

## Synchronous occurrence of a hepatic myelolipoma and two hepatocellular carcinomas

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**Supported by the National Basic Research Program (973 Program) in China, No. 2013CB531403; and the National Natural Science Foundation of China, No. 81572307.**

**Institutional review board statement:** The study was reviewed and approved by the Institutional Review Board of the First Affiliated Hospital, School of Medicine, Zhejiang University.

**Informed consent statement:** Informed consent was obtained from the patient.

**Conflict-of-interest statement:** No commercial or associative interest in any form has been received or will be received from a commercial party related directly or indirectly to the subject of this paper.

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**Manuscript source:** Unsolicited manuscript

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**Received:** September 7, 2016  
**Peer-review started:** September 8, 2016  
**First decision:** September 28, 2016  
**Revised:** October 10, 2016  
**Accepted:** October 19, 2016  
**Article in press:** October 19, 2016  
**Published online:** November 21, 2016

### Abstract

Myelolipoma is a rare tumor composed of fat and bone marrow components, most of which are located in the adrenal gland. Myelolipoma in the liver is extremely rare. To date, only 10 cases have been reported in the English-language medical literature. In one of these cases, the hepatic myelolipoma was found within a hepatocellular carcinoma (HCC). In the present study, we report the first case of the synchronous occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient, a 26-year-old female who was admitted to our hospital because of a 4-d history of upper abdominal pain. The unenhanced computed tomography (CT) images showed a well-defined low-density mass with adipose components in the right liver lobe, 4.2 cm × 4.1 cm in size. Two inhomogeneous low-

density masses were found in the left liver lobe, 8.6 cm × 7.7 cm and 2.6 cm × 2.6 cm in size. The masses in both the right and left liver lobes were heterogeneously enhanced in the contrast-enhanced CT images. Based on the results of the imaging examination, the mass in the right liver lobe was preliminarily considered to be a hamartoma, and the two masses in the left liver were preliminarily considered to be HCCs. We performed a right hepatectomy, a left hepatic lobectomy, and a cholecystectomy. Microscopic and immunohistochemical results revealed that the tumor in the right liver lobe was a hepatic myelolipoma, and that the two tumors in the left liver lobe were HCCs.

**Key words:** Liver; Myelolipoma; Hepatocellular carcinoma; Hepatectomy; Hepatic lobectomy

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**Core tip:** Hepatic myelolipoma is extremely rare. To date, only 10 cases have been reported in the English-language medical literature. In the present study, we report the first case of the synchronous occurrence of a hepatic myelolipoma and two hepatocellular carcinomas in different liver sections of one patient, who received a right hepatectomy, a left hepatic lobectomy, and a cholecystectomy. We also highlight the diagnosis and treatment of a hepatic myelolipoma and conduct a literature review to deepen the understanding of the subject.

Xu SY, Xie HY, Zhou L, Zheng SS, Wang WL. Synchronous occurrence of a hepatic myelolipoma and two hepatocellular carcinomas. *World J Gastroenterol* 2016; 22(43): 9654-9660 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v22/i43/9654.htm> DOI: <http://dx.doi.org/10.3748/wjg.v22.i43.9654>

## INTRODUCTION

Myelolipoma is a rare benign tumor composed of fat and bone marrow components. The adrenal gland is the most common location<sup>[1,2]</sup>. Myelolipoma in the liver is extremely rare. To our knowledge, 10 cases have been reported in the English-language medical literature as individual case reports<sup>[3-12]</sup>. In one of the cases, the hepatic myelolipoma was found within a hepatocellular carcinoma (HCC)<sup>[6]</sup>. Hepatic myelolipomas are usually incidentally discovered by ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI), or autopsy examination. The first case of hepatic myelolipoma was reported in France by Grosdidier *et al.*<sup>[13]</sup> in 1973, and it was found on a plain abdominal X-ray during a regular checkup for diabetes and obesity. Although hepatic imaging modalities will lead to detection of the tumor, the diagnosis of a hepatic myelolipoma

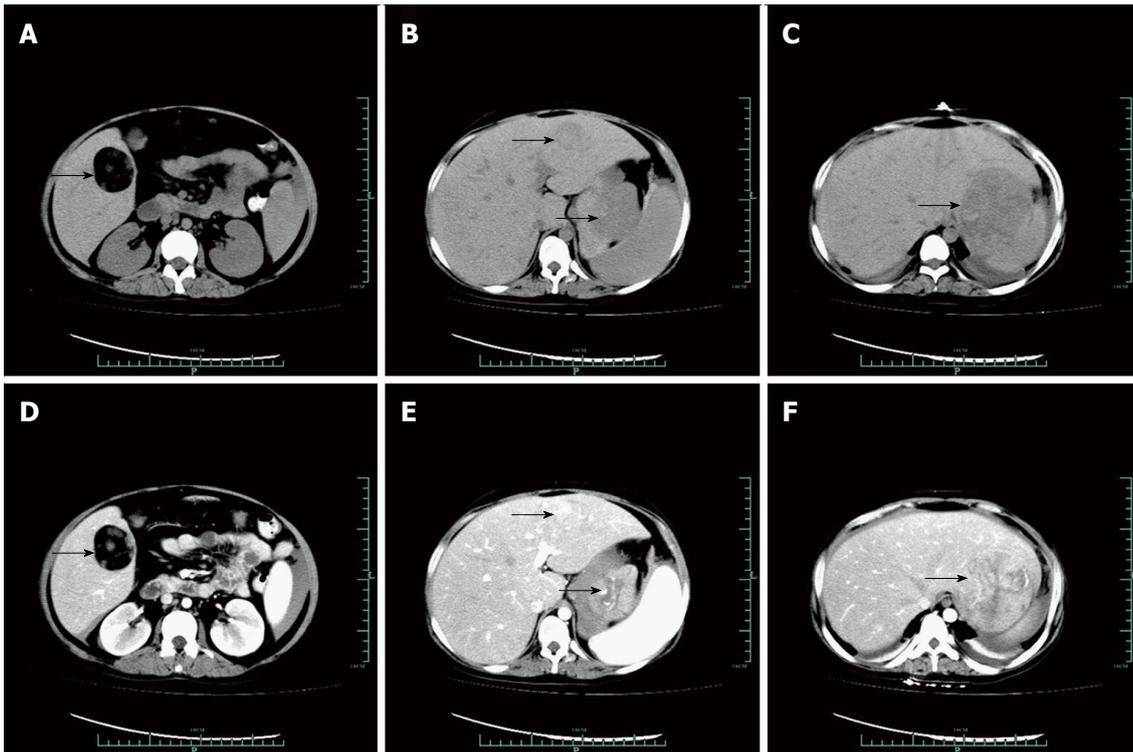
has to be confirmed by a histopathologic examination of the resected specimen. In the present study, we present the eleventh case of hepatic myelolipoma to be reported in the English-language medical literature. This is also the first case of the synchronous occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient. The clinical, imaging, and pathologic features of this case are described, and the subject of hepatic myelolipoma is briefly reviewed to deepen our understanding of it.

## CASE REPORT

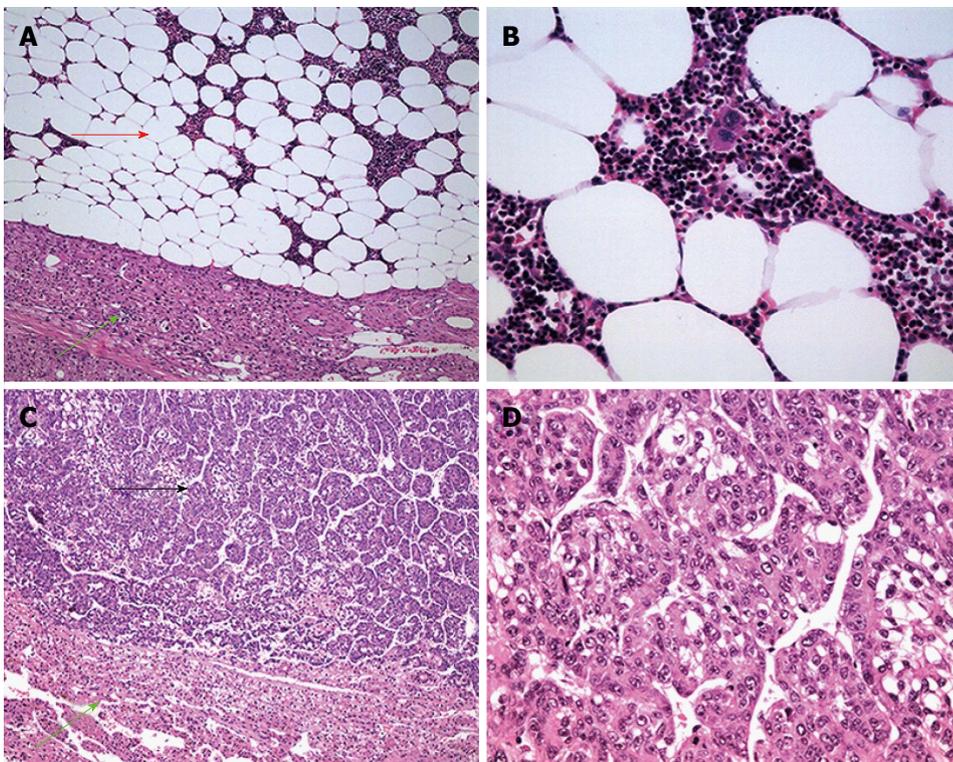
On November 28, 2014, a 26-year-old female was admitted to our hospital because of a 4-d history of upper abdominal pain. Her abdomen was soft, lax, and non-distended, with no palpable mass. The patient had no history of hepatitis B virus infection, hepatitis C virus infection or non-alcoholic fatty liver disease (NAFLD). Her family history was not significant. Abnormal laboratory results including alpha fetoprotein (AFP), 7529.2 ng/mL (normal, 20); carbohydrate antigen 125, 99.4 U/mL (normal, 0-35); serum creatinine, 42 μmol/L (normal, 45-84); serum sodium, 131 mmol/L (normal, 136-145); glutamyl transpeptidase, 103 U/L (normal, 7-32); fibrinogen, 4.45 g/L (normal, 2.00-4.00); and D-2-dimer, 9611 μg/L (normal, 0-700). The unenhanced CT images showed a well-defined low-density mass with adipose components in the right liver lobe, 4.2 cm × 4.1 cm in size (Figure 1A). Two inhomogeneous low-density masses were found in the left liver lobe, 8.6 cm × 7.7 cm and 2.6 cm × 2.6 cm in size (Figure 1B and C). In the contrast-enhanced CT images, the masses in both the right and the left liver lobe were heterogeneously enhanced (Figure 1D-F). Based on the results of the imaging examination, the mass in the right liver lobe was preliminarily considered to be a hamartoma, and the two masses in the left liver lobe were preliminarily considered to be HCCs.

After sufficient pre-operative preparation, a laparotomy was performed. One mass was found in the V section of the right liver lobe, and two masses were found in the left liver lobe, reflecting what was seen in the CT scan. We completed a right hepatectomy and a left hepatic lobectomy. Because the gallbladder was close to the tumor, a cholecystectomy was also performed. The intraoperative frozen pathology revealed that the tumor in the right liver lobe was a hepatic myelolipoma, and that the two tumors in the left liver lobe were HCCs.

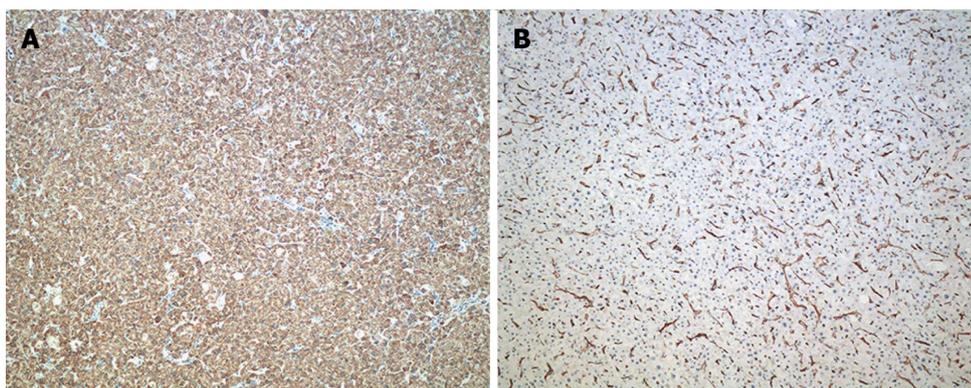
Macroscopically, the mass in the right liver lobe had a solid capsule that was 5.0 cm × 4.0 cm. The two masses in the left liver lobe were solid and were 9.5 cm × 6.5 cm × 5 cm and 3.2 cm × 2.0 cm in size, respectively. Microscopically, the tumor in the right liver lobe consisted of adipose tissue and hematopoietic elements containing erythroid tissue, megakaryocytes and myeloid colonies, consistent with a myelolipoma (Figure 2A and B). Tumor cells



**Figure 1 Computed tomography findings.** A: An unenhanced computed tomography (CT) image showing a well-defined low-density mass (arrow) with adipose components in the right liver lobe, 4.2 cm × 4.1 cm in size; B and C: Two inhomogeneous low-density masses (arrows) are shown in the left liver lobe, 8.6 cm × 7.7 cm and 2.6 cm × 2.6 cm in size, respectively; D, E and F: In the contrast-enhanced CT image, the masses in both the right and left liver lobes are heterogeneously enhanced.



**Figure 2 Microscopic examination.** A and B: The tumor (red arrow) in the right liver lobe consists of adipose tissue and hematopoietic elements containing erythroid tissue, megakaryocytes and myeloid colonies, consistent with a myelolipoma (A: HE, 100 ×; B: HE, 400 ×); C and D: The tumor cells (black arrow) in the left liver lobe are in a trabecular arrangement and are growing invasively with significant atypia, compatible with a malignant hepatocellular carcinoma (C: HE, 100 ×; D: HE, 400 ×). The areas marked by green arrows are normal liver tissue. HE: Hematoxylin and eosin.



**Figure 3** Immunohistochemical investigation. Hepatocyte (A) and CD34 (B) proteins were positive in the tumors of the left liver lobe (100 ×).

in the left liver lobe were in a funicular arrangement and showed invasive growth with significant atypia, compatible with malignant hepatic cancers (Figure 2C and D). Immunohistochemical investigation showed that hepatocyte and CD34 proteins were positive in the tumors of the left liver lobe (Figure 3), while AFP, GPC-3, HMB45, Melan-A and SMA were negative. Finally, the tumor in the right liver lobe was diagnosed as a hepatic myelolipoma, and the tumors in the left liver lobe were diagnosed as HCCs. After surgery, the patient developed an intra-abdominal infection and was hospitalized for 27 d. Unfortunately, two months later, a CT scan of the liver suggested the recurrence of the HCC. The patient received four transcatheter arterial chemoembolization (TACE) procedures and one iodine 131I metuximab injection in our hospital. However, the HCC metastasized to the lung eight months after surgery. The patient was then lost after nine months of follow-up.

## DISCUSSION

Myelolipoma is a rare type of benign, nonfunctioning tumor of mesenchymal origin, which is composed of various proportions of fat and hematopoietic cells<sup>[14]</sup>. As such, it resembles a site of extramedullary hematopoiesis. The adrenal gland is the most common site of myelolipomas; autopsy series have revealed the prevalence of myelolipomas in the adrenal gland at autopsy to be 0.08%-0.8%<sup>[2,15,16]</sup>. Extraadrenal myelolipomas are very rare<sup>[17]</sup>. They have been reported in the parietal pleura<sup>[18]</sup>, presacral area<sup>[19]</sup>, intrathoracic paravertebral area<sup>[20]</sup>, mediastinum<sup>[21,22]</sup>, gastric antrum<sup>[23]</sup>, perirenal tissue<sup>[24]</sup>, and right iliac fossa<sup>[25]</sup>. To date, only ten cases of hepatic myelolipomas have been reported in the English-language medical literature<sup>[3-12]</sup> (Table 1). In one of these cases, the hepatic myelolipoma was found in a HCC<sup>[6]</sup>. In the present study, we report the first case of the synchronous occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient. Table 2 summarizes the clinical data from all 11 cases of hepatic myelolipoma reported in the English-

language medical literature, including the present study. Continuous variables were summarized as the mean  $\pm$  the standard deviation (SD) and the range. Statistical analyses were conducted using SPSS version 20.0 for Windows (SPSS Inc., Chicago, IL, United States). The mean age of these patients was  $51.45 \pm 16.74$  years (range 25-76 years) and the male-female ratio was 5:6. Forty percent of patients were asymptomatic; most patients were symptomatic. The right liver lobe was the reported site of the myelolipoma in nine (81.82%) of the patients; the left liver lobe was the reported site in 2 patients. The mean tumor size was  $6.69 \pm 4.71$  cm (range 1.4-15 cm). Seven patients (63.64%) underwent tumor resection.

The etiology of hepatic myelolipoma remains uncertain. An ectopic adrenal gland is one hypothesis<sup>[8]</sup>. Most myelolipomas are reported in the adrenal gland. Anatomically, the right adrenal gland is adjacent to the right lobe of the liver, and an ectopic adrenal gland rarely appears in liver parenchyma<sup>[8]</sup>. Except for two cases, hepatic myelolipomas were found in the subcapsular region of the right liver lobe, including in our case. Emboli from bone marrow represent another hypothesis for the histogenesis of these lesions<sup>[4]</sup>. Although the gross appearance of a myelolipoma suggests a neoplastic origin, light and electron microscopy studies have revealed the polyclonal character of the hematopoietic cells<sup>[26]</sup>. The definitive stimulus that causes the hematopoietic and fat cells to proliferate remains enigmatic. Several studies have suggested that tissue necrosis is the basic stimulus<sup>[6,26]</sup>. For example, Van Hoe *et al*<sup>[6]</sup> speculated that the presence of foci of tumor necrosis may be associated with the development of a myelolipoma. Malignant tumors, hypertension, obesity, burns, and endocrinopathies have also been reported to be associated with the development of a myelolipoma<sup>[26]</sup>.

The preoperative diagnosis of a hepatic myelolipoma is challenging. The appearance of myelolipomas on US, CT, and MRI images depends on the proportions of fat relative to myelogenous components<sup>[6]</sup>. US imaging reveals the myelolipoma to be a hyperechoic lesion<sup>[5,8]</sup>. Unenhanced CT images usually show

**Table 1 Summary of clinical data on patients with hepatic myelolipoma in the English literature**

Ref.	Year	Sex/age	Symptom	location	Imaging method	Number	Size (cm)	Treatment
Present case	2016	F/26	Upper abdomen pain	Right liver lobe	CT	Solitary	5.0	Resection
Menozzi <i>et al</i> <sup>[5]</sup>	2016	F/72	Asymptomatic	Right liver lobe	US, CT, CEUS	Solitary	3.5	NA
Radhi <sup>[4]</sup>	2010	M/76	Symptoms related to a urinary tract infection	Segment VIII of the right liver	US, CT	Solitary	3.2	NA
Savoie-Coll <i>et al</i> <sup>[5]</sup>	2000	M/25	Asymptomatic	Segment IV	MRI	Solitary	9.0	Left hepatectomy
Van <i>et al</i> <sup>[6]</sup>	1994	M/57	Asymptomatic	Right liver lobe	US, CT	Solitary	1.4	Hemihepatectomy
Moreno <i>et al</i> <sup>[7]</sup>	1991	M/40	Malaise, anorexia, fever	Right liver lobe	X-rays, CT, Radioisotope scan	Solitary	15.0	Right hepatic lobectomy
Nishizaki <i>et al</i> <sup>[8]</sup>	1989	F/56	Right upper abdominal pain	Right post segment subcapsule	US; CT, Hepatic arteriography	Solitary	5.5	Right posterior segmentectomy
Kaurich <i>et al</i> <sup>[9]</sup>	1988	F/42	Asymptomatic	Left liver lobe	US; CT, Hepatic arteriography	Solitary	6.0	Resection
Mali <i>et al</i> <sup>[10]</sup>	1986	M/63	Hepatomegaly	Right liver lobe subcapsule	US; CT	Solitary	15.0	No treatment
Rubin <i>et al</i> <sup>[11]</sup>	1984	F/56	Abdominal pain, RUQ tenderness	Right post segment subcapsule	CT, Hepatic arteriography	Solitary	8.0	Resection
AFIP case <sup>[12]</sup>	1976	F/53	NA	Left liver lobe	NA	Solitary	2.0	NA

AFIP: Armed Forces Institute of Pathology; M: Male; F: Female; NA: Not available; US: Ultrasound; CT: Computed tomography; MRI: Magnetic resonance imaging; CEUS: Contrast-enhanced ultrasound.

**Table 2 Summary of clinical data from all 11 cases of hepatic myelolipoma**

	<i>n</i> (%) or mean ± SD (range)
Age (yr) ( <i>n</i> = 11)	
Mean	51.45 ± 16.74 (25-76)
Sex (male/female), (male %) ( <i>n</i> = 11)	5/6 (45.45)
Symptoms ( <i>n</i> = 10)	
Asymptomatic	4 (40.00)
Symptomatic ( <i>n</i> = 10)	
Abdominal pain	3 (30.00)
Symptoms related to a urinary tract infection	1 (10.00)
Malaise	1 (10.00)
Anorexia	1 (10.00)
Fever	1 (10.00)
Hepatomegaly	1 (10.00)
Location ( <i>n</i> = 11)	
Right liver lobe	9 (81.82)
Left liver lobe	2 (18.18)
Mean size (cm) ( <i>n</i> = 11)	6.69 ± 4.71 (1.4-15)
Operation ( <i>n</i> = 11)	
Resection	7 (63.64)
No resection	1 (9.09)
Not available	3 (27.27)

that the tumor is well-encapsulated and has low-density areas varying from -69 to 28 HU as a result of intratumoral hemorrhage and varying proportions of fat and bone marrow elements<sup>[6,9]</sup>. On enhanced CT images, the tumor appears moderately enhanced. The area of low density remains hypoattenuated<sup>[27]</sup>. On T1-weighted MR images, the mass usually appears well margined with a capsule, shows heterogeneous hyperintensity and contains necrosis. Hepatic arteriography reveals a hypervascular mass with an avascular zone<sup>[8,11]</sup>. On T2-weighted images, the

mass shows heterogeneous low-signal intensity. After the administration of a gadolinium bolus, the lesion may show delayed heterogeneous enhancement<sup>[5,28]</sup>. Hepatic myelolipoma should be distinguished from other hepatic lesions that cause lipomatous masses, including lipomas, angiomyolipomas, metastatic dermoid tumors, Langerhans cell histiocytosis, and focal fatty infiltration<sup>[29]</sup>. Areas of fatty degeneration can also be observed occasionally in HCCs and hepatic adenomas<sup>[30]</sup>.

Although myelolipomas are benign, these types of tumor can be symptomatic and may increase in size. Thus, surgical intervention is warranted when the tumor is symptomatic or difficult to diagnose. In the present study, the hepatic myelolipoma could not be preoperatively diagnosed precisely. Furthermore, two HCCs were synchronously found in the left liver lobe. HCC is the sixth most common malignancy worldwide and has the third highest mortality among cancer patients<sup>[31,32]</sup>, for whom surgical resection is the most common and effective therapeutic method. Accordingly, we performed a right hepatectomy and a left hepatic lobectomy to completely resect the hepatic myelolipoma and HCCs. Because the gallbladder was close to the tumor, a cholecystectomy was also performed. Histopathologic and immunohistochemical analyses of the surgical specimen confirmed the diagnosis of hepatic myelolipoma and HCCs. Microscopically, the hepatic myelolipoma was composed of fat cells and hematopoietic cells, including mature and developing myeloid, erythroid, and megakaryocytic cells. Marrow-like areas were also clearly observed.

In conclusion, hepatic myelolipoma is extremely rare. To our knowledge, only 10 cases have been

reported in the English-language medical literature. In one of these cases, the myelolipoma was found within a HCC. In the present study, we report the first case of the synchronous occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient, who received a right hepatectomy, a left hepatic lobectomy, and a cholecystectomy.

## COMMENTS

### Case characteristics

A 26-year-old female was admitted to our hospital because of a 4-d history of upper abdominal pain.

### Clinical diagnosis

Abdomen was soft, lax, and non-distended, with no palpable mass.

### Differential diagnosis

Differential diagnoses included lipomas, angiomyolipomas, metastatic dermoid tumor, and Langerhans cell histiocytosis.

### Laboratory diagnosis

Abnormal laboratory results: alpha fetoprotein (AFP), 7529.2 ng/mL (normal, 20); carbohydrate antigen 125, 99.4 U/mL (normal, 0-35); serum creatinine, 42  $\mu$ mol/L (normal, 45-84); serum sodium 131 mmol/L (normal, 136-145); glutamyl transpeptidase, 103 U/L (normal, 7-32); fibrinogen, 4.45 g/L (normal, 2.00-4.00); and D-2-dimer, 9611  $\mu$ g/L (normal, 0-700).

### Imaging diagnosis

The unenhanced computed tomography (CT) images showed a well-defined low-density mass with adipose components in the right liver lobe, 4.2 cm  $\times$  4.1 cm in size. Two inhomogeneous low-density masses were found in the left liver lobe, 8.6 cm  $\times$  7.7 cm and 2.6 cm  $\times$  2.6 cm in size. In the contrast-enhanced CT images, the masses in both the right and left liver lobes were heterogeneously enhanced. Based on the results of the imaging examination, the mass in the right liver lobe was preliminarily considered to be a hamartoma, and the two masses in the left liver lobe were preliminarily considered to be hepatocellular carcinoma (HCC).

### Pathological diagnosis

Macroscopically, the two masses in the left liver lobe were solid and were 9.5 cm  $\times$  6.5 cm  $\times$  5 cm and 3.2 cm  $\times$  2.0 cm in size, respectively. The mass in the right liver lobe had a capsule, was solid and 5.0 cm  $\times$  4.0 cm in size. Microscopically, the tumor in the right liver lobe consisted of adipose tissue and hematopoietic elements containing erythroid tissue, megakaryocytes and myeloid colonies, which was consistent with a myelolipoma. The tumor cells in the left liver lobe were in a funicular arrangement and had invasive growth with significant atypia, which was compatible with malignant hepatic cancer. Immunohistochemical investigation showed that hepatocyte and CD34 proteins were positive in the tumors of the left liver lobe, while AFP, GPC-3, HMB45, Melan-A, and SMA were negative. Finally, the tumor in the right liver lobe was diagnosed as a hepatic myelolipoma, and the tumors in the left liver lobe were diagnosed as HCCs.

### Treatment

The authors performed a right hepatectomy, a left hepatic lobectomy and a cholecystectomy.

### Related reports

Hepatic myelolipoma is extremely rare. To date, only 10 cases have been reported in the English-language medical literature.

### Experiences and lessons

In the present study, the authors present the first case of the synchronous

occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient. Preoperative diagnosis of hepatic myelolipoma is challenging. Surgery is the most effective treatment for the tumor.

### Peer-review

This study highlights the diagnosis and treatment of the first case of the synchronous occurrence of hepatic myelolipoma and HCCs in different liver sections of one patient. This study also presents a literature review to deepen our understanding of hepatic myelolipoma. The information included is worthwhile to the reader.

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**P- Reviewer:** Goral V, Lee CL    **S- Editor:** Gong ZM    **L- Editor:** A  
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