

## Original Article

# Lesions of biliary hamartoms can be diagnosed by ultrasonography, computed tomography and magnetic resonance imaging

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Received August 7, 2014; Accepted September 15, 2014; Epub October 15, 2014; Published October 30, 2014

**Abstract:** Aims: This study is to compare the value of ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) in the diagnosis of biliary hamartomas. Methods: From 2003 to 2013, 15 cases of liver biopsies were found to have biliary hamartomas, including 3 cases excluded from this study. The remaining 12 patients were 7 women and 5 men aged from 28 to 66 years (mean age, 53 years). Ultrasonography examinations were performed by two different scanners using 3.5- to 5.0-MHz convex array transducers. Eight patients were examined by plain and contrast CT including 2 cases with Sensation Cardiac 64 and 6 cases with Somatom definition dual source CT. MRI was performed by a 3 T system using an eight-channel phased-array torso coil. Using pathology slides, lesions were classified into class 1 (predominantly solid), class 2 (intermediate, mixed solid and cystic), and class 3 (predominantly cystic). Results: Patients with biliary hamartomas have distributed lesions. Ultrasonography can be used to diagnose biliary hamartomas, with occasional mistakes. CT is effective in the diagnosis of biliary hamartomas. MRI is capable of diagnosing biliary hamartomas. Histopathological examination provides a direct means to classify the degrees of lesions caused by biliary hamartomas. Conclusions: Biliary hamartomas showed characteristic features on imaging findings by ultrasonography, CT, and MRI. Although abdominal ultrasonography could detect suspected biliary hamartomas, the best choice for further diagnosis is MRI examination instead of CT. In addition, follow-up ultrasonography examinations are necessary.

**Keywords:** Biliary hamartoms, ultrasonography, computed tomography, magnetic resonance imaging

## Introduction

Biliary hamartomas are benign bile duct malformations that are also referred to as Von Meyenburg complex [1]. The lesions of biliary hamartomas contain a variable number of dilated and twisty bile ducts that are lined by a single layer of columnar or cuboidal epithelium embedded within a hyalinized fibrous stroma. Biliary hamartomas are considered to be benign liver lesions, but they are possibly misdiagnosed as liver metastases, cirrhosis, microabscesses, etc. Therefore, it is important to apply differential diagnosis methods for biliary hamartomas according to their radiological features.

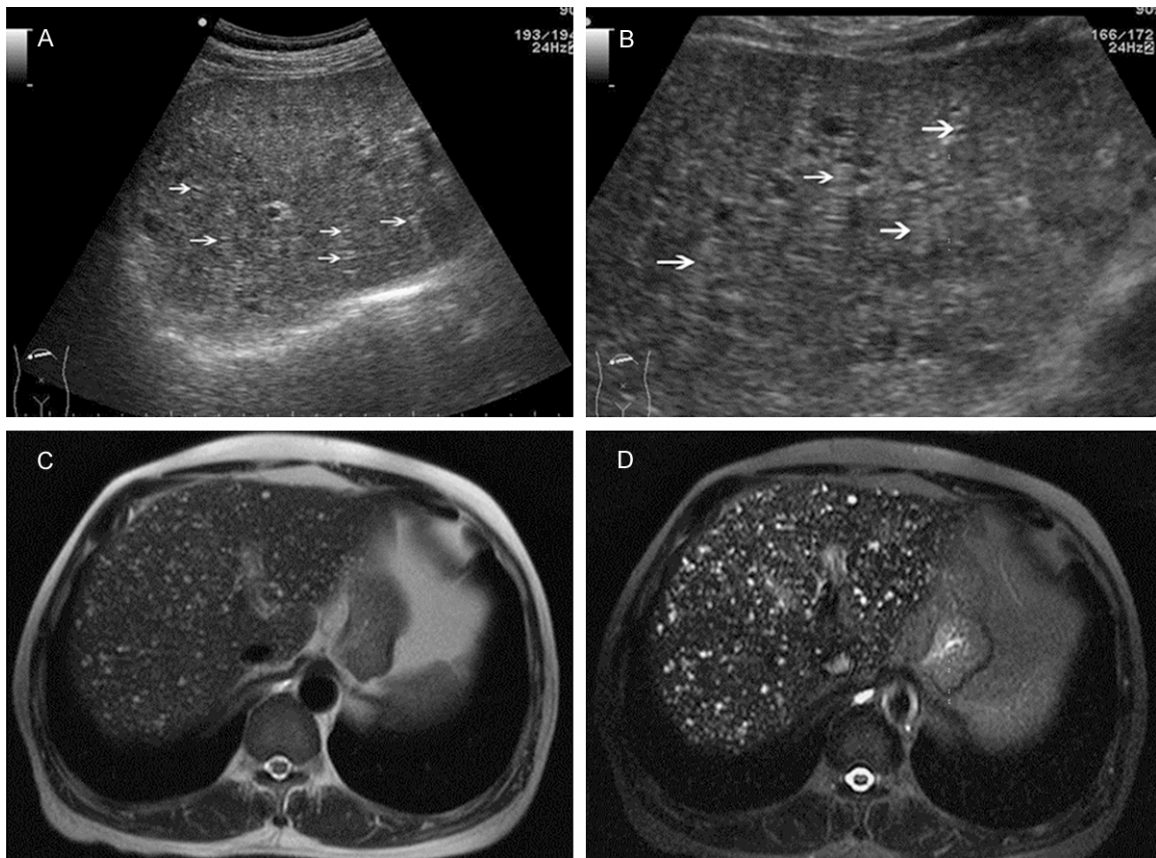
Biliary hamartomas are considered to be congenital bile duct malformations and a conse-

quence of interrupted remodeling of ductal plates during the phase of embryologic development of small intra-hepatic bile ducts [2]. The incidence of biliary hamartomas is very low, ranging between 0.6% and 5.6% of all cases according to autopsy [3]. Lin S et al. [4] reported that only six patients (0.35%) were confirmed to have biliary hamartomas among 1697 liver biopsies. The rate increases with age and chronic liver disease [5]. In gross specimens, biliary hamartomas demonstrate small, whitish or gray-yellow lesions with diameters usually smaller than 5 mm. In addition, lesions of biliary hamartomas can also coalesce into larger cystic lesions. Biliary hamartomas typically appear as multiple lesions and scatter throughout the liver or predominantly in either of the liver lobe. However, solitary lesions have been reported by

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**Table 1.** Information and test results of patients

No.	Sex/Age (yr)	Clinical data	Distribution	Ultrasonography	Imaging findings				
					Computed tomography		Magnetic resonance imaging		
					Plain scan	Enhancement	T1WI	T2WI	Enhancement
1	M/56	Gastric tumor	In the right anterior lobe and peripherally located	Hypoechoic with comet-tail echoes	Hypodense	Rim-like enhancement	Hypo-intense	Hyper-intense	Rim-like enhancement
	F/61	Colorectal tumor	Uniformly throughout the whole liver	Hypo- and hyperechoic lesions with equal sign	Hypodense	No	Hypo-intense	Hyper-intense	No
3	M/66	Gastric tumor	Uniformly throughout the left lobe	Hypoechoic with comet-tail echoes	Hypodense	No	Hypo-intense	Hyper-intense	No
4	F/44	Hepatitis B	The whole liver and peripherally located	Heterogeneous and hyperechoic signal	Hypodense	No	Hypo-intense	Hyper-intense	Rim-like enhancement
5	F/65	Colorectal tumor	Uniformly throughout the whole liver	Hypo- and hyperechoic lesions with equal sign	-	-	Hypo-intense	Hyper-intense	No
6	F/28	No symptom	In the right anterior lobe and peripherally located	Heterogeneous and hyperechoic signal	Hypodense	Circular enhancement	Hypo-intense	Hyper-intense	Rim-like enhancement
7	F/53	Thyroid tumor	Uniformly throughout the whole liver	Hypoechoic lesions with comet-tail echoes	Hypodense	No	Hypo-intense	Hyper-intense	Rim-like enhancement
8	M/48	No symptom	Uniformly throughout the whole liver	Hypo- and hyperechoic lesions with equal sign	-	-	Hypo-intense	Hyper-intense	Rim-like enhancement
9	F/57	Lung cancer	In the left lobe and peripherally located	Heterogeneous and hyperechoic signal	Hypodense	Rim-like enhancement	Hypo-intense	Hyper-intense	Rim-like enhancement
10	F/49	Hepatitis B	Uniformly throughout the whole liver	Hypo- and hyperechoic lesions with equal sign	-	-	Hypo-intense	Hyper-intense	No
11	M/62	Colorectal tumor	The whole liver and peripherally located	Heterogeneous and hyperechoic signal	Hypodense	No	Hypo-intense	Hyper-intense	No
12	M/45	Hepatitis B	Uniformly throughout the whole liver	Hypoechoic lesions with comet-tails	-	-	Hypo-intense	Hyper-intense	Rim-like enhancement



**Figure 1.** A 48-year-old male patient with biliary hamartomas distributed uniformly throughout the whole liver. (A) Ultrasound image showing uniformly small hypo- or hyper-echoic lesions presented as “equal sign” (white arrows) with comet-tail echoes. (B) Image in (A) after using zoom function, showing posterior acoustic enhancement clearly (white arrows). (C) T2-weighted magnetic resonance image showing multiple small hyperintense lesions. (D) “Heavily” T2-weighted magnetic resonance image with fat suppression sequences.

Saul H and Semelka RC [6, 7]. Under the microscope, biliary hamartomas demonstrate groups of tortuous, dilated intra-hepatic bile ducts that are lined by a single layer of columnar, cuboidal or flattened epithelium and embedded in a dense fibrous stroma. Bile materials can be observed in some of the cystic ducts [8]. Biliary hamartomas are benign asymptomatic lesions without clinical significance, but are complicated with microscopic polyangiitis [9] and their malignant transformation to cholangiocarcinoma has been reported [10, 11]. Imaging features of biliary hamartomas are various [7, 8, 12, 13] and have not been well illustrated yet.

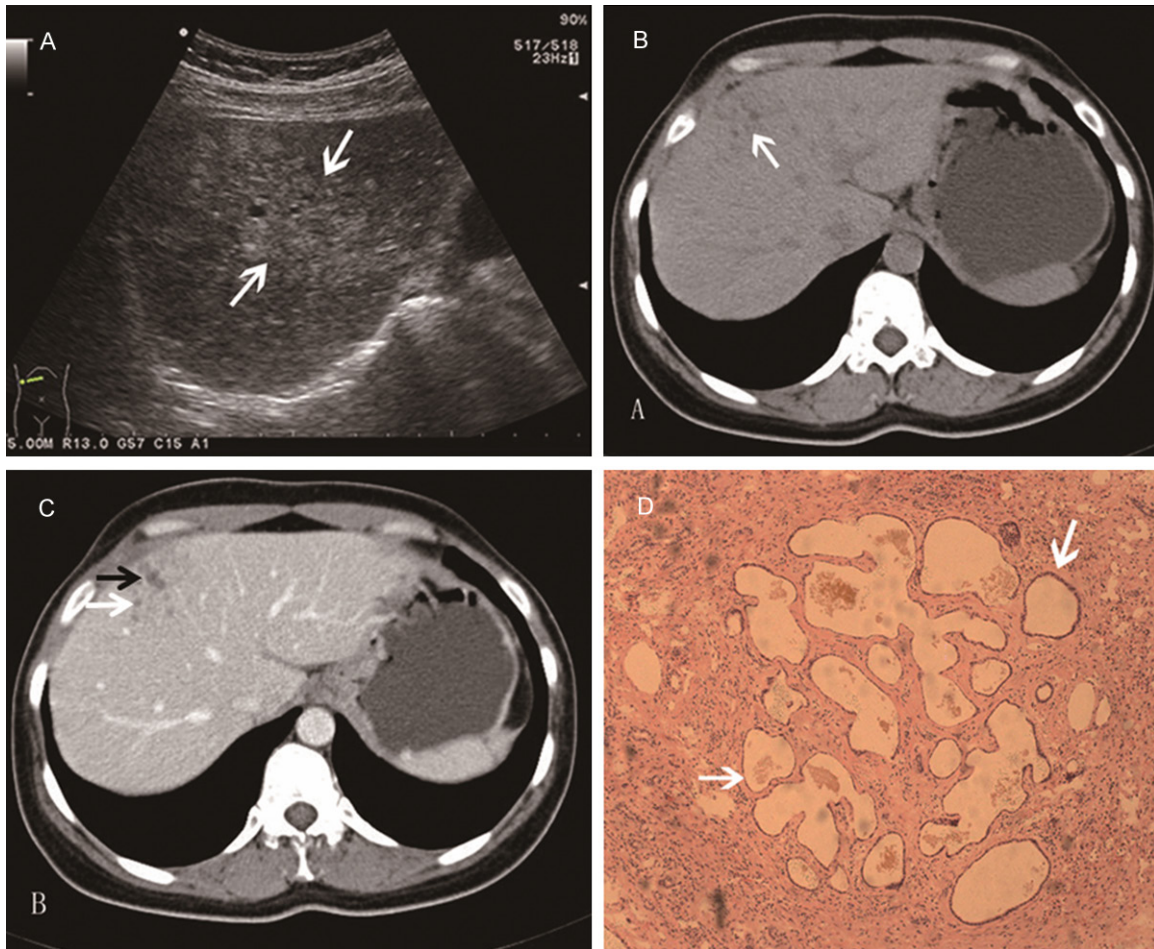
In this study, we retrospectively analyze the clinical and imaging features of 12 cases uncovered in health check-up or pre-operative examinations by ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI), and summarize the imaging characteristics. To our knowledge, only a few studies have evaluated the features of biliary

hamartomas, and there is no literature that compares the value of ultrasonography, CT and MRI in the diagnosis of biliary hamartomas.

## Materials and methods

### Patients

After reviewing pathologic records from 2003 to 2013, 15 cases of liver biopsies were found to have biliary hamartomas, including 3 cases without imaging studies at our hospital that were excluded from this study. The remaining 12 patients were 7 women and 5 men aged from 28 to 66 years (mean age, 53 years). Among the 15 patients, hepatic lesions were first found by ultrasonography in 11 cases, including 2 cases found accidentally during routine physical check-up, 3 cases found in abdominal ultrasonography examination for hepatitis B virus infection and 6 cases diagnosed during treatment for primary tumors (2 cases of gastric tumor, 3 cases of colorectal



**Figure 2.** A 28-year-old female patient with biliary hamartomas scattered in the right anterior liver lobe. A: Ultrasonography showing biliary hamartomas with multiple small cysts less than 10 mm in diameter. The white arrows indicate heterogeneous and slightly hyperechoic signals. B: Axial CT plain scan showing several hypoattenuated lesions (white arrow) with irregular or oval shapes. C: CT image showing lesions with no enhancement (white arrow) in portal venous phase of contrast CT, but with sharp border. A few lesions showed circular enhancement in portal venous phase (black arrow). D: Histological examination showing lesions containing a variable number of irregular and tortuous dilated bile ducts (arrows) embedded in a dense fibrous stroma.

tumor and 1 case of thyroid tumor). Only 1 patient was first detected by CT for lung cancer. All imaging studies including ultrasonography, CT and MRI were performed in 8 patients. Both of ultrasonography and MRI scans were performed in 4 patients. Patient information and all test results are given in **Table 1**. All procedures were approved by the Ethics Committee of Shandong University. Informed consents were obtained from all patients or their families.

#### *Ultrasonography*

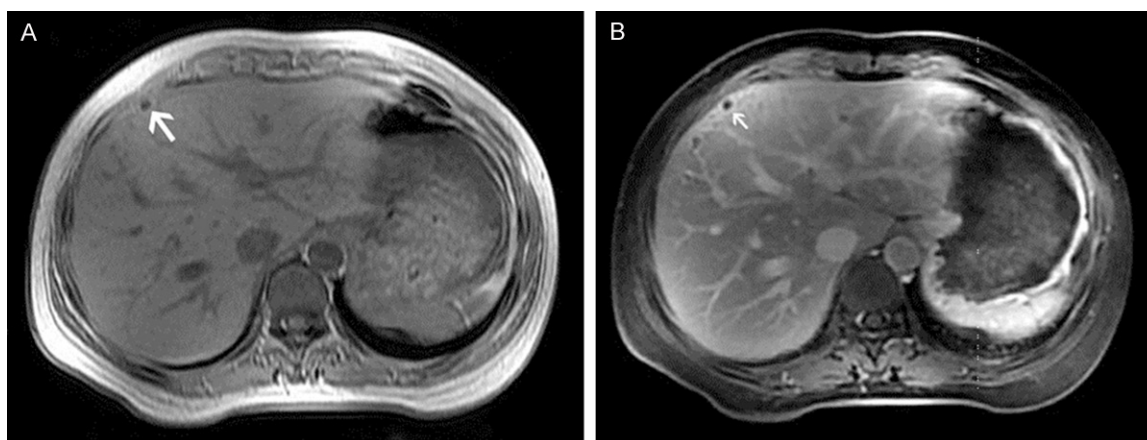
Ultrasonography examinations were performed by two different scanners (GE LOGIQ 9, GE Healthcare, Milwaukee, WI; and Aloka Prosound

Alpha 10, Aloka, Tokyo, Japan) using 3.5- to 5.0-MHz convex array transducers. In 11 cases, two- to ten-time follow-up ultrasonography examinations were performed during the following 1-9 years to verify the diagnosis.

#### *CT*

Eight patients were examined by plain and contrast CT including 2 cases with Sensation Cardiac 64 (Siemens, Forchheim, Germany) and 6 cases with Somatom definition dual source CT (Siemens, Forchheim, Germany). For enhanced CT, contrast medium was injected at a rate of 3.0 ml/s through the antecubital vein using a power injector. A dynamic enhancement





**Figure 3.** A 56-year-old male with biliary hamartomas. A: T1-weighted magnetic resonance image showing a small lesion located in the subcapsula with low signal intensity (arrow). B: T1-weighted magnetic resonance image showing thin peri-lesional rim enhancement (arrow) that is apparent in portal venous phase.

scan was performed for hepatic arterial, portal venous and delayed phases.

## MRI

MRI was performed by a 3 T system (Signa Excite HDx, GE Healthcare, Milwaukee, Wisconsin, USA) using an eight-channel phased-array torso coil. SE T1WI and FSE T2WI sequences with and without fat suppression were performed in all cases. Enhanced SE T1WI with and without fat suppression was also performed. A high-pressure syringe was used to administer Gadolinium-diethylene triamine pentacetate acid (0.1 mmol/kg) at a rate of 3 ml/s through intravenous catheter. Data were obtained in arterial, portal venous and delayed phases.

## Histopathological examinations

The original pathology slides were reevaluated. Lesions were subsequently classified into class 1 (predominantly solid lesions with narrow bile channels), class 2 (intermediate, with mild or focal dilatation of bile channels), and class 3 (predominantly cystic) using previous described nomenclature [14].

## Results

### *Patients with biliary hamartomas have distributed lesions*

To observe how biliary hamartomas cause lesions on patients, histological investigation

was performed. The results showed that biliary hamartomas led to innumerable tiny lesions that were distributed evenly throughout the whole liver in 8 patients, and distributed predominantly in the right anterior liver lobe in 2 cases and in the left liver lobe in 2 cases. Among these patients, 7 patients showed equally distributed peripheral and central lesions, and the other 5 patients showed predominantly peripherally located lesions. The lesions varied in size from 1 to 10 mm in diameter. In addition, several common round or oval cysts that were larger than 10 mm in diameter were noted in 5 cases. These results demonstrated that patients with biliary hamartomas had distributed lesions.

### *Ultrasonography can be used to diagnose biliary hamartomas, with occasional mistakes*

To further investigate the lesions caused by biliary hamartomas, ultrasonography was performed. According to ultrasound images, all cases had numerous tiny hypo- or hyperechoic lesions with comet-tail echoes. A new phenomenon called “equal sign” was observed for the first time. Some dot-like lesions were presented as “two short parallel lines (equal signs)” corresponding to their front and rear wall with lateral echoic loss (**Figure 1A**). When zoom function was available, micro-cystic lesions with posterior acoustic enhancement were observed (**Figure 1B**). In contrast to normal liver, the areas with biliary hamartomas were heterogeneous and slightly hyperechoic (**Figure 2A**). Of

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**Table 2.** Histopathological types and imaging findings

Type	Cases	Imaging findings					
		Ultrasonography	Computed tomography		Magnetic resonance imaging		
			Plain Scan	Enhancement	T1WI	T2WI	Enhancement
Class 1	0	-	-	-	-	-	-
Class 2	8	Hypo- and hyperechoic lesions with equal sign	Hypodense	3 cases enhancement	Hypo-intense	Hyper-intense	7 cases enhancement
Class 3	4	Hypoechoic lesions with comet-tail echoes	Hypodense	No	Hypo-intense	Hyper-intense	No

note, 3 cases were mistaken for hepatic fibrosis by preoperative ultrasonography examination. These data indicated that ultrasonography could be used to diagnose biliary hamartomas, with occasional mistakes.

### *CT is effective in the diagnosis of biliary hamartomas*

To assist the diagnosis of biliary hamartomas by ultrasonography, CT examination was used on 8 cases in this study. On plain CT, biliary hamartomas were presented as multiple hypodense lesions with irregular or oval shapes. Of all the patients, 4 had lesions distributed throughout the liver, 2 had lesions located in the right anterior lobe (**Figure 2B**), and 2 had lesions located in the left lobe. After intravenous injection of contrast medium, 5 cases showed no enhancement on any phases of contrast CT, but the border became sharper in portal venous and delayed phases. In 3 cases, several lesions showed thin rim-like enhancement in the delayed phase (**Figure 2C**). These data suggested that CT was also effective in the diagnosis of biliary hamartomas.

### *MRI is capable of diagnosing biliary hamartomas*

To investigate the lesions of biliary hamartomas on another aspect, MRI was employed. According to MRI, biliary hamartomas were presented as hypo-intense on T1-weighted images (**Figure 3A**) and hyper-intense on T2-weighted images (**Figure 1C**) with or without fat-suppression. On “heavily” T2-weighted sequences, the signal intensity of the lesions was enhanced and the lesions became more conspicuous (**Figure 1D**). Gadolinium-enhanced images showed peripheral rim-like enhancement (**Figure 3B**) in 7 patients but no enhancement in the other 5 patients. These data demonstrated that MRI was also capable of diagnosing biliary hamartomas.

### *Histopathological examination provides a direct means to classify the degrees of lesions caused by biliary hamartomas*

To complement imaging investigations by ultrasonography, CT and MRI, histopathological examination was also used. Histological diagnosis was based on wedge biopsy at surgery on 6 patients. For the other 6 patients, the diagnosis was performed by core-needle biopsy following sonographic guidance. Histological examinations showed that multiple irregular and tortuous dilated bile ducts were lined by a single layer of columnar epithelium embedded within a dense fibrous stroma (**Figure 2D**). Most lesions (8 cases) were classified as intermediate (class 2), showing mild focal dilatation of bile channels. For the other 4 patients, cystic lesions were predominantly observed with prominent dilated bile channels (class 3) (**Table 2**). These data indicated that histopathological examination provided a direct means to classify the degrees of lesions caused by biliary hamartomas.

## Discussion

Using ultrasound, previous studies have described biliary hamartomas as non-specific hypo- or hyperechoic tiny lesions [15, 16]. In this study, a new phenomenon called “equal sign” was first described, which might be due to the front and rear walls of these small foci with lateral echoic loss. Luo et al. [15] speculated that the sign of multiple comet-tail echoes might be specific ultrasonography feature. The cystic feature of dilated bile duct most likely accounted for this appearance that resulted in good transmission of sound beam.

On plain CT images, biliary hamartomas are usually depicted as hypodense small foci. On contrast-enhanced CT images, biliary hamartomas are described as non-enhancing struc-

tures in most of the reported cases [12, 14]. In our study, 5 cases showed no enhancement in artery phase, but the lesions became more conspicuous in portal and delayed phases. The other 3 cases showed thin rim-like enhancement in delayed phase. The reason might be that more imaging details were manifested with advanced spiral CT with higher resolution or newer scanning techniques such as faster rates of contrast administration.

On MRI images, with respect to the normal liver parenchyma, the lesions were presented as small cystic nodular structures and were hypointense on T1-weighted images and hyperintense on T2-weighted images. On “heavily” T2-weighted images, the signal intensity was increased and almost equaled to that of cerebrospinal fluid. According to magnetic resonance cholangiopancreatography, the lesions did not demonstrate communications with bile duct that shows normal appearance [7, 12]. On diffusion-weighted imaging, the multiple lesions displayed decreased signal intensity with increased b-values that indicated free diffusion [17]. Previous studies described the lesions as rim enhancement on post-gadolinium images [7, 18]. Tohme-Noun C et al. [19] reported that gadolinium-enhanced images showed mural nodal enhancement in 9 of 10 patients. In our study, we observed peripheral rim-like enhancement in 7 cases during the arterial phase with persistence of the enhancement pattern on the late images. The other 5 cases showed no enhancement in any contrasted phases. According to histopathological examinations, there were no prominent vessels within or surrounding the biliary hamartoma lesions. The rim-like enhancement pattern corresponded to the peri-lesional compressed hepatic parenchyma and inflammatory cell infiltration. In addition, we found that the 7 rim enhancement cases belonged to class 2 (mild focal dilatation of bile channels), implying more inflammatory cell infiltration. In the 7 cases, 5 patients underwent CT scanning, but only 3 cases showed thin rim-like enhancement in delayed phase, probably due to the fact that MRI had more soft tissue contrast resolution than CT.

The most important value of the imaging features of biliary hamartomas is to differentiate the lesion from multiple liver metastases.

Commonly speaking, small metastases usually show various degrees of enhancement on contrast CT or MRI. Typically, metastasis lesions vary in size and are not evenly distributed. Diffuse primary hepatocellular carcinoma often occurs in cirrhotic patients and is rarely shown as cystic lesions on ultrasonography or CT. Considered as part of the spectrum of fibropolycystic liver diseases, biliary hamartomas may be confused with simple hepatic cyst and polycystic liver disease. Simple hepatic cyst is usually presented as round shape with random distribution. In addition, simple hepatic cyst is larger in diameter and fewer in number. According to histological examinations, both lesions are lined with bile duct epithelium and are of congenital development origin, but the cystic biliary hamartoma is surrounded by a thicker zone of fibrous tissue that separates it from peri-lesional normal hepatic parenchyma. Hepatic fibrosis is easy to be confused with small, dot-like lesions of biliary hamartomas on ultrasound images because the liver echo texture is heterogeneous. However, they can be easily distinguished by CT and MRI. Microabscesses may appear as multiple widely scattered lesions and hypoechoic nodules or poorly defined areas, but they usually appear as little or no enhancement through transmission.

Some researchers pointed out that it might be possible to make an accurate diagnosis of biliary hamartomas by imaging while liver biopsy was not necessary. In our study, we demonstrated that accurate diagnosis of biliary hamartomas could be made via advanced imaging modalities and long-term imaging follow-ups. Among the 12 cases examined only by ultrasonography, 6 cases were diagnosed as biliary hamartomas, 3 cases were mistaken for hepatic fibrosis and the remaining 3 cases were suggested to be diffusion disease. For the 8 cases with CT scanning, only 3 cases were diagnosed as biliary hamartomas. A study showed that about 44% of biliary hamartomas remained occult on CT [14]. MRI exhibited higher diagnosis rate with 10 cases being diagnosed as biliary hamartomas because of its higher soft tissue contrast resolution. When all imaging results were comprehensively analyzed, 11 cases of biliary hamartomas were revealed.

In conclusion, biliary hamartomas showed characteristic features on imaging findings, such as multiple small comet-tail echoes and

“equal sign” on ultrasonography, innumerable tiny hypodense lesions on CT, high signal on T2-weighted images, and peripheral rim-like enhancement on post-gadolinium images on MRI. Through comprehensive analysis of all images, a correct diagnosis of biliary hamartomas might be obtained. Currently, more and more people go to hospital for health examination and most of them choose abdominal ultrasonography, which detects suspected biliary hamartomas. The best choice for further diagnosis is MRI examination instead of CT. In addition, follow-up ultrasonography examinations are necessary.

## Acknowledgements

This work was supported by Shandong Province Government Medical Grant (No. 2012BSB-14068).

## Disclosure of conflict of interest

None.

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