Liver Tumor: A Case Report and Literature Review

Mary Potkonjak1, John T. Miura1, Abdulrahman Y. Hammad2, Kiyoko Oshima3 and T. Clark Gamblin1

1Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin Milwaukee, WI, USA
2Department of Pathology, Medical College of Wisconsin, Milwaukee, WI, USA
3Corresponding author: T. Clark Gamblin, Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin Milwaukee, WI, USA, Tel: +414-805-5020, Fax: +414-805-5771 E-mail: tcgamblin@mcw.edu

Rec date: Mar 24, 2015; Acc date: May 07, 2015; Pub date: May 12, 2015

Copyright: © 2015 Potkonjak M. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

PEComas are an uncommon group of mesenchymal neoplasms that exhibit perivascular epithelioid cell differentiation. The term PEComa includes a collection of different subcategories, such as lymphangioleiomyomatosis, clear cell tumor of the lung, and angiomyolipoma (AML) which is the topic of discussion in this article. The main problem concerning the diagnosis of hepatic AML is the wide non-specific imaging findings, stressing the need for a tissue diagnosis. Histological examination of a hepatic AML shows different types of tissues such as smooth muscle cells, fat cells (adipocytes), and blood vessels. The ultimate method for diagnosing an AML case is through immunohistochemical examination. AML displays positive immunoreactivity to HMB-45 and Melan-A, and negative to CAM5.2 and AE1/AE3 as well as S100 of the melanoma. The management of hepatic AML has been a matter of debate between different groups, and in this article we discuss a hepatic AML case that presented to our group and was treated with a minimally invasive surgical procedure.

Keywords: Liver tumor; Hepatic angiomyolipoma; Angiomyolipoma; PEComa; Laparoscopic resection

Introduction

In 2002, the World Health Organization described PEComas as neoplasms with perivascular epithelioid cell differentiation [1]. Defined as a family of mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells, the PEComa class is comprised of angiomyolipoma (AML), lymphangioleiomyomatosis (LAM), clear cell “sugar” tumor of the lung (CCTL), and other unusual clear cell tumors subclasses[2]. PEComas of hepatic origin are often misdiagnosed as hepatocellular carcinoma, nodular hyperplasia, or liver hemangioma due to their variable composition and infrequent occurrence [3,4]. The disease was previously thought to be rare; however, a recent publication from China described 178 cases spanning 11-years and raised questions stressing the need for a tissue diagnosis. Histological examination of a hepatic AML shows different types of tissues including foamy macrophages, and no evidence of necrosis (Figure 3). Stains revealed the tumor to be positive for HMB-45, Melan-A, and negative to CAM5.2 and AE1/AE3 as well as S100 of the melanoma. The diagnostic uncertainty of the lesion, lead to a core needle biopsy, which yielded the diagnosis of angiomyolipoma.

Due to concern over the potential for malignant transformation, the patient underwent a laparoscopic right hepatic lobectomy. Gross examination showed a 7.2 × 4.7 × 4.7 cm well-circumscribed mass exhibiting a soft pink to yellow-tan to red cut surface (Figure 2). The remaining liver parenchyma had no additional masses or lesions, but it contained evidence of mild macrovesicular steatosis. Microscopic examination showed the lesion with sheets of epithelioid cells with clear cytoplasm, often indented nuclei with stippled chromatin, and discernible nucleoli. Adjacent to the nuclei were condensed eosinophilic material. There were occasional foci of inflammatory cells including foamy macrophages, and no evidence of necrosis (Figure 3).

Clinical Presentation and Imaging

Hepatic angiomyolipoma is an unusual tumor of the perivascular epithelioid class of tumors. It is more commonly seen in women than men and can cause symptoms such as dull, right upper abdominal pain, discomfort, nausea, and/or fever [5]. However, the majority of patients with hepatic AML remain asymptomatic and are typically incidental findings on abdominal imaging studies [7]. Due to its variable composition and vascularity, hepatic AML can yield varying results across multiple imaging modalities, contributing to the frequency of its misdiagnosis [8]. Frequently, AML with minimal surveillance was recommended, however follow up imaging at 5 months demonstrated no change in the size of the mass (Figure 1). The diagnostic uncertainty of the lesion, lead to a core needle biopsy, which yielded the diagnosis of angiomyolipoma.

Illustrative Case

A 46 year old woman with a BMI of 30 presented with intermittent bouts of abdominal pain. Concerned for appendicitis, the patient underwent a computed tomography (CT) scan, which demonstrated a 7 × 5 cm solid appearing mass in the right hepatic lobe. To further delineate the lesion, a magnetic resonance imaging (MRI) was subsequently obtained, which revealed a lack of intense early phase enhancement, most consistent with focal nodular hyperplasia. Routine imaging demonstrated no change in the size of the mass (Figure 1). The diagnostic uncertainty of the lesion, lead to a core needle biopsy, which yielded the diagnosis of angiomyolipoma.
amounts of fat can often be confused for hepatocellular carcinoma. In the present case, the tumor was initially mistaken for focal nodular hyperplasia.

Figure 1: Magnetic resonance imaging (MRI) demonstrating a (A) hypointense tumor measuring 5.2 cm on T1-weighted images. (B,C) MRI enhanced scans revealing dramatic homogenous enhancement of tumor on early arterial phase followed by contrast wash out on delayed phases.

Figure 2: Gross specimen; Tumor is well circumscribed, measuring 7.2 × 4.7 × 4.7 cm in size.

Figure 3: Tumor is composed of sheets of epithelioid cells with clear cytoplasm (right side). Left side shows normal hepatic parenchyma. Immunohistochemical stain for melanocytic markers (Mart-1/ Melan A) is positive (inset).

In 2013, Yang et al. reviewed the imaging of 178 hepatic AML cases in an attempt to solidify its characteristics on ultrasound, CT, and MRI and decrease the frequency of misdiagnosis. They found several unifying characteristics—hyperechoic foci on ultrasound, low-density lesions on a plain CT, low intensity lesions on T1 scans and high intensity lesions on T2 scans [5]. Other studies examining the ultrasound features of the disease reported that the lesion appears hyperechoic in 56-80% of the cases [7,9,10]. Doppler ultrasound demonstrates arterial signal in 75% of the cases with filiform or punctiform vascular distribution pattern [9-11]. Further evaluations of AML cases utilizing SonoVue contrast enhanced ultrasound showed enhancement on the arterial phase (100%). On portal and late phases of the ultrasound, enhancement defects was seen in 28.1% of the cases, while the rest (71.9%) were iso- to hyperechoic in the portal phase [12]. AML cases appear hypodense on precontrast CT, while enhancement is seen in arterial phase of contrast enhanced CT in the majority of cases. Few cases continue showing enhancement in the portal venous phase [7-9,10]. The presence of central fat inside the AML appears as non-enhancement following contrast injection on CT, and in one of the articles examining CT findings of AML cases, Low et al. reported that this feature might aid in differentiating AML cases from hepatocellular carcinoma ones [8,9]. MRI examination is able to increase the diagnostic accuracy pre-operatively for AML, showing hypointensity in most cases on T1-weighted images and hyperintensity on T2-weighted image, according to the amount of adipose tissue within the lesion [6,9,13]. Furthermore, MRI are more sensitive than CT in showing the fat component of the lesion as compared to CT [6]. Unfortunately hepatic AML may exhibit a wide range of radiographic characteristics, as previously discussed. Similarly, the current study’s patient possessed only a few of the classic characteristics. Besides, these findings are not specific to hepatic AML, thus reaching a diagnosis from imaging alone is actually difficulty. A previous study examining a cohort of 79 AML cases were able to reach the diagnosis in 52% of the patients utilizing a combination of ultrasound, CT, MRI and/or angiography [14]. Currently, pathological and immunohistochemical analysis, either from a core-needle biopsy or the surgical specimen, are necessary to confidently distinguish hepatic AML from other, more aggressive tumors.

Histopathology

Hepatic angiomyolipomas are comprised of three different cell types—smooth muscle cells (SMC), adipocytes, and blood vessels—that may be further sub classified based on the differing ratios of each component giving rise to mixed, angiomatous, lipomatous and myomatous types [15-17]. Other features that can be observed include infiltration of lymphocytes, foamy macrophages, extramedullary hematopoiesis, and both thick and thin walled blood vessels [18-20].

In our case, sheets of epithelioid cells with a clear cytoplasm were demonstrated in the lesion on microscopic examination. The nuclei were often indented nuclei and contained stippled chromatin, and visible nucleoli. Condensed osinophilic material was found adjacent to the nuclei. There were occasional foci of inflammatory cells including foamy macrophages, and no evidence of necrosis.

Immunohistochemistry

Immunohistochemical (IHC) analysis is the key for definitive AML diagnosis. AML characteristically stains positive for Melan-A and HMB-45, and negative for CAM5.2 and AE1/AE3. A positive stain for HMB-45 is diagnostic for primary hepatic AML as no other primary
hepatic tumors demonstrate this finding. The tissue is also negative for SI100, differentiating it from other mature adipocytes, and distinguishing it from metastatic melanoma. The angiomatous components will characteristically stain positive for CD34 and factor VIII [21,22]. Our case demonstrated the characteristically positiveHMB-45Melan-A, and SMA needed for diagnosis, while testing for glypican-3, HEPPAR-1, AE1 AE3, DOG-1, SI100, and CD117 was found to be negative. Based on this immunohistochemical profile, the diagnosis of angiomyolipoma was confirmed.

Treatment

Hepatic AML is thought to be a benign tumor; however, in recent years there have been an increasing number of reports of invasive, malignant, and/or recurrent disease that has led to controversy regarding the optimal course of treatment [23-25]. Attempts have been made to delineate factors that might prompt surveillance over resection. Factors proposed include asymptomatic presentation, tumor size smaller than 5 cm, lack of tumor growth over time, confirmed AML via a core needle biopsy, and/or reliable patient compliance for scans [6,26]. In contrast, factors indicating possible malignant disease include the presence of coagulative necrosis, a tumor size >10 cm, evidence of metastasis, and lack of CD117 receptor expression. Additional features including cytologic atypia, invasive growth pattern also indicate a malignant disease [27]. Despite these proposals, the majority of tumors are removed due to concern of malignancy or inconclusive diagnostic results [20]. Most patients with hepatic AML in the literature undergo open surgical resection [14,20]. To our knowledge there are only three cases of laparoscopic resection of hepatic AML in the literature [28-30]. In our case, we opted to pursue a laparoscopic resection due to its potential benefits, such as smaller incision, shorter recovery time and hospital stay. The patient stayed in the hospital 4 days post-operatively.

Non-surgical treatment options in the literature are generally limited to surveillance. There is one report of neoadjuvant sirolimus administered to a woman with a large hepatic AML with malignant characteristics, which achieved favorable tumor reduction allowing surgical resection [31]. This decision was made based on reports of PEComas arising from other anatomical locations showing susceptibility to mTOR inhibitors [32,33]. Despite this, surgical resection with negative margins remains the favored and only curative treatment [4,31].

Conclusion

Hepatic angiomyolipomas are uncommon tumors with few recommendations regarding the best treatment option. Despite attempts to establish radiographic imaging characteristics, it remains frequently misdiagnosed. Different treatment modalities attempting to delineate the best treatment are still ongoing. This case adds to the growing number of cases depicting hepatic AML treated with a minimally invasive surgical approach.

References


