells that
have a high propensity for local recurrence and metastases. It accounts for 1-2% of primary liver tumors, which occur 3 times more often in men than women in their sixth or seventh decade of life. The prognosis for patients with liver angiosarcoma is extremely grim with mean survival around 6 months due to early distant metastasis to other organs such as the lungs, spleen, and colon [9-11]. There are some environmental risk factors linked to liver angiosarcomas such as the use of an oral contraceptive pill or anabolic steroids, radiation exposure, arsenic, vinyl chloride, and Thorotrast (a suspension of radioactive compound thorium dioxide, that was used as a radiocontrast agent until 1950s) which contribute to the incidence of hepatic angiosarcoma [12,13]. Diagnosis of hepatic angiosarcoma is challenging since patients usually present with nonspecific symptoms including right upper quadrant abdominal pain, weight loss, fever, and fatigue. The physical exam could be useful in the detection of tumors by revealing hepatomegaly, ascites, and hemothorax [14-16].

Imaging modalities are used for the diagnosis, determining the extent of the lesion, and detecting distant metastases. Ultrasonography of hepatic angiosarcoma can present as a solitary or multiple mass(es) with different echogenicity inside tumors due to bleeding or necrosis. CT scan is considered the modality of choice in many studies. Liver lesions appear as hypodense masses and some may be hypervascular. They usually show early arterial enhancement followed by progressive filling in of contrast within the lesion, contrary to washout seen in hepatocellular carcinoma [17]. On MRI, the tumors appear as a heterogeneous area, and hemorrhage is reflected by hyperintense spots or patchy signals on T1 and T2-weighted images. PET/CT scan has a major role in staging the tumor and detection of distant metastasis, appearing FDG-avid on PET-CT [17-19]. Cinematic rendering is a recently described 3-dimensional (3D) imaging technique that generates photorealistic images based on a new lighting model [20]. Chu et al applied CR to focal liver masses, and showed the potential of CR to improve the visualization of enhancement patterns and internal architecture, local tumor extension, and global disease burden [20].

Histopathological examination in the close correlation of radiologic imaging helps to confirm the diagnosis. Immunohistological markers including CD31/34, factor VIII, and vascular endothelial growth factor receptor-3 (VEGFR-3) can be used to support the vascular endothelial origin of malignancy. The treatment of liver angiosarcoma is challenging with poor long-term prognosis since there are usually multiple metastatic lesions at the time of diagnosis. At present, surgical resection is the primary method of treatment for single and local lesions however chemotherapy and/or radiation therapy or transarterial chemoembolization can be an important part of the palliative treatment plan in case of metastases [8,21].

Inoue et al [22] reported one of the latest cases of hepatic angiosarcoma in June 2020. The patient was a man in his 50s admitted with jaundice, abdominal distention, and lower extremity edema. Imaging evaluation showed multiple mass-like lesions with mixed homogeneous and heterogeneous enhancement in the right lobe of the liver. Unfortunately, the patient died on the 20th day of admission due to liver failure complications. The pathology report after

Fig. 2 – (a, b). Contrast-enhanced arterial phase (a) coronal and (b) sagittal reformatted computed tomography images show a heterogeneous ill-defined mass (black asterisk) in the posterior inferior right hepatic lobe extending to the heterogeneous subcapsular fluid collection (black asterisk) and multiple scattered hypoattenuating lesions throughout the liver. Right pleural metastases with multiloculated heterogeneous malignant right pleural effusion (white asterisk) are also seen. Right hemidiaphragm (white arrowheads) is compressed between the right pleural metastases with loculated pleural lesion and subcapsular hepatic lesion.
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Noor et al [23] reported a case of a 71-year-old man who presented with right upper quadrant abdominal pain. Large multifocal liver angiosarcoma was detected in contrast-enhanced CT and MRI scans. The diagnosis was confirmed by liver core biopsy. The pathological analysis demonstrated large, abnormal CD31+ endothelial cells surrounding small groups of hepatocytes. Averbukh et al [24] described a 54-year-old male with weight gain, increased abdominal girth, and lower extremity edema. Two incidental hypoattenuating foci in the liver were found on an abdominal CT scan. The diagnosis of hepatic angiosarcoma was confirmed by immunohistochemical staining showing positive vascular markers and the patient was started on a cycle of gemcitabine. Unfortunately, he passed away 7 months after diagnosis due to cancer complications.

Compared to the available case reports in the literature, our patient was unique in terms of the occurrence of hepatic angiosarcoma with the past medical history of Wilms tumor. Wilms tumor is the most common kidney malignancy in children less than 5 years old. Primary management includes surgery, chemotherapy, and radiation therapy depending on the stage and histology of the tumor. The 5-year survival rate with proper treatment is more than 90% [25]. Incidence of secondary malignant neoplasms such as solid tumors and leukemia are increased in survivors of Wilms tumor compared to the general population, however, the risk is relatively small in comparison with other cancers in children. The risk of developing solid tumors increased with time since diagnosis of Wilms tumor but for leukemia [25–27]. In the British Childhood Cancer Survivor Study, Wong et al [26] analyzed 1441 survivors of Wilms tumors and reported the cumulative risk of developing secondary neoplasm is 3.7% by 30 years after Wilms tumor diagnosis, which increased to 16.4% by 50 years. These tumors which arise 40 to 50 years after radiotherapy are predominantly digestive (41%) and breast (6%) origins. Kovalic et al [27] reported 4 patients of hepatocellular carcinoma (HCC) who were treated for Wilms tumor in childhood. These tumors developed 15 to 20 years after the treatment of Wilms tumor. Repullo et al [28] also reported a 49-year-old man with HCC in the inferior right hepatic lobe as a potential late side effect of radiotherapy in a patient treated for Wilms tumor at the age of 6 weeks.

In our case, a history of radiation exposure for the treatment of Wilms tumor is thought to be the main risk factor for developing liver angiosarcoma. Abdominal CT with contrast as the first step of investigation revealed a large heterogeneous mass in the posterior right hepatic lobe with malignant right pleural effusion, which was compatible with the diagnosis of hepatic angiosarcoma in this case. Liver tumor biopsy confirmed the diagnosis by positive immunohistochemistry for neoplastic cells CD31, ERG, and FL1-1. Therefore, a combination of radiologic images and pathology evaluation played an essential role in identifying the tumor. Generally, the best treatment is decided based on the size of the tumor, metastasis to distant organs such as the lungs and spleen, and its complications. In the current case, surgical intervention was not appropriate due to the spread of the tumor to other organs and complications like liver failure. Although liver angiosarcoma is extremely rare, it should be considered among the differential diagnoses of an aggressive liver tumor particularly with the presence of risk factors since late diagnosis is associated with a grave prognosis.

**Patient consent statement**

No specific consent is available for publication. No personal data is presented in the whole text and/or figure, fulfilling anonymity standards.
Acknowledgment

The authors thank senior science writer Edmund Weisberg, MS, MBE, who helped us to review and edit the article.

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