CASE REPORT

Hepatic angiomyolipoma masquerading as hepatocellular carcinoma

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SUMMARY

We reported a relatively unusual case of hepatic angiomyolipoma (HAML), which originated from a progenitor mesenchymal cell with pluripotent potential. It commonly affects middle-aged women and imitates various liver tumours radiologically. This case report aims to emphasise the value of histopathology and immunohistochemistry in diagnosing HAML and for further prognostication. Herein, we describe a case of HAML in a 54-year-old woman with its radiological manifestations, immunochemistry findings and management.

INTRODUCTION

Hepatic angiomyolipoma (HAML) is an unusual triphasic mesenchymal tumour that consists of dysmorphic blood vessels, smooth muscle, adipose tissue and occasional foci of extramedullary haemopoiesis. It belongs to part of perivascular epithelioid cell tumours. The most common extrarenal site is the liver. Renal angiomyolipoma (AML) is associated with tuberous sclerosis in 20% of cases; on the contrary, only 6% of cases of HAML are related to tuberous sclerosis.[1] Multiple HAMLs are usually seen in tuberous sclerosis, especially in cases with bilateral diffuse renal AML.[2]

CASE REPORT

A 54-year-old Malay woman with underlying multiple uterine fibroids, bronchial asthma, acute gastritis and hypertension, presented with deranged liver function test in March 2020, which was associated with weight loss of approximately 10 kg in 2 months. Per abdominal examination was unremarkable. Biochemical investigations showed normal serum albumin and alkaline phosphatase. Alanine transaminase and aspartate transaminase were slightly above the upper normal limit. Her hepatitis B surface antigen and hepatitis C virus antibody were non-reactive. Tumour markers levels such as alpha-fetoprotein (AFP) and cancer antigen 19-9 were within the normal range. Abdominal computed tomography (CT) demonstrated a segment V/VIII mixed density mass, measuring 4.6 cm × 3.4 cm × 4.5 cm (AP × W × CC). This lesion appeared to be of mixed soft tissue-fat density on the plain, heterogenous progressive enhancement on the arterial and porto-venous and hypodense on the delayed phase, which was initially suspicions of hepatocellular carcinoma (Figure 1). Magnetic resonance imaging (MRI) of the liver revealed a heterogeneously hyperintense mass on T2WI and hypointense mass on T1 fat-saturated image. There is identifiable fat within the tumour evidenced by the significant signal drop in the opposed phase, rim enhancement in the early arterial phase, progressive enhancement from the late arterial till equilibrium phase and hypointense in the 10-minute and 20-minute images (Figure 2). The intra-operative findings demonstrated a generalised fatty liver with a palpable tumour at the anterior surface of segment VII which extended to segment VIII. There were no peritoneal nodules or ascites. The patient underwent non-anatomical liver resection of segments VII and VIII. The diagnosis of hepatic AML was confirmed by histopathology examination (Figure 3).

DISCUSSION

The primary hepatic tumour may emanate from different elements, including hepatocytes, bile ducts, mesenchymal cells, epithelial and neuroendocrine cells. The mesenchymal cell is a progenitor and pluripotent cell, which shows multilineage differentiation. Therefore, a mesenchymal tumour comprises mixed components of vascular, adipose tissue, fibrous and smooth muscle. Owing to the varying difference in proportions of these three histological components in each HAML, this poses a diagnostic challenge in radiology. HAML is rarely diagnosed pre-operatively and is commonly misdiagnosed as hepatocellular carcinoma (HCC), adenoma or focal nodular hyperplasia. Here, we discuss the clinical, radiological, histopathological, and immunohistochemical examinations; although it is not fully pathognomy, they can be used as guidance in diagnosing HAML.

HCC can be distinguished from HAML by several clinical features. HAML predominantly occurs in middle-aged women (83.3%) without underlying liver disease, whereas HCCs are commonly found in men (75%) with either chronic Hepatitis B, Hepatitis C, or alcoholic liver disease.[3] Only 68.8% of HCC demonstrated elevated AFP and none of HAML showed abnormal AFP, which makes HCC another possible differential diagnosis in this AFP normal patient. Patients with either HAML or HCC usually present with non-specific symptoms such as abdominal distension, abdominal pain, and weakness. Some are asymptomatic and diagnosed incidentally during clinical screening.[4]

Differentiating HAML from HCC is notoriously difficult by imaging. However, there are several radiological

This article was accepted: 28 June 2023
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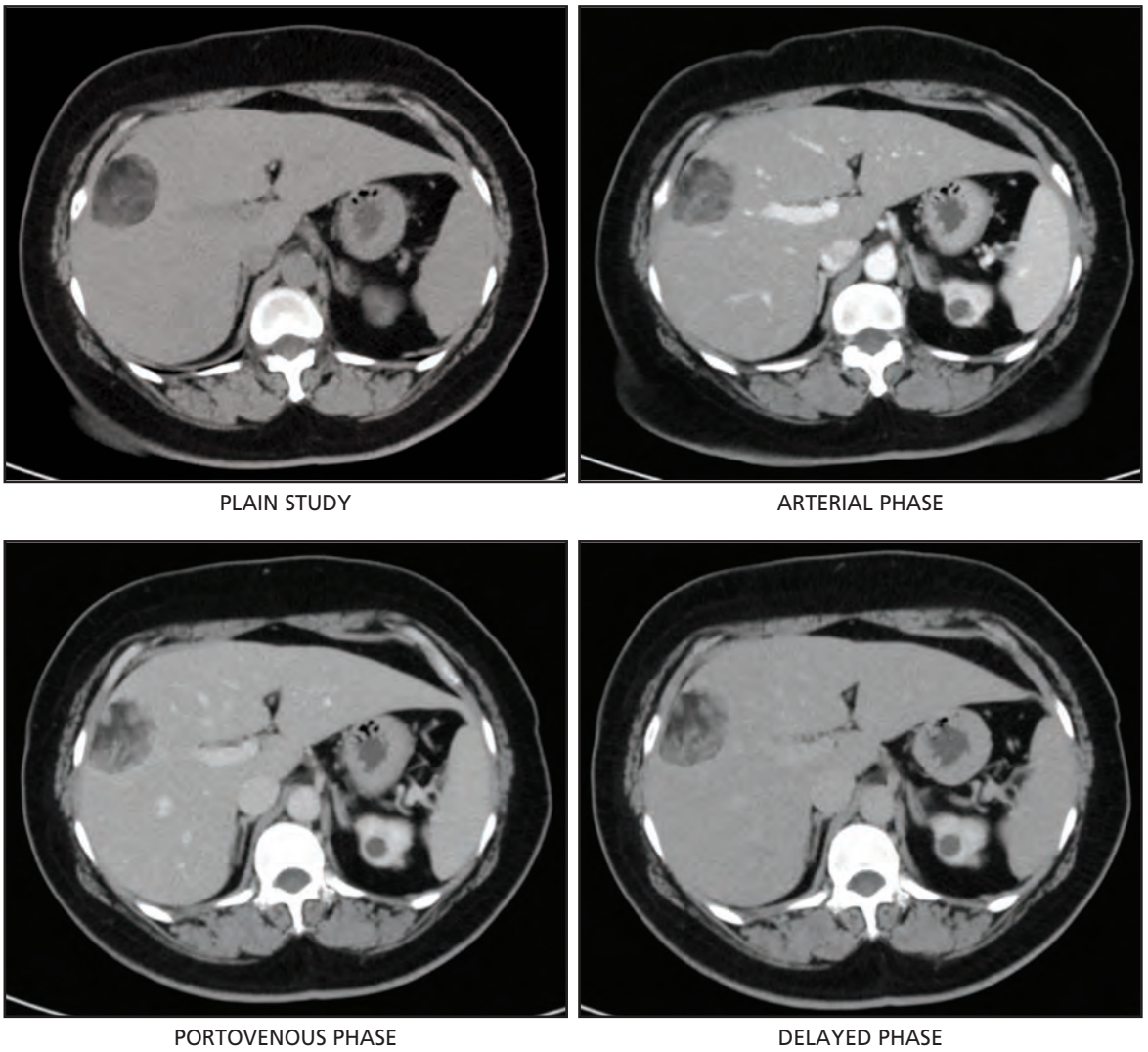
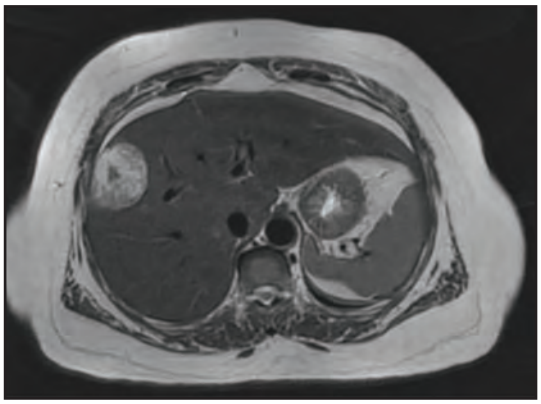


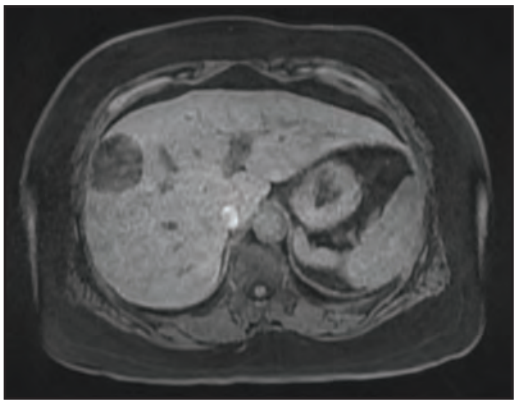
Fig. 1: Multiphasic computed tomography (CT) imaging findings of HAML: A segment VIII mixed soft tissue-fat density mass, with heterogenous progressive enhancement on the arterial and porto-venous and hypodense on the delayed phase

characteristic features that can help to differentiate it. The characteristic imaging features of HAML include visible intralesional fat, prominent draining vessel, and absence of capsule.[3,5] The typical HAML is regarded as a benign tumour, which shows the characteristic features of a large amount of fat content within a plain study. The other possible differential diagnosis of the fat-containing benign liver lesion with soft tissue component comprises adenoma, hepatic adrenal rest tumour and teratoma; however, the malignant liver lesion encompasses HCC, primary liposarcoma and metastatic deposit. Furthermore, another typical radiological feature is the presence of a prominent central vessel, but in fact, the HAML and HCC are also hypervascular tumours, some showing similar enhancement patterns. The radiological enhancement pattern solely depends on the number of intralesional blood vessels, and no specific enhancement pattern is seen in HAML. The lesion with ample central vessels will show rapid enhancement and washout in the subsequent phase; besides, the lesion with a tiny or devoid vessel will show prolonged enhancement in portal venous/ delayed phases. But Lee et al[3] also mentioned that only portovenous phase is significantly different between these two entities, where hypointensity on portovenous phase is depicted in 61.1% of HAML versus 88.9% of HCC. In this case, the lesion showed continued enhancement on portovenous and equilibrium phases in MRI images, which should be the salient characteristics to differentiate HAML from HCC and cavernous haemangioma. Nonetheless, the presence of enhancing capsule in the portal or delayed phase is near pathognomonic for HCC.[6]

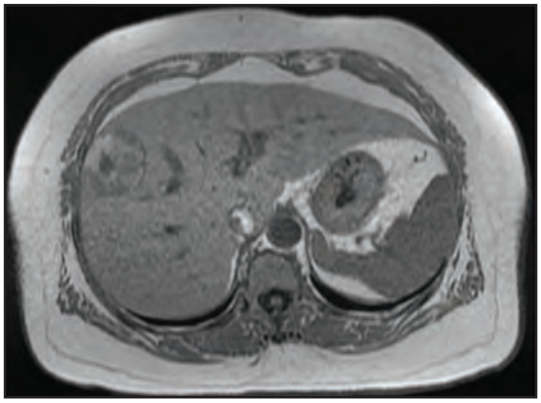
The radiologist must be aware of the spectrum of morphologic features of HAML, which have been subcategorised as classic, fat-poor, HAML with the epithelial cyst, and lastly, epithelioid HAML (Epi-HAML). Epi-HAML was regarded as a tumour of unpredictable malignant potential. It will appear as a well-defined, unencapsulated lesion with a paucity of adipose tissue, which engenders more than 50% of the fat-poor HAML cases to be misdiagnosed as HCC.[5] MRI is more sensitive in detecting small amounts of



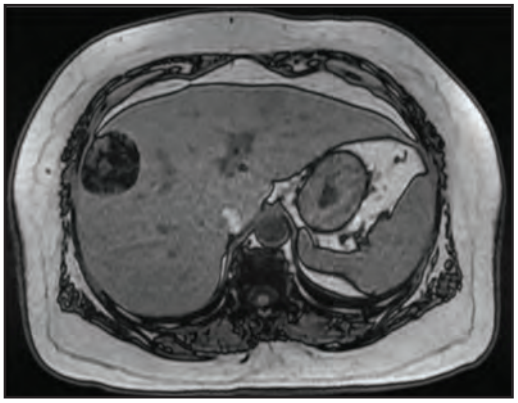
T2-WEIGHTED IMAGE



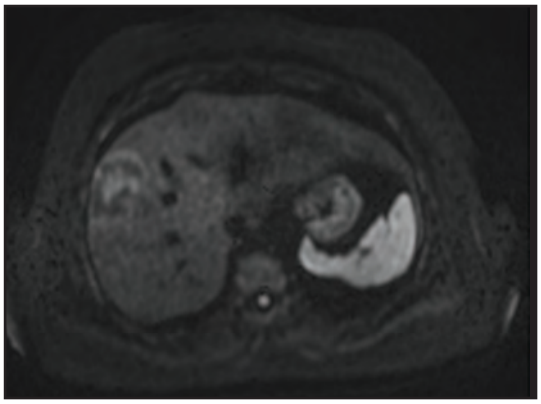
PRE-LAVA T1-WEIGHTED



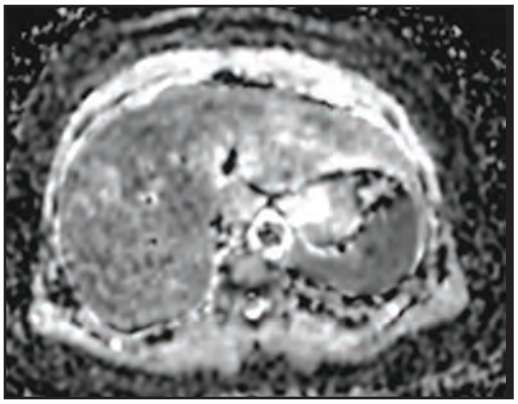
IN-PHASE



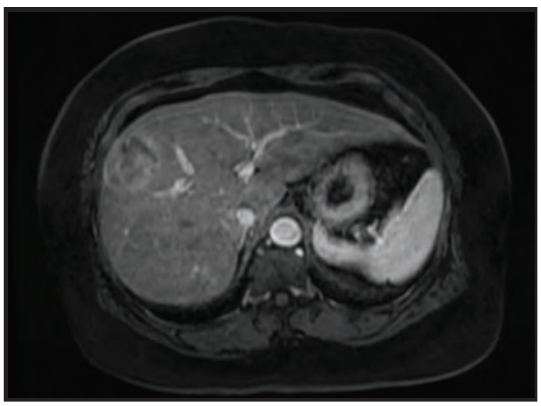
OUT-PHASE



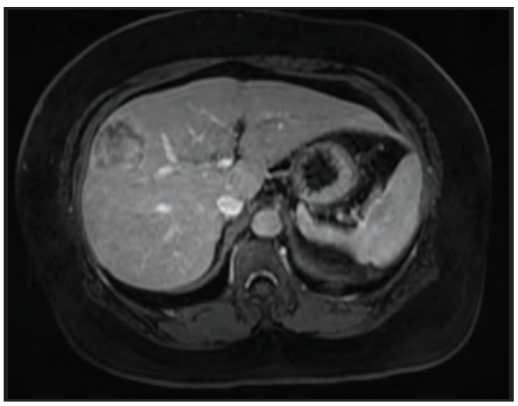
DWI



ADC



EARLY ARTERIAL



LATE ARTERIAL

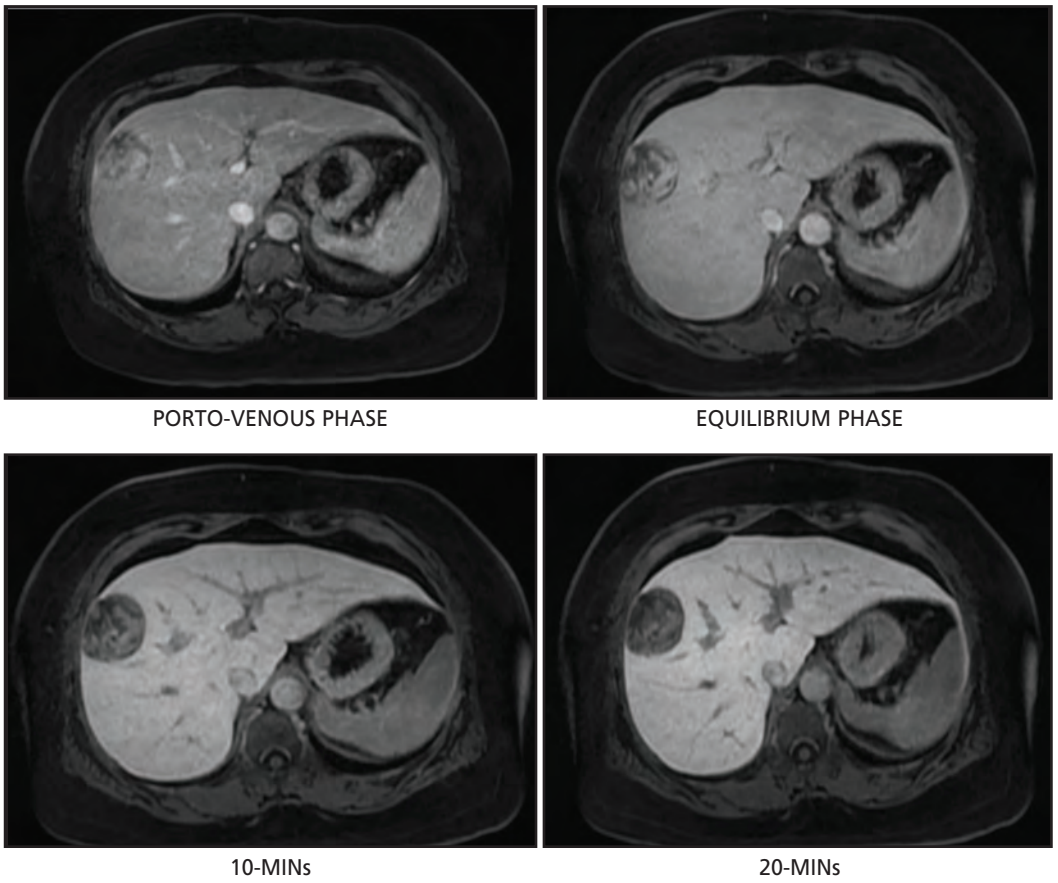


Fig. 2: Magnetic resonance imaging (MRI) features of HAML: The mass is heterogeneously hyperintense on T2WI and hypointense on T1 fat-saturated image. The presence of significant signal drop on the opposed phase indicates fat content, with rim enhancement in the early arterial phase, progressive enhancement from the late arterial till equilibrium phases and hypointense in the 10-minute and 20-minute images

intra-tumoral fat by relying on the different precession frequencies of water and fat proton. Conversely, the conspicuousness of microscopic fat on CT might be affected by volume averaging. On high b-value DWI, the epi-HAML mainly manifests mild hyperintense, while HCC manifests as a marked hyperintense lesion. Indeed, another distinctive feature of epi-HAML is rich intra-tumoral blood vessels at different phases, draining hepatic vein during the arterial phase and prolonged enhancement pattern. It is worth noting that the enhancement intensity of the sectional area within the tumour is higher than surrounding liver parenchyma during the delayed phase, which should not be interpreted as a wash-out pattern. It is imperative for radiologists accustomed to the classifications of HAML to avert improper treatment such as transhepatic arterial chemoembolisation and liver transplantation in HCC cases.[4]

Histologically, HAML displays variable and deviant features, which can be further subclassified into mixed, lipomatous (≥70 % fat), myomatous (≤10%) and angiomatous types. This reported case belongs to the mixed type. The diagnosis of AML can be confirmed by using histopathologic and immunohistochemical features as in this reported case, whereby more than 90% expressing melanocytic antigens, i.e. human melanoma black (HMB)– 45 and Melan-A staining; as well as smooth muscle cell markers i.e. actin and/or desmin. However, the uncertain malignant potential of HAML should not be disregarded. The prognostication of HAML can be further evaluated by using the mitotic marker, i.e. Ki-67 or P53 immunoreactivity or mutation,[7,8] which was not performed for this patient.

Although almost all the HAMLs are benign, the possibility of malignant transformation needs to be taken into consideration. Invasive/infiltrated growth in HAML is hitherto not indicative of malignancy. Indeed, actual malignant HAML is rare, and only a few cases have been reported. Delle et al.[9] reported the first case of malignant HAML in 2000, in a 70-year-old female patient with a right liver lobe hypervascular mass and HPE-proven HAML, which showed positivity in HBM-45/NKIC-3. In view of recurrent abscess formation, the mass was resected 5 years later. Histologically, it showed epithelioid AML with prominent vascular invasion. Unfortunately, the patient passed away due to recurrent disease. Nguyen et al[10] also described a case of recurrent localised HAML after 6 months post-operation, followed by second-look surgery showed local recurrence and extensive intraabdominal metastases. Furthermore, HAML also has the potential risk of enlargement, imposing the mass-compression effect, and the patient has a high

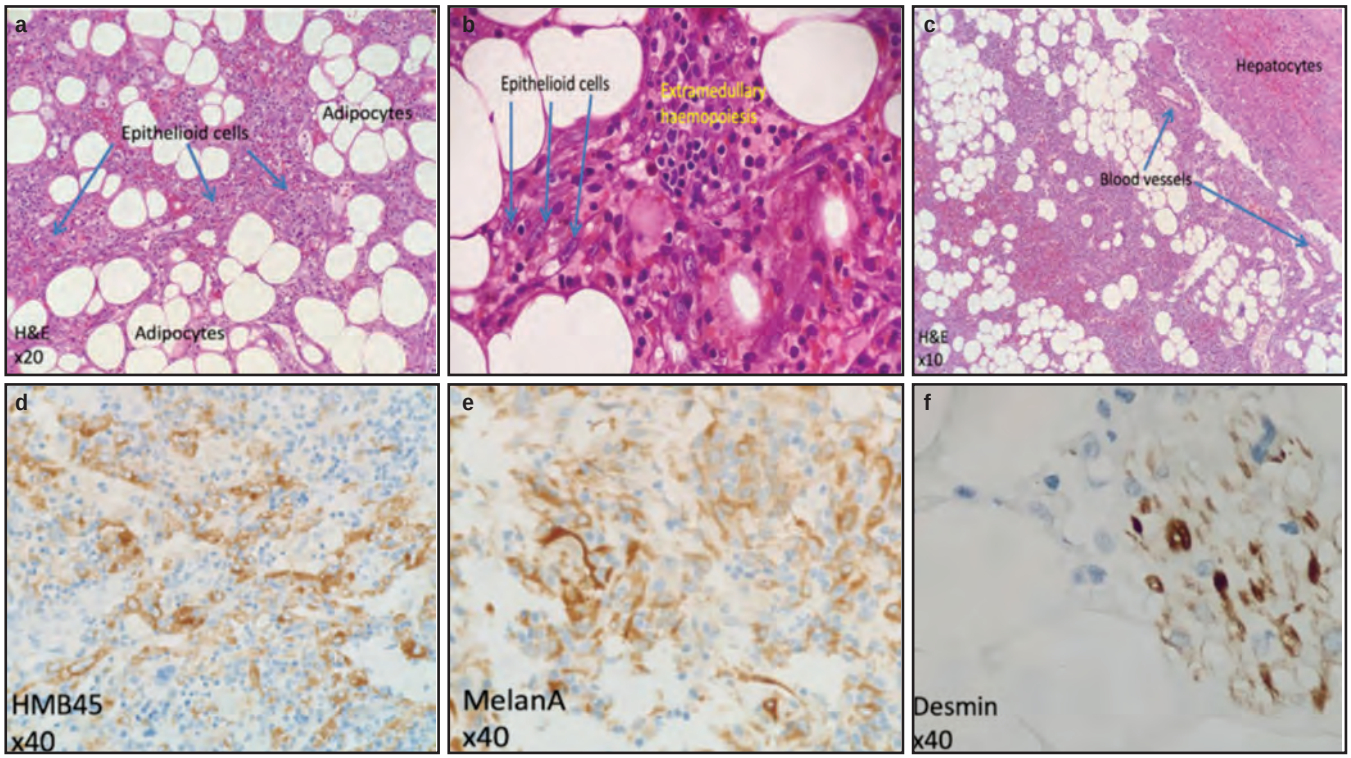


Fig. 3: Histopathological findings—the liver nodule is formed by an admixture of adipocytes (a), epithelioid tumour cells (a, b) and scattered thick-walled blood vessels (c). Extramedullary haematopoiesis is also observed (b). The epithelioid tumour cells show positivity for HMB45 (d) and Melan A (e) with focal positivity for desmin (f). No overt features of malignancy were seen

propensity of being symptomatic. Enlarging tumours will also make the surgery become more complicated, thus early operation is recommended once diagnosed with large HAML.

Malignant transformation features of HAML can be supported by using either radiology or immunohistochemistry. The common features of benign and malignant HAML encompass three basic histology components (mature adipose tissue, blood vessels, spindle and epithelioid cells), immunochemistry (immunoreactivity in melanocytes markers (ie. S100, HMB-45, Melan-A), and smooth muscle antigens (ie. SMA, Desmin)), sinusoidal spaces and circumjacent portal blood vessels invasion and cytology atypia, which are not a definitive benchmark for predicting malignancy in HAML. Notwithstanding, large (>10 cm), coagulative necrosis and metastases are radiological manifestations of malignancy. Loss of CD-117 (c-kit) expression, which is tyrosine kinase growth factor receptor is a feature of malignancy.[10] Borderline cases should be categorised as AML of uncertain malignant potential, and further close follow-up is warranted. Other than the loss of CD-117 expression, Ki-67 and P53, which were not performed in our centre, none of the features were found in our cases, suggesting that this is probably a benign lesion and she is still under surveillance imaging.

CONCLUSION

This case report is helpful to increase awareness among managing teams of HAML with diverse prognoses. Concordance imaging correlation with pathology results is important in making the diagnosis explicitly. Resection is advisable for the symptomatic, large HAML (>5 cm), non-compliance patient or hepatitis B virus carrier who endures the risk of hepatoma. Close imaging follow-up is suggested for patients under conservative management. Eventually, curative resection is an ideal choice for this patient because the tumour size is borderline big, and the patient defaulted to all the follow-ups for many reasons, but the latest ultrasound was done 1 year after resection, which revealed a normal study with no focal liver lesion.

ACKNOWLEDGEMENT

Special thanks to Dr. Nurul Akmar Misron, a pathologist from Sultanah Bahiyah Hospital, Alor Setar, Kedah for preparing the histopathological pictures.

CONFLICT OF INTERESTS

No financial arrangement or affiliation with any organisation that may have a direct influence on their work. Patient consent for publication: Obtained.

REFERENCES

1. Cha I, Cartwright D, Guis M, Miller TR, Ferrell LD. Angiomyolipoma of the liver in fine-needle aspiration biopsies: its distinction from hepatocellular carcinoma. Cancer 1999; 87(1): 25-30.
2. Fricke BL, Donnelly LF, Casper KA, Bissler JJ. Frequency and imaging appearance of hepatic angiomyolipomas in pediatric and adult patients with tuberous sclerosis. Am J Roentgenol. 2004; 182(4): 1027-30.

3. Lee SJ, Kim SY, Kim KW, Kim JH, Kim HJ, Lee MG, et al. Hepatic angiomyolipoma versus hepatocellular carcinoma in the noncirrhotic liver on gadoxetic acid–enhanced MRI: a diagnostic challenge. Am J Roentgenol. 2016; 207(3): 562-70.
4. Liu W, Wang J, Huang Q, Lu Q, Liang W. Comparison of MRI features of epithelioid hepatic angiomyolipoma and hepatocellular carcinoma: imaging data from two centers. Front Oncol. 2018; 8: 600.
5. Kim MU, Kim SH, Kim HC, Lee JY, Kim MA, Han JK, et al. Hepatic angiomyolipoma: dual-contrast mri findings using superparamagnetic iron oxide (SPIO) and gadolinium agents. J Korean Soc Radiol. 2010; 63: 537-46.
6. Ji JS, Lu CY, Wang ZF, Xu M, Song JJ. Epithelioid angiomyolipoma of the liver: CT and MRI features. Abdom. Imaging 2013; 38(2): 309-14.
7. Hwang I, Yu E, Cho KJ. Hepatic angiomyolipoma with variable histologic features: 8 cases resembling hepatocellular carcinoma or inflammatory pseudotumor. Korean J Gastroenterol 2012; 60(4): 242-8.
8. Kobayashi Y, Kamimura K, Nomoto M, Sugitani S, Aoyagi Y. Immunohistochemical character of hepatic angiomyolipoma: for its management. Case Rep Med 2013; 298143.
9. Dalle I, Sciot R, de Vos R, Aerts R, van Damme B, Desmet V, et al. Malignant angiomyolipoma of the liver: A hitherto unreported variant. Histopathology 2000; 36(5): 443-50.
10. Nguyen TT, Gorman B, Shields D, Goodman Z. Malignant hepatic angiomyolipoma: report of a case and review of literature. Am J Surg Pathol. 2008; 32(5): 793-8.