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Laparoscopic Resection of Hepatic Angiomyolipoma – An Uncommon Primary Liver Tumor: A Case Report and Literature Review

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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 lymphangioleimyomatosis, 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, focal nodular hyperplasia, or liver hemangioma due to their variable composition and infrequent occurence [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 regarding geographic incidence and prevalence of this unusual tumor As a result, the paucity of literature surrounding PEComas has generated debate regarding the best course of treatment [4-6]. This project sought to share a representative case of an AML that was managed by a laparoscopic resection, and provide a review of the current literature contributing to our knowledge.

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 central 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 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.

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 mildmacrovesicular 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). Stains revealed the tumor to be positive for HMB-45, Melan-A, and SMA and negative for glypican-3, HEPPAR-1, AE1 AE3, DOG-1, S100, and CD117. Based on this immunohistochemical profile, the diagnosis of angiomyolipoma was confirmed. Six months following resection, routine cross sectional imaging demonstrated no evidence of tumor recurrence.

Clinical Presentation and Imaging

Hepatic angiomyolipoma is anunusual 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

amounts of fat can often be confused for hepatocellular carcinoma. In the present case, the tumor was initially mistaken for focal nodular hyperplasia.

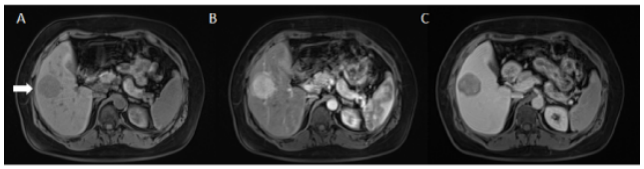

Figure 1: Magnetic resonance imaging (MRI) demonstrating a **(A)** hypointense tumor measuring 5.2 cm on T1-weighted images. **(B,C)** MRI enhanced scans revealing dramatic homogenous enhancement of tumor on early arterial phase followed by contrast wash out on delayed phases.

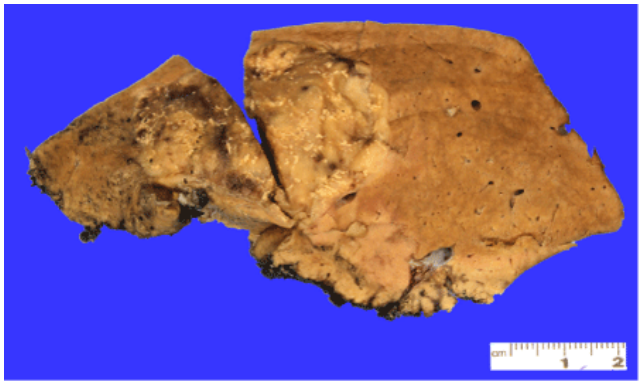

Figure 2: Gross specimen; Tumor is well circumscribed, measuring 7.2 × 4.7 × 4.7 cm in size.

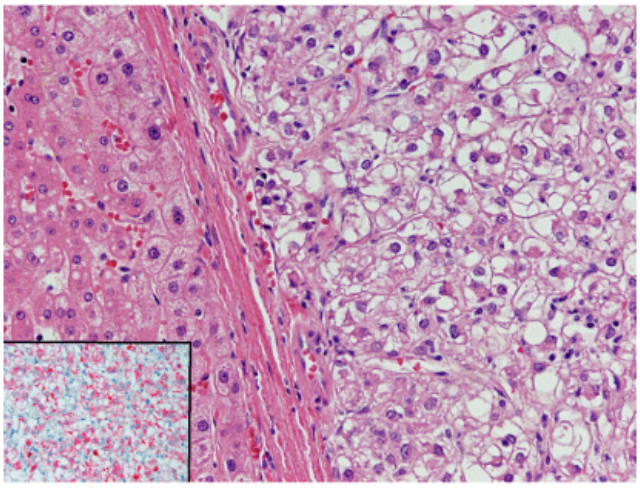

Figure 3: Tumor is composed of sheets of epithelioid cells with clear cytoplasm (right side). Left side shows normal hepatic parenchyma. Immunohistochemical stain for melanocytic markers (Mart-1/ Melan A) is positive (inset).

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 puncitiform 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 examinationis able to increase the diagnostic accuracy pre-operatively for AML, showing hypointensityin 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 eosinophilic 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 S100, 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-45 Melan-A, and SMA needed for diagnosis, while testing for glypican-3, HEPPAR-1, AE1 AE3, DOG-1, S100, 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 patientcompliance 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

1. Folpe A. (2002) Neoplasms with perivascular epithelioid cell differentiation (PEComas). World Health Organization Classification of Tumors: Pathology and Genetics of Tumors of Soft Tissue and Bone 221-222.
2. Yu D, Tang S (2013) Hepatic perivascular epithelioid cell tumor: a case report and review of the literature. Intern Med 52: 1333-1336.
3. Zhao LJ, Yang YJ, Wu H, Huang SM, Liu K (2013) Perivascular epithelioid cell tumor of the liver: a case report and literature review. Eur Rev Med Pharmacol Sci 17: 1665-1668.
4. Liu D, Shi D, Xu Y, Cao L1 (2014) Management of perivascular epithelioid cell tumor of the liver: A case report and review of the literature. Oncol Lett 7: 148-152.
5. Yang X, Li A, Wu M (2013) Hepatic angiomyolipoma: clinical, imaging and pathological features in 178 cases. Med Oncol 30: 416.
6. Hu WG, Lai EC, Liu H, Li AJ, Zhou WP, et al. (2011) Diagnostic difficulties and treatment strategy of hepatic angiomyolipoma. Asian J Surg 34: 158-162.
7. Zhou YM, Li B, Xu F, Wang B, Li DQ, et al. (2008) Clinical features of hepatic angiomyolipoma. Hepatobiliary Pancreat Dis Int 7: 284-287.
8. Low SC, Peh WC, Muttarak M, Cheung HS, Ng IO (2008) Imaging features of hepatic angiomyolipomas. J Med Imaging Radiat Oncol 52: 118-123.
9. Li T, Wang L, Yu HH, Sun HC, Qin LX, et al. (2008) Hepatic angiomyolipoma: a retrospective study of 25 cases. Surg Today 38: 529-535.
10. Ren N, Qin LX, Tang ZY, Wu ZQ, Fan J (2003) Diagnosis and treatment of hepatic angiomyolipoma in 26 cases. World J Gastroenterol 9: 1856-1858.
11. Wang Z, Xu HX, Xie XY, Xie XH, Kuang M, et al. (2010) Imaging features of hepatic angiomyolipomas on real-time contrast-enhanced ultrasound. Br J Radiol 83: 411-418.
12. Wei RX, Wang WP, Ding H, Huang BJ, Li CL, et al. (2012) Hepatic angiomyolipoma: contrast patterns with SonoVue-enhanced real-time gray-scale ultrasonography. Asian Pac J Cancer Prev 13: 493-497.
13. Krebs S, Esposito I, Lersch C, et al. (2011) Preoperative radiological characterization of hepatic angiomyolipoma using magnetic resonance imaging and contrast-enhanced ultrasonography: a case report. J Med Case Rep 5:481.
14. Ding GH, Liu Y, Wu MC, Yang GS, Yang JM, et al. (2011) Diagnosis and treatment of hepatic angiomyolipoma. J Surg Oncol 103: 807-812.
15. Nonomura A, Mizukami Y, Kadoya M (1994) Angiomyolipoma of the liver: a collective review. J Gastroenterol 29: 95-105.
16. Chang Z, Zhang JM, Ying JQ, Ge YP (2011) Characteristics and treatment strategy of hepatic angiomyolipoma: a series of 94 patients collected from four institutions. J Gastrointestin Liver Dis 20: 65-69.
17. Nonomura A, Enomoto Y, Takeda M, et al. (2012) Angiomyolipoma of the liver: a reappraisal of morphological features and delineation of new characteristic histological features from the clinicopathological findings of 55 tumours in 47 patients. Histopathology 61:863-880.
18. Agaimy A, Vassos N, Croner RS, et al. (2012) Hepatic angiomyolipoma: a series of six cases with emphasis on pathological-radiological correlations and unusual variants diagnosed by core needle biopsy. Int J Clin Exp Patho 5:512-521.
19. Liu Y, Wang J, Lin XY, Xu HT, Qiu XS, et al. (2012) Inflammatory angiomyolipoma of the liver: a rare hepatic tumor. Diagn Pathol 7: 122.
20. Du S, Li Y, Mao Y, Sang X, Lu X, et al. (2012) Diagnosis and treatment of hepatic angiomyolipoma. Hepatobiliary Surg Nutr 1: 19-24.
21. Petrolla AA, Xin W (2008) Hepatic angiomyolipoma. Arch Pathol Lab Med 132: 1679-1682.
22. Tsui WM, Colombari R, Portmann BC, Bonetti F, Thung SN, et al. (1999) Hepatic angiomyolipoma: a clinicopathologic study of 30 cases and delineation of unusual morphologic variants. Am J Surg Pathol 23: 34-48.
23. Selvaggi F, Risio D, Claudi R, Cianci R, Angelucci D, et al. (2011) Malignant PEComa: a case report with emphasis on clinical and morphological criteria. BMC Surg 11: 3.
24. Grant C, Lacy JM, Strup SE (2013) A 22-year-old female with invasive epithelioid angiomyolipoma and tumor thrombus into the inferior vena cava: case report and literature review. Case Rep Urol 2013: 730369.
25. Yang L, Xu Z, Dong R, Fan J, Du Y, et al. (2013) Is surgery necessary for patients with hepatic angiomyolipoma? Retrospective analysis from eight Chinese cases. J Gastroenterol Hepatol 28: 1648-1653.

26. Yang CY, Ho MC, Jeng YM, Hu RH, Wu YM, et al. (2007) Management of hepatic angiomyolipoma. J Gastrointest Surg 11: 452-457.
27. Nguyen TT, Gorman B, Shields D, Goodman Z (2008) Malignant hepatic angiomyolipoma: report of a case and review of literature. Am J Surg Pathol 32: 793-798.
28. Mima K, Beppu T, Chikamoto A, Ishiko T, Horino K, et al. (2011) Laparoscopy-assisted resection of an undiagnosed liver tumor and ascending colon cancer via mini median laparotomy: report of a case. Surg Today 41: 1633-1638.
29. Saito Y, Shimada M, Utsunomiya T, et al. (2013) Hepatic epithelioid angiomyolipoma with arterioportal venous shunting mimicking hepatocellular carcinoma: report of a case. J Med Invest 60:262-266.
30. Ramia JM, De la Plaza R, Quiñones J, Sanchez-Tembleque MD, Caminoa A, et al. (2011) Three trocars laparoscopic resection of angiomyolipoma of the liver. Int J Hepatol 2011: 150691.
31. Bergamo F, Maruzzo M, Basso U, Montesco MC, Zagonel V, et al. (2014) Neoadjuvant sirolimus for a large hepatic perivascular epithelioid cell tumor (PEComa). World J Surg Oncol 12: 46.
32. Hofbauer GF, Marcollo-Pini A, Corsenca A, Kistler AD, French LE, et al. (2008) The mTOR inhibitor rapamycin significantly improves facial angiofibroma lesions in a patient with tuberous sclerosis. Br J Dermatol 159: 473-475.
33. Italiano A, Delcambre C, Hostein I, Cazeau AL, Marty M, et al. (2010) Treatment with the mTOR inhibitor temsirolimus in patients with malignant PEComa. Ann Oncol 21: 1135-1137.