CASE REPORT

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

MRI diagnosis of perivascular epithelioid cell tumor (PEComa) of the liver

HUA-QIANG SHENG[1)], DONG-FENG CHEN[2)], XIN-HAI SUN[1)], XIAN LI[1)], JIE XU[1)], XI-BIN HU[1)], MEI-QIN LI[1)], TAO WU[1)], REN-YA ZHANG[3)], KAI-ZHI LI[3)]

[1)]*Department of Radiology*
[2)]*Department of Ultrasonography*
[3)]*Department of Pathology*
Affiliated Hospital of Jining Medical College, Jining, China

Abstract

Introduction: Perivascular epithelioid cell tumor (PEComa) has been rarely reported in the liver. *Patient, Methods and Results*: We present a liver PEComa case diagnosed by magnetic resonance imaging (MRI) findings. The patient was incidentally found to have an abnormal mass in the liver. MRI revealed early and strikingly homogeneous enhancement of the lesion. Partial hepatectomy was performed, and a pathological examination revealed signs of typical of PEComa. The patient was closely monitored for 12 months after the surgery, with no clinical or radiographic evidence of recurrence or metastatic disease. *Conclusion*: MRI diagnosis is applicable for PEComa.

Keywords: liver, neoplasm, perivascular epithelioid cell tumor (PEComa), magnetic resonance imaging, diagnosis.

Introduction

PEComa is a mesenchymal tumor that is especially rare in the liver [1–11]. Few case reports have described the imaging profiles of this type of tumor [7, 11–13]. The perivascular epithelioid cell tumor (PEComa) has no known normal tissue counterpart. PEComa is a rare example of an emerging class of hepatic PEC tumors, and has been defined as a mesenchymal tumor composed of histologically and immunohistochemically distinctive perivascular epithelioid cells (PECs) [14]. Firstly reported in the liver in 2000 [15], epithelioid angiomyolipoma (EAML) is yet another recently described, rare, variant of an angiomyolipoma (AML). EAML often resembles AML or HCC, both in terms of radiographic and histologic characteristics. PEComas are now classified as a family of tumors that includes classic AML, lymph-angioleiomyomatosis, and clear epithelioid cell tumors, including EAML, pulmonary and extrapulmonary clear cell sugar tumor, and PEComa [16]. Immunohistochemical tests reveal that the tumors are positive for melanocytic HMB-45 (an anti-melanoma monoclonal antibody) and α-smooth muscle actin [4, 12, 17]. According to the line of differentiation and predominance of tissue components, AML in hepatic regions has been subcategorized into mixed, lipomatous (≥70% fat), myomatous (≤10% fat), and angiomatous subtypes [18] (reviewed in Table 1).

Table 1 – ***Reported cases of hepatic PEComas in literature***

Sex/Age [years]	Site	Imaging appearance	Pathological features	Immunohistochemical staining	Tumor recurrence	Outcome
F/60	Liver	Computerized tomography (CT) imaging demonstrated lesions in the liver.	Cells arranged in solid sheets and nests, invested with a prominent capillary vasculature.	The tumor cells demonstrated strong and diffuse positivity for human melanoma black-45 (HMB-45), Melan-A, and α-smooth muscle actin (α-SMA).	Hepatic recurrence and pulmonary, pancreatic and muscular metastases at nine years; bladder metastases at 10 years.	Alive with disease at 10 years.
F/56	Liver	On contrast-enhanced CT, a well-demarcated mass was found with significant and heterogeneous enhancement, more strikingly enhanced on portal venous phase than on arterial phase.	Photomicrograph shows polygonal or short spindle cells with oval nuclei and clear abundant cytoplasm.		No recurrence.	Neither primary recurrence nor metastasis was found during two-year follow-up.
F/63	Liver	Contrast-enhanced CT showed significantly and heterogeneously patchy enhancement of the lesion on arterial phase.	The tumor cells were polygonal with eosinophilic cytoplasm.		No recurrence.	Neither primary recurrence nor metastasis could be found during one-year follow-up.

Sex/Age [years]	Site	Imaging appearance	Pathological features	Immunohistochemical staining	Tumor recurrence	Outcome
F/36	Left lateral segment	CT scan showed a well-demarcated, heterogeneous mass.	Largely of polygonal epithelioid cells with sheets or a vague trabecular pattern separated by a rich sinusoidal vascular network.	The epithelioid cells were diffusely positive for HMB-45 and α-SMA, and weakly reactive for S-100 protein.	No recurrence.	Alive, not evidence of disease.
F/36	Segment 2	Contrast-enhanced ultrasonography showed the tumor was enhanced in early arterial phase and the reagent rapidly flowed into drainage veins in no more than one second after the infusion.	Tumor was highly cellular, consisting of fascicles of large polygonal cells with abundant cytoplasm.	Immunohistochemical studies showed a strong and diffuse expression of HMB-45 and partial expression of α-SMA within tumor cells.	No recurrence.	Without recurrence or metastasis for 18 months.
F/46	Segment 3	Strongly hyperintense on T2 and hypointense on T1 homogeneous and intense contrast enhancement in the arterial phase and persisted as slightly hyperintense in portal phase.	Pleomorphic epithelioid clear cells intermingled with fat and vascular tissue.	Showed immuno-reactivity for α-SMA, HMB-45, and Melan-A, and negative findings for S-100 protein and desmin.	No recurrence.	No signs of malignancy were confirmed.

Here we describe a rare case of a 55-year-old man with magnetic resonance imaging features. We retrospectively analyzed the clinical presentation, imaging characteristics, and reviewed the related literature. Further, we studied the imaging characteristics and performed differential diagnosis of the tumor.

Patient, Methods and Results

A 55-year-old man was incidentally found to have a lesion in the liver during ultrasonography (US) performed as part of a physical examination. Clinical examination revealed no significant abnormalities, and no abnormal findings were observed in routine blood tests. Results of liver function tests were normal. US revealed an oval, homogeneous, hyperechoic mass located in the posterior inferior segment of the right lobe of the liver. Computed tomography (CT) showed a homogeneous, hypoattenuating lesion measuring 1.5×1.6 cm at the maximal cross-sectional diameter in segment VI. Magnetic resonance imaging (MRI) was performed in our hospital by using a 1.5-T unit (Magnetom Avanto, Siemens Medical Solutions), and it revealed a focal lesion in the right inferior lobe of the liver. MRI scans were acquired using a 1.5-T whole-body magnet equipped with 25-mT/m gradient coils and phased array surface coils (Magnetom Avanto, Siemens). Vibe sequence: field of view, 350 mm; thickness 2.5 mm, matrix: 256×256; TR 5.77 ms, TE 2.63 ms; flip angle [FA], 10^0; bandwidth 250. Contrast material is injected at a rate of 3.5 mL/s by means of a power injector, a test bolus to calculate more exact timing after the start of injection. Arterial phase scanning began about 15–20 seconds after injection, venous phase scanning began at 35 seconds, and delayed phase scanning began at 5 minutes.

The lesion was homogeneous and appeared as a hypointense area on T1-weighted images. It appeared as a hypo- and hyperintense area on T2-weighted images and as a hyperintense area on diffusion-weighted images (Figure 1, A–C). The lesion was not found to contain fat in the fat tissue suppression sequence.

On dynamic MRI performed after bolus injection of 30 mL of gadolinium-diethylene-triamine penta-acetic acid (Gd-DTPA 3.5 mL/s through an auto-injector), the lesion showed a striking and homogeneous enhancement during the arterial phase, indicating a relatively hyper-vascular, heterogeneous composition. This enhancement was rapidly attenuated during the portal venous and equilibrium phases, and hypoenhancement was observed in the late parenchymal phase (Figure 1, D–F). Additionally, a vessel was noted to be passing through the lesion. Based on this data, we presumptively diagnosed the lesion as a PEComa. However, these findings were similar to the imaging findings observed in cases of hepatocellular carcinoma (HCC), and therefore, surgical resection was recommended.

For the surgery, oblique incision was made at the right costal margin 15 cm under the right costal margin, cutting through the skin, subcutaneous fat, and the three layers of muscle and then peritoneum. Then open laparotomy; cut liver round ligament and free falciform ligament, the right coronary ligament, the right triangular ligament, free bare area of liver, revealed the liver right posterior lobe. According to surgery ultrasound in the display, the tumor was located in segment VI of the liver close to the inferior vena cava, about 2 cm in size; cut the tumor with a 2 cm excision margin. Liver incision was sutured and hemostasised. Specimen was cut open, a diameter about 2 cm gray solid mass was found (benign).

For histology, the tissue sample was fixed in formalin and embedded in paraffin. Full tissue sections (4 mm thick) were used for immunohistochemistry. HE staining and immunohistochemical staining was performed according to standard techniques on a Ventana Benchmark XT Autostainer (Ventana Medical System Inc., Tucson, AZ, USA). Briefly, antigen retrieval was done with EGTA-based solution for five minutes cooking with microwave (evaporated water replaced) and cooled down for 30 minutes. Then, the slices were incubated with 3% H_2O_2 of deionized water for 10 minutes, to block endogenous peroxidase in prior to the primary

antibody incubation for overnight at 4^0C [mouse-anti-HMB-45 (Sig-3116, 1:100, Covance, Priceton, NJ, USA), mouse-anti-Melan-A (A103, 1:50, Sigma, Shanghai, China), mouse-anti-actin (AC-40, 1:100, Sigma, Shanghai, China)], followed by polyperoxidase anti-mouse IgG (W4021, Promega, Beijing, China) incubation for two hours at room temperature, and finally the DAB based visualization (Pierce Peroxidase IHC Detection Kit, 36000, Thermo Fisher Scientific, Rockford, IL, USA). The selected normal tissues were used as the control. Hematoxylin staining was used for counterstaining for the background. Under microscope visualization, the tumor is sharply demarcated from the surrounding liver parenchyma as can be seen in low power scan of the glass slide. The tumor is composed of nests and sheets of epithelioid and some spindled cells with clear to granular eosinophilic cytoplasm and a focal association with blood vessel walls, showing immunoreactivity for both melanocytic (HMB-45 and Melan-A) and α-smooth muscle actin (α-SMA) markers. Histological analysis showed sheets of large epithelioid cells, small amounts of adipose cells, and blood vessels with abundant eosinophilic cytoplasm (Figure 2, A–C). On immunohistochemical staining, the cells were found to be positive for a melanocytic cell-specific monoclonal antibody HMB-45 (Figure 2D).

The diagnosis of hepatic PEComa was thus established (Figure 3). A review MRI performed 12 months after the surgery showed no sign of the lesion.

This study was approved by the Institutional Review Board of the Affiliated Hospital of Jining Medical College (Jining, China) and written informed consent was obtained from every participant.

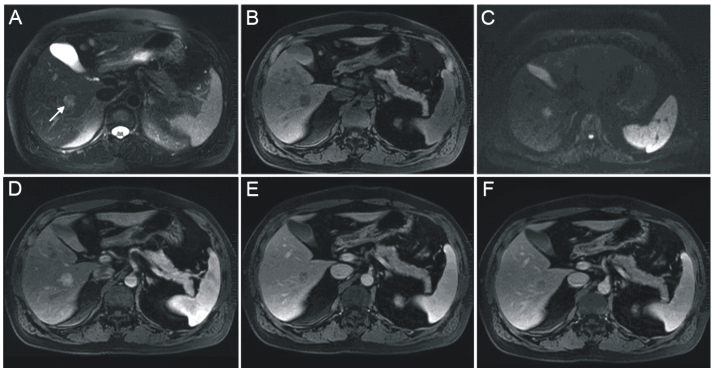

Figure 1 – *(A–C) Magnetic resonance imaging showed a homogeneous tumor appeared as a hypo- and hyperintense area on T2-weighted images (arrow); hypointense area on T1-weighted images, and as a hyperintense area on diffusion-weighted images. (D–F) Enhanced magnetic resonance imaging showed the tumor with early-phase hyperattenuation and late-phase hypo-attenuation on gadolinium-diethylene-triamine penta-acetic acid enhanced MRI.*

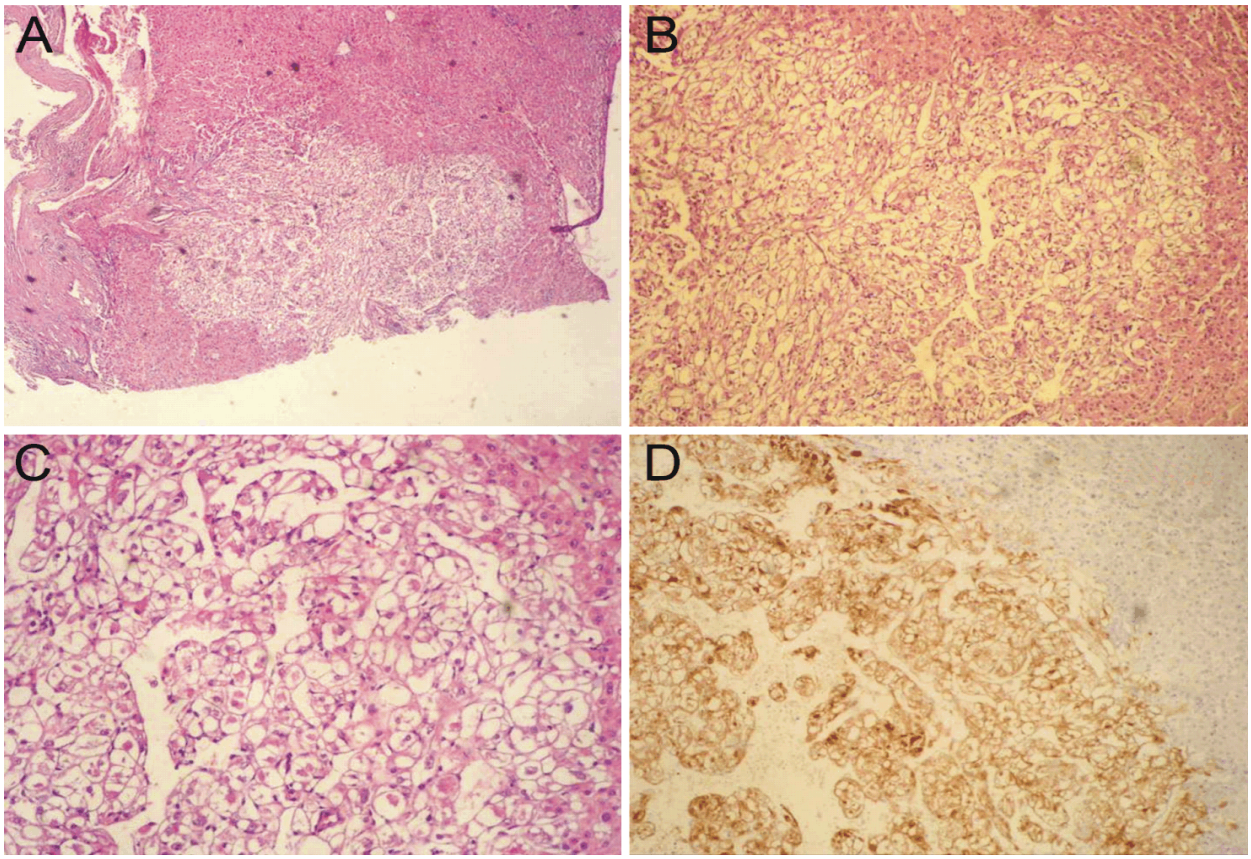

Figure 2 – *(A) On microscopic examination, the tumor appears to be well-circumscribed and without a capsule compressing the adjacent liver tissue (HE staining, ob. ×4). (B) Nests and sheets of epithelioid cells with clear and granular eosinophilic cytoplasm (HE staining, ob. ×10). (C) Typical perivascular nests of PEComa cells (HE staining, ob. ×40). (D) Immunostaining with HMB-45 antibody. The tumor cells show a strong, characteristic positive labeling in a granular cytoplasmic pattern (ob. ×10).*

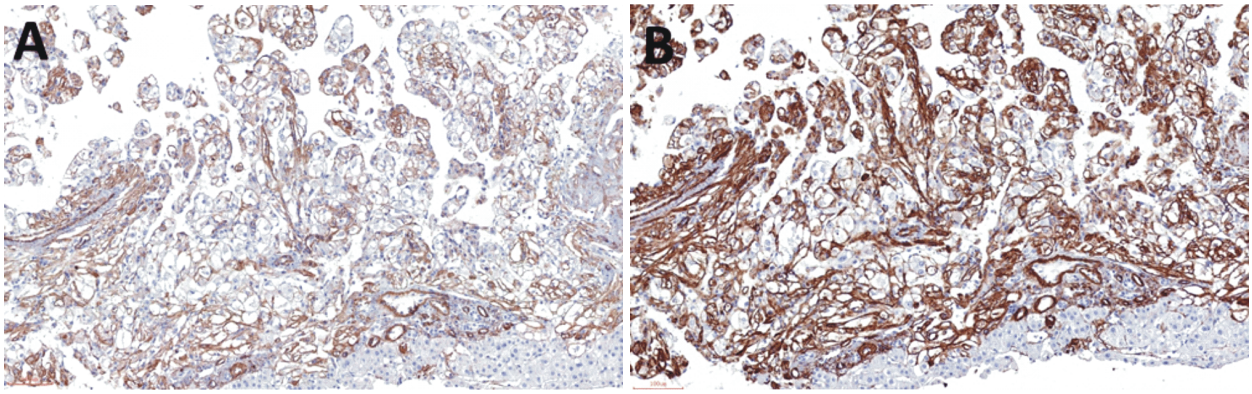

Figure 3 – ***The tumor cells show a strong, characteristic positive immunoreactivity for actin (A) and SMA (B) as myogenic differentiation markers at ob. ×10.***

Discussion

Confusion and controversy surrounding the use of the term "PEComa" remains. Some authors have suggested that the term should be more broadly applied to include AML and lymphangioleiomyomatosis [19, 20], while others have included EAML as a subtype of PEComa [21]. Researchers have now defined PEComa as a neoplasm without adipocytes, and thus distinguish it from classic AML [22]. Most PEComas follow a benign clinical course, but malignant PEComas and distant metastasis after surgical resection of the original tumors have been reported [4–9, 12, 23, 24]. Due to the characteristic morphology and positive staining with melanocytic marker HMB-45, we use the term PEComa in this case report.

With advances in MRI and CT, there is an increasing awareness of this technique as a diagnostic tool. However, PEComas exhibit a wide spectrum of imaging findings, and few radiological features of PEComa of the liver have been described in the literature. In tumors with a much lower fatty content (or in EAMLs), definitive diagnosis may be difficult. The common differential diagnoses for hypervascular lesions include hemangioma and HCC. MRI provides the greatest tissue contrast with the highest specificity, allowing more accurate detection of lipomatous components, and thus aids the diagnosis of PEComas. Moreover, it has been suggested that dynamic imaging would be the most reliable method for differentiating AML from HCC [25], because the amount of adipose tissue present in hepatic AMLs can vary greatly. Previous reports have suggested that hypervascularity and arteriovenous characteristics in contrast-enhanced CT or MRI is a useful diagnostic feature of PEComa [24, 26–28].

Fang SH *et al.* [27] reported two cases of liver PEComa. In one of these two cases, the tumor showed striking and homogeneous enhancement during the arterial phase and venous phase. Xu PJ *et al.* [29] reported 10 immunohistochemically verified cases of PEComa. In these cases, eight epithelioid angiomyolipoma (Epi-HAML) and 13 non-Epi-HAML lesions were imaged, and they showed obvious enhancement during the arterial phase. Furthermore, punctate or curved vessels could be seen within 10 Epi-HAML as well as nine non-Epi-HAML lesions in the arterial or/and portal phases. Outer rim enhancement was found in eight Epi-HAML on enhanced imaging.

In our study, the lesion lacked a significant fatty component and had none of the characteristic features of AML. There were some similarities between our study and the reports mentioned above, most notably the pattern of enhancement; however, since we also saw rapid attenuation during the portal venous and equilibrium phases, the radiographic findings can be confused with those of HCC. However, the imaging features of the tumor helped to distinguish it from HCC, since HCC does not usually have such a mixed intensity on T2-weighted images and does not display such hyperintensity on diffusion-weighted images. Moreover, the early influx into the tumor and the rapid drainage of arterial blood to the veins, along with the absence of a distinguishable capsule, helped to rule out typical HCC.

Conclusions

The present study demonstrated the use of MRI in early recognition of liver PEComas. However, to definitively diagnose PEComa, histological findings determined using melanocytic markers, such as HMB-45, are essential. In order to achieve this, fine-needle aspiration biopsy (FNAB) or laparoscopy may be needed, and long-term periodic follow-up is reasonable in cases presenting with PEComa.

References

[1] Fang S, Dong D, Jin M, *Perivascular epithelioid cell tumor (PEComa) of the kidney: MR features*, Eur Radiol, 2007, 17(7):1906–1907.

[2] Rouquie D, Eggenspieler P, Algayres JP, Béchade D, Camparo P, Baranger B, *Malignant-like angiomyolipoma of the liver: report of one case and review of the literature*, Ann Chir, 2006, 131(5):338–341.

[3] Yamamoto H, Oda Y, Yao T, Oiwa T, Kobayashi C, Tamiya S, Kawaguchi K, Hino O, Tsuneyoshi M, *Malignant perivascular epithelioid cell tumor of the colon: report of a case with molecular analysis*, Pathol Int, 2006, 56(1):46–50.

[4] Bing Z, Yao Y, Pasha T, Tomaszewski JE, Zhang PJ, *p53 in pure epithelioid PEComa: an immunohistochemistry study and gene mutation analysis*, Int J Surg Pathol, 2012, 20(2): 115–122.

[5] Selvaggi F, Risio D, Claudi R, Cianci R, Angelucci D, Pulcini D, D'Aulerio A, Legnini M, Cotellese R, Innocenti P, *Malignant PEComa: a case report with emphasis on clinical and morphological criteria*, BMC Surg, 2011, 11:3.

[6] Ahn JH, Hur B, *Primary perivascular epithelioid cell tumor (PEComa) of the liver – a case report and review of the literature*, Korean J Pathol, 2011, 45(S1):S93–S97.

[7] Akitake R, Kimura H, Sekoguchi S, Nakamura H, Seno H, Chiba T, Fujimoto S, *Perivascular epithelioid cell tumor (PEComa) of the liver diagnosed by contrast-enhanced ultrasonography*, Intern Med, 2009, 48(24):2083–2086.
[8] Strzelczyk JM, Durczynski A, Szymanski D, Jablkowski M, Dworniak D, Sporny S, *Primary perivascular epithelioid cell tumor (PEComa) of the liver: report of a case*, Surg Today, 2009, 39(10):916–921.
[9] Priola MA, Priola MS, Cataldi A, Marci V, Fava C, *Acute abdomen as an unusual presentation of hepatic PEComa. A case report*, Tumori, 2009, 95(1):123–128.
[10] Paiva CE, Moraes Neto FA, Agaimy A, Custodio Domingues MA, Rogatto SR, *Perivascular epithelioid cell tumor of the liver coexisting with a gastrointestinal stromal tumor*, World J Gastroenterol, 2008, 14(5):800–802.
[11] Svajdler M, Bohus P, Goc V, Tkácová V, *Perivascular epithelioid cell tumor (PEComa) of the liver: a case report and review of the literature*, Cesk Patol, 2007, 43(1):18–22.
[12] Tan Y, Xiao EH, *Hepatic perivascular epithelioid cell tumor (PEComa): dynamic CT, MRI, ultrasonography, and pathologic features – analysis of 7 cases and review of the literature*, Abdom Imaging, 2012, 37(5):781–787.
[13] Larbcharoensub N, Karnsombut P, Jatchavala J, Wasutit Y, Nitiyanant P, *Primary hepatic clear cell myomelanocytic tumor. Case report and review of the literature*, APMIS, 2007, 115(12):1454–1459.
[14] Folpe AL, Neoplasms with perivascular epithelioid cell differentiation (PEComas). In: Fletcher CDM, Unni KK, Epstein J, Mertens F (eds), *Pathology and genetics of tumours of soft tissue and bone*, IARC Press, Lyon, 2002, 221–222.
[15] Yamasaki S, Tanaka S, Fujii H, Matsumoto T, Okuda C, Watanabe G, Suda K, *Monotypic epithelioid angiomyolipoma of the liver*, Histopathology, 2000, 36(5):451–456.
[16] Pan CC, Chung MY, Ng KF, Liu CY, Wang JS, Chai CY, Huang SH, Chen PC, Ho DM, *Constant allelic alteration on chromosome 16p (TSC2 gene) in perivascular epithelioid cell tumour (PEComa): genetic evidence for the relationship of PEComa with angiomyolipoma*, J Pathol, 2008, 214(3):387–393.
[17] Tanaka Y, Ijiri R, Kato K, Kato Y, Misugi K, Nakatani Y, Hara M, *HMB-45/melan-A and smooth muscle actin-positive clear-cell epithelioid tumor arising in the ligamentum teres hepatis: additional example of clear cell 'sugar' tumors*, Am J Surg Pathol, 2000, 24(9):1295–1299.
[18] Tsui WM, Colombari R, Portmann BC, Bonetti F, Thung SN, Ferrell LD, Nakanuma Y, Snover DC, Bioulac-Sage P, Dhillon AP, *Hepatic angiomyolipoma: a clinicopathologic study of 30 cases and delineation of unusual morphologic variants*, Am J Surg Pathol, 1999, 23(1):34–48.
[19] Bonetti F, Martignoni G, Colato C, Manfrin E, Gambacorta M, Faleri M, Bacchi C, Sin VC, Wong NL, Coady M, Chan JK, *Abdominopelvic sarcoma of perivascular epithelioid cells. Report of four cases in young women, one with tuberous sclerosis*, Mod Pathol, 2001, 14(6):563–568.
[20] Tazelaar HD, Batts KP, Srigley JR, *Primary extrapulmonary sugar tumor (PEST): a report of four cases*, Mod Pathol, 2001, 14(6):615–622.
[21] Zimmermann A, von der Brelie C, Berger B, Kappeler A, Candinas D, *Primary perivascular epithelioid cell tumor of the liver not related to hepatic ligaments: hepatic PEComa as an emerging entity*, Histol Histopathol, 2008, 23(10):1185–1193.
[22] Martignoni G, Pea M, Reghellin D, Zamboni G, Bonetti F, *PEComas: the past, the present and the future*, Virchows Arch, 2008, 452(2):119–132.
[23] Dalle I, Sciot R, de Vos R, Aerts R, van Damme B, Desmet V, Roskams T, *Malignant angiomyolipoma of the liver: a hitherto unreported variant*, Histopathology, 2000, 36(5):443–450.
[24] Parfitt JR, Bella AJ, Izawa JI, Wehrli BM, *Malignant neoplasm of perivascular epithelioid cells of the liver*, Arch Pathol Lab Med, 2006, 130(8):1219–1222.
[25] Murakami T, Nakamura H, Hori S, Nakanishi K, Mitani T, Kozuka T, Kimura Y, Monden M, Wakasa K, Sakurai M, *Angiomyolipoma of the liver. Ultrasound, CT, MR imaging and angiography*, Acta Radiol, 1993, 34(4):392–394.
[26] Högemann D, Flemming P, Kreipe H, Galanski M, *Correlation of MRI and CT findings with histopathology in hepatic angiomyolipoma*, Eur Radiol, 2001, 11(8):1389–1395.
[27] Fang SH, Zhou LN, Jin M, Hu JB, *Perivascular epithelioid cell tumor of the liver: a report of two cases and review of the literature*, World J Gastroenterol, 2007, 13(41):5537–5539.
[28] Takahara M, Miyake Y, Matsumoto K, Kawai D, Kaji E, Toyokawa T, Nakatsu M, Ando M, Hirohata M, *A case of hepatic angiomyolipoma difficult to distinguish from hepatocellular carcinoma*, World J Gastroenterol, 2009, 15(23):2930–2932.
[29] Xu PJ, Shan Y, Yan FH, Ji Y, Ding Y, Zhou ML, *Epithelioid angiomyolipoma of the liver: cross-sectional imaging findings of 10 immunohistochemically-verified cases*, World J Gastroenterol, 2009, 15(36):4576–4581.

Corresponding author
Hua-qiang Sheng, Professor, Department of Radiology, Affiliated Hospital of Jining Medical College, 79 Guhuai Road, Jining 272000, China; Phone/Fax +86–537–2903189, e-mail: huaqiang_sheng@163.com

Received: September 5, 2012

Accepted: July 2, 2013