Received: 29 August 2021 | Revised: 28 November 2021 | Accepted: 14 January 2022

DOI: 10.1002/ccr3.5327

CASE REPORT

Clinical Case Reports Open Access WILEY

Puzzling hepatic tumor: Epithelioid angiomyolipoma

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Funding information
The authors did not receive any financial support for the publication of this article

Abstract

Hepatic epithelioid angiomyolipomas are uncommon mesenchymal neoplasms. They are difficult to diagnose by imaging, especially when the fatty component is scant or absent. The gold standard for the diagnosis is histologic examination coupled with an immunohistochemical study. Positive HMB45 immunostaining of the myoid cells is a major diagnostic feature.

KEYWORDS

epithelioid angiomyolipoma, immunohistochemistry, liver, pathology, tumor

1 | INTRODUCTION

Hepatic angiomyolipomas are rare mesenchymal neoplasms, which can potentially exhibit an aggressive clinical behavior. They are composed of an admixture of smooth muscle cells, adipose tissue, and blood vessels.[1] Epithelioid angiomyolipoma is a rare variant of angiomyolipoma where the epithelioid smooth muscle cells predominate.[2] Due to their varying composition, particularly their frequent paucity of fat, diagnosis can be challenging both radiologically and histologically resulting in misdiagnosis prior to excision.[3]

Herein, the authors report a case of hepatic epithelioid angiomyolipoma with a minor adipocytic component mimicking a hepatocellular carcinoma.

2 | CLINICAL HISTORY

A 37-year-old previously healthy woman, presented with a 5-month history of weight loss anorexia, abdominal distention, and discomfort. The patient had no prior history of hepato-biliary disease or tuberous sclerosis. Physical examination disclosed hepatomegaly with a liver span

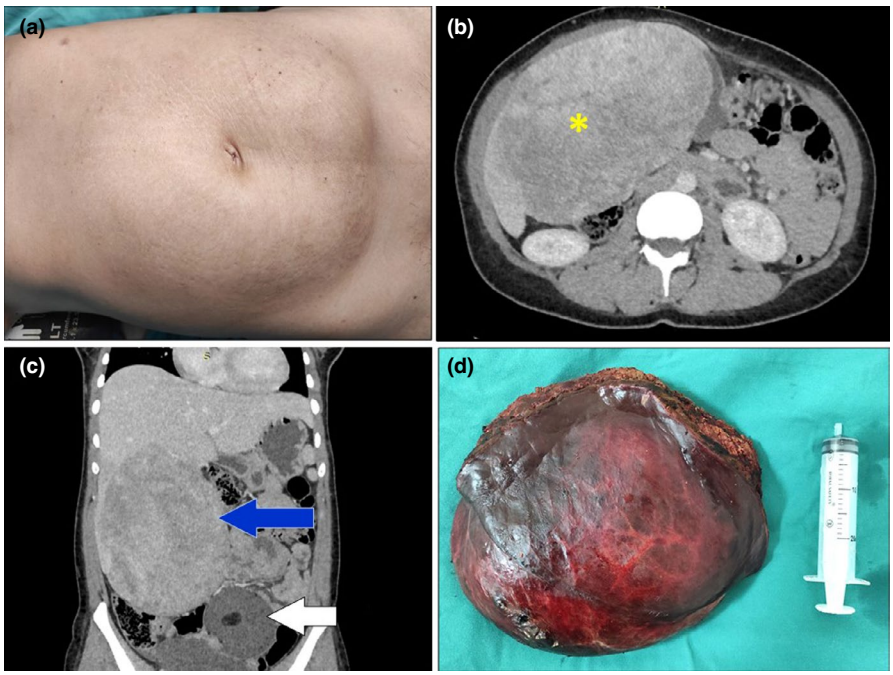

FIGURE 1 (A) Physical examination disclosed hepatomegaly with an increased liver span =20 cm. (B) Axial Contrast-enhanced computed tomography scan demonstrated a hepatic mass (yellow asterisk) located in segments IV, V, and VI, with exophytic development, moderate, and heterogeneous arterial enhancement, continuing in the portal and late stages, without detectable washout or late capsular enhancement. (C) Coronal computed tomography scan demonstrating a hepatic mass (blue arrow) located in segments IV, V, and VI and a left ovarian mass suggestive of teratoma (white arrow). (D) Per-operative gross findings of the hepatic mass

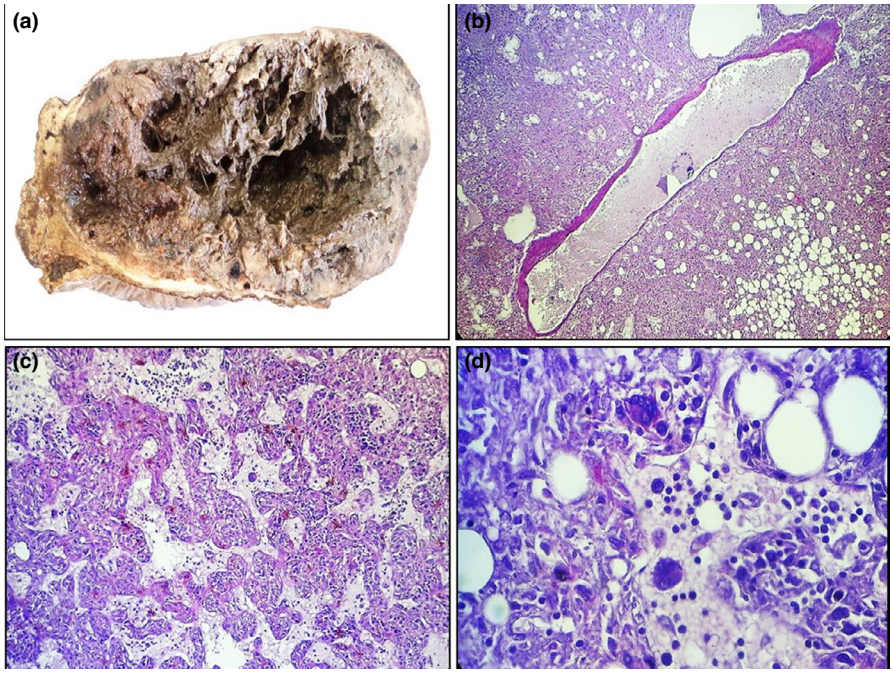

FIGURE 2 (A) On gross examination (after formalin fixation), the cut surface of the liver showed a well-demarcated cystic mass measuring 16 cm in diameter with a hemorrhagic appearance and gray white firm areas in the periphery. (B) Histological findings of the hepatic tumor showing an admixture of sheets of epithelioid myoid cells, thick-walled abnormal blood vessels, and islands of mature adipocytes. The blood vessels are surrounded by mantles of epithelioid myoid cells (Hematoxylin and eosin staining, ×40). (C) Tumor cells were arranged in a trabecular pattern (Hematoxylin and eosin, magnification ×200). (D) Some tumor cells exhibited clear or granular cytoplasm and were in relation with adipocytes. Note the extramedullary hematopoiesis (Hematoxylin and eosin, magnification ×400)

equal to 20 cm (Figure 1A). On palpation of the abdomen, there was a renitent firm mass in the upper right quadrant mobile with respect to the superficial planes and fixed with respect to the deep planes. Tumor markers, including alpha-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19–9, were all within normal limits. Aspartate aminotransferase, alanine aminotransferase, and total bilirubin were within the normal range. Viral serologies for hepatitis B and C were negative. Contrast-enhanced computed tomography scan demonstrated a

hepatic mass located in segments IV, V, and VI, with exophytic development, moderate, and heterogeneous arterial enhancement, continuing in the portal and late stages, without detectable washout or late capsular enhancement (Figure 1B,C). This mass measured 170 × 110 mm in the axial plane and 200 mm in height. It had a close vascular contact with the right hepatic artery, the cystic artery, and the right portal branch as well as its segmental portal branches of IV and VI, which remained permeable, without real invasion. Computed tomography scan also disclosed a left ovarian mass measuring 90 × 60 × 90 mm suggestive of teratoma (Figure 1C). On abdominal magnetic resonance imaging (MRI), low intensity was observed on a T1-weighted image and high intensity on a T2-weighted image. The patient underwent fine-needle biopsy of the hepatic mass and histopathological examination was suggestive of hepatocellular carcinoma because of the epithelioid morphology of the tumor cells which were arranged in a trabecular pattern. There were neither adipocytes nor vessels on the biopsy specimen. Foci of extramedullary hematopoiesis were conspicuous. The immunohistochemical study showed negative staining of tumor cells for cytokeratin 7 and 20. Because of the small size of the biopsy, we could not perform other antibodies. Right hepatectomy was performed with informed consent of the patient. Intraoperatively, a relatively soft dark red giant tumor was found to occupy the whole right lobe of the liver (Figure 1D). There was no infiltration of the right hepatic artery and the right portal vein. The surgical specimen weighed 1050 grams and was measured after formalin fixation 17 × 15.5 × 6.5 cm. Cut section showed a well-circumscribed cystic mass measuring 16 cm in diameter with a hemorrhagic appearance and focal gray white firm areas in the periphery (Figure 2A). Histologically, the mass was composed of an admixture of smooth muscle cells, adipose tissue, and blood vessels (Figure 2B). Sheets of mature adipocytes were seen in some of the sections focally. The tumor proliferation consisted of 100% of epithelioid cells arranged in a trabecular pattern (Figure 2C) or in sheets. Extensive extramedullary hematopoiesis was noted in several sections with hematopoietic elements, including megakaryocytes as well as erythroid and myeloid precursors (Figure 2D). The vascular component was abundant and was composed of thick- (Figure 2B) and thin-walled vessels with a striking peliotic pattern in some areas (Figure 3A). The epithelioid cells showed round nuclei, and abundant eosinophilic or clear cytoplasm (Figure 3B). Brown melanin granules were focally found within the tumor (Figure 3C). The non-neoplastic liver showed mild nonspecific mononuclear infiltration in the portal tracts. There were no histological signs suggestive of chronic liver disease. The immunohistochemical study showed that HMB45 (Figure 3D), MelanA, Smooth Muscle Actin, and Desmin showed diffuse strong positive staining. However, the tumor cells were negative for anti-hepatocyte and CD34. The postoperative course was uneventful, and the patient was discharged on postoperative day 10. The patient was referred to the gynecology department for resection of the left ovarian mass. Histopathological examination of the resection specimen established the diagnosis of a benign mature ovarian teratoma. Currently, the patient is systematically monitored on an outpatient basis with a follow-up period of 2 months.

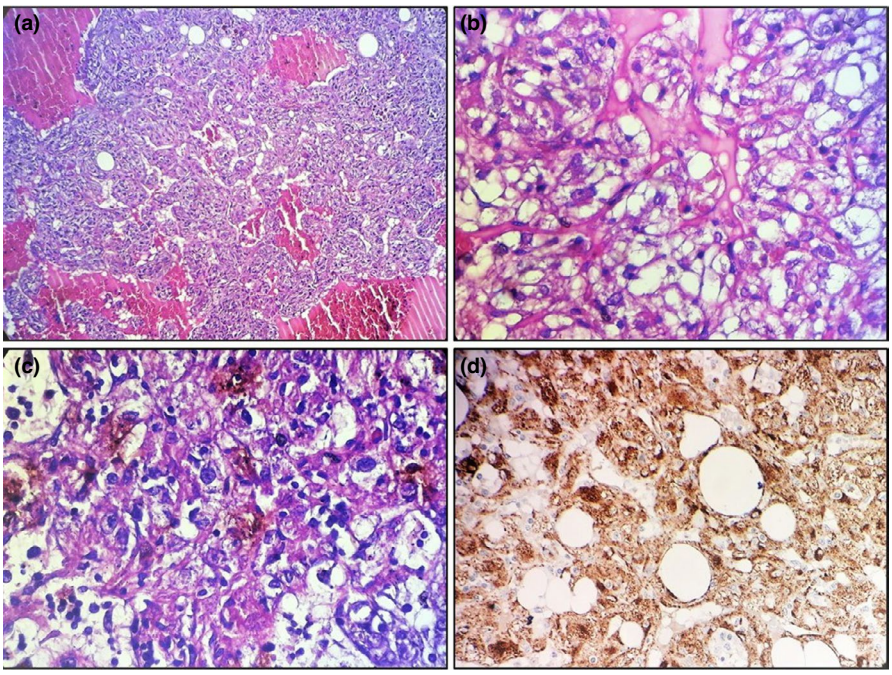

FIGURE 3 (A) Striking peliotic pattern was focally noted (Hematoxylin and eosin, magnification ×40). (B) Epithelioid myoid cells had bland vesicular nuclei and a clear cytoplasm (Hematoxylin and eosin, magnification ×400). (C) Epithelioid myoid cells had bland vesicular nuclei and eosinophilic cytoplasm. Note the melanin pigment (Hematoxylin and eosin, magnification ×400). (D) Immunohistochemical study showing positive immunostaining of the tumor cells with the HMB45 antibody, (Immunohistochemistry, magnification ×400)

3 | DISCUSSION

Epithelioid hepatic angiomyolipoma is classified as a perivascular epithelioid cell tumor with a malignant potential.[4] It occurs most commonly in the kidneys and rarely involves the liver. More than 200 cases of hepatic angiomyolipomas have been reported in the English language literature so far. The age at diagnosis ranges from 10 to 80 years.[5] Our patient was 37 years old. In contrast to renal angiomyolipomas, which are associated with tuberous sclerosis in up to 20% of patients, hepatic angiomyolipomas are associated with tuberous sclerosis in only 6% of patients, with a female predominance.[6,7] Our patient had no past medical history of tuberous sclerosis. Most patients with hepatic angiomyolipomas are asymptomatic, and their tumors are found incidentally during routine health check-ups.[1,5,6] Our patient presented with a 5-month history of weight loss, anorexia, abdominal distention, and discomfort. There are no helpful laboratory tests for this disease. The liver function is normal, tumor and hepatitis markers are negative as it was the case in our patient. The imaging features of hepatic angiomyolipomas depend on the internal composition of the tumor and specifically on the variable amounts of intralesional fat (from <10% to more than 90%), smooth muscle, and proliferating vessels present. MRI is the most specific imaging technique to detect both macroscopic and microscopic fat.[8] Angiomyolipomas with abundant fat are hypoattenuating on noncontrast CT with absent or minimal enhancement after contrast injection, whereas they are hyperintense on T1- and T2-weighted MRI sequences.[8,9] These lesions, which are hypervascular and with a large amount of fat, have a characteristic appearance and may be somewhat easier to distinguish from other tumors. In contrast, fat-poor lesions are more difficult to differentiate from hepatocellular carcinoma. They are hypointense on T1-weighted, precontrast MRI sequences and tend to enhance after contrast injection.[8-10] The lack of a capsule, bulky fat, and prominent intratumoral vessels seem to be the most helpful findings for distinguishing angiomyolipoma from hepatocellular carcinoma, especially in the noncirrhotic liver.[10,11] There is limited literature on nuclear medicine imaging of hepatic angiomyolipoma; however, there are case reports of hepatic angiomyolipomas demonstrating uptake on ^{11}C-acetate positron-emission tomography (PET)-CT, similar to renal angiomyolipomas and 2-[18F]-fluoro-2-deoxy-D-glucose (FDG) PET-CT.[12,13]

Macroscopically, hepatic angiomyolipomas with significant fat content tend to be soft and yellow, whereas tumors with predominantly smooth muscle content tend to be firm, with a tan-white cut surface. Necrosis and hemorrhage may occur. Cystic appearance with hemorrhagic areas is rare, which added to the diagnostic difficulty in our case.[1,14] Histologically, hepatic angiomyolipomas contain a variable amount of fat, vessels, and smooth muscle cells.[1,6,7,14] Four types of smooth muscle cell can be found histologically within angiomyolipomas including spindle, intermediate, epithelioid, and pleomorphic cells.[6] The percentage of epithelioid cells that is required to make a diagnosis of epithelioid angiomyolipoma was not defined in the published studies. A study by Aydin et al. proposed that using 10% of epithelioid component as the cutoff value was preferred.[14] In our patient, 100% of the tumor cells were epithelioid. Hepatic angiomyolipoma often contains hematopoietic elements, including megakaryocytes as well as erythroid and myeloid precursors. In our case, there were extensive foci of extramedullary hematopoiesis. The pathognomonic feature of angiomyolipoma is the positivity of smooth muscle cells for HMB45 along with the positivity for muscle markers.[15,16] In our patient, HMB45, MelanA, Smooth Muscle Actin, and Desmin showed diffuse strong positive staining. The main differential diagnosis of epithelioid angiomyolipoma is hepatocellular carcinoma or hepatocellular adenoma.[1,17] Hepatic epithelioid angiomyolipomas, especially those with atypical epithelioid cells, have an invasive growth potential with a tendency for local recurrence and distant metastasis.[18] Given the poorly understood potential for malignancy and complications, the optimum management of hepatic angiomyolipoma is controversial, with some authors advocating surgical resection for all suspected hepatic angiomyolipomas whereas others suggest guidelines for when imaging follow-up alone may be appropriate.[19,20]

In conclusion, hepatic epithelioid angiomyolipomas can lead to considerable diagnostic problems clinically, radiologically, and pathologically because of their diverse morphology. Diagnostic confusion arises when the fat cell component is inconspicuous and the smooth muscle component assumes an unusual morphologic phenotype. The diagnostic difficulty escalates in a fine-needle aspiration setting as it was the case in our patient since the biopsy specimen is not representative of the entire tumor. Histopathological diagnosis is relatively easy on the surgical specimen with adequate sampling of the lesion. The striking feature in our case was the unusual macroscopic appearance of the tumor mimicking a vascular neoplasm. It was also characterized by the prominence of extramedullary hematopoiesis. The possibility of angiomyolipoma should be considered whenever unfamiliar hepatic tumors are encountered. The existence of extramedullary hematopoiesis on biopsy specimens should raise the suspicion of angiomyolipoma.

ACKNOWLEDGEMENTS

The corresponding author would like to offer her special thanks to her friend Mrs Saïda Jerbi who prepared the microscopic slides.

CONFLICTS OF INTERESTS

None declared.

AUTHOR CONTRIBUTION

Dr Faten LIMAIEM, Dr Nadia BOUJELBENE, and Pr Saadia BOURAOUI prepared, organized, wrote, and edited all aspects of the manuscript. They performed the gross and microscopic, pathologic evaluation of the pathology specimen. They prepared all of the histology figures in the manuscript. They read, edited, and approved the final version of the manuscript.

Dr Seifeddine BACCOUCH, Dr Aziz ATALLAH, Dr Mohamed HAJRI, Dr Sofiène GABSI, and Leila BEN FARHAT participated in:

1. The conception and design of the study,
2. The acquisition of data, analysis and interpretation of the data,
3. The drafting of the article and revising it critically for important intellectual content,
4. Final approval of the manuscript before its submission

ETHICAL APPROVAL

All procedures performed were in accordance with the ethical standards. The examination was made in accordance with the approved principles.

CONSENT

Published with written consent of the patient.

DATA AVAILABILITY STATEMENT

In accordance with the DFG Guidelines on the Handling of Research Data, we will make all data available upon request.

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How to cite this article: Limaiem F, Baccouch S, Boujelbene N, et al. Puzzling hepatic tumor: Epithelioid angiomyolipoma. *Clin Case Rep*. 2022;10:e05327. doi:10.1002/ccr3.5327