Review

Management of simple hepatic cyst

Running title: simple hepatic cyst

Key words: simple hepatic cyst, fenestration, aspiration, diagnosis, management

Tetsuya Shimizu, Masato Yoshioka, Yohei Kaneya, Tomohiro Kanda, Yuto Aoki, Ryota Kondo, Hideyuki Takata, Junji Ueda, Youichi Kawano, Atsushi Hirakata, Akira Matsushita, Nobuhiko Taniai, Yasuhiro Mamada, Hiroshi Yoshida

Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery,
Nippon Medical School, Tokyo, Japan

Corresponding author: Tetsuya Shimizu, MD

Address: Department of Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

Telephone: 81-3-5814-6239, Facsimile: 81-3-5685-0989

E-mail address: tetsuya@nms.ac.jp

Key words: simple hepatic cyst, fenestration, aspiration, diagnosis, management
Abstract

Simple hepatic cysts are typically saccular, thin-walled masses with fluid-filled epithelial lined cavities that arise from aberrant bile duct cells during embryonic development. With the development of diagnostic modalities such as ultrasonography, computed tomography and magnetic resonance imaging, simple hepatic cysts are seen with relative frequency in daily clinical examination. US is the most useful and noninvasive tool for the diagnosis of simple hepatic cysts, and can generally differentiate simple hepatic cysts from abscesses, hemangiomas and malignancies. Cysts with irregular walls, septations, calcifications or daughter cysts on US should be evaluated with enhanced CT or MRI to differentiate simple hepatic cysts from cystic neoplasms or hydatid cysts.

Growth and compression of hepatic cysts cause abdominal discomfort, pain, distension and dietary symptoms such as nausea, vomiting, a feeling of fullness and early satiety. Complications of simple hepatic cysts include infection, spontaneous hemorrhage, rupture, and external compression of biliary tree or major vessels.

Asymptomatic simple hepatic cysts should be observed. Treatment for symptomatic simple hepatic cysts includes percutaneous aspiration, aspiration followed by sclerotherapy, and surgery. The American College of Gastroenterology clinical guidelines recommend laparoscopic fenestration based on its high success rate and low invasiveness. Percutaneous procedures for treatment of simple hepatic cysts are particularly effective for the immediate palliation of patient symptoms; however, they are not generally recommended because of the high rate of recurrence.

Management of simple hepatic cysts requires correct differentiation from neoplasms and infections, and the selection of a reliable treatment.
Introduction

Simple hepatic cysts are typically thin-walled masses, with fluid-filled epithelial lined cavities that arise from aberrant bile duct cells during embryonic development\textsuperscript{1,2}. Now that diagnostic modalities such as ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) are widely available, simple hepatic cysts are seen with relative frequency in daily clinical examination. However, these are rarely treated and are often overlooked. Enlarged simple hepatic cysts are associated with symptoms such as abdominal distension and pain, and mechanical compression of adjacent structures may cause organ disfunction.

Treatment for symptomatic hepatic cysts is indicated, and this review focuses on the management of simple hepatic cysts.

Epidemiology

Before the widespread appearance of diagnostic modalities, hepatic cyst was diagnosed in surgery. In 1974, Sanfelippo et al.\textsuperscript{3} reported the incidence of hepatic cystic lesion as 17 per 10,000 explorations. With the increased use of diagnostic modalities including US and CT, hepatic cyst is diagnosed easily and encountered frequently in daily medical examinations. The prevalence of simple hepatic cyst ranges from 3-5\% on ultrasononography to as high as 18\% on CT\textsuperscript{4}. Large hepatic cysts tend to be found more frequently in women aged older than 50 years, and the female to male ratio is 4:1\textsuperscript{5}.

Clinical presentation

The radiographic presentation of hepatic cyst varies from solitary to multiple and from small to large. Simple hepatic cysts range in size from < 1 cm to 30 cm, and tend to occur more frequently in the right hepatic lobe\textsuperscript{5}. The presence of more than 20 hepatic cysts is arbitrarily defined as polycystic liver disease (PLD).

Generally, simple hepatic cyst is clearly differentiated from PLD.

In microscopical examination, simple hepatic cysts have an outer layer of thin fibrous tissue and an inner layer of cuboid or columnar epithelium lining resembling biliary epithelium without mesenchymal stroma or cellular atypia\textsuperscript{4,6}. The diameter of hepatic cysts gradually increases because of continuous fluid produce by secretory epithelial cells, and enlarged hepatic cysts cause symptomatic or complicated disease. The
mortality rate for simple hepatic cysts is generally very low; however, the rate increases when cyst-related complications develop.\textsuperscript{3, 7}

The majority of patients with simple hepatic cysts have no common symptoms. Although complications are rare, hepatic cysts increasing in size may cause symptoms. Patient with large hepatic cyst may have a palpable abdominal mass or hepatomegaly and increased abdominal girth on physical examination.\textsuperscript{6} Clinical symptoms occur in 5\% of patients due to progressive enlargement or compression of adjacent structures.\textsuperscript{8}

Symptomatic hepatic cysts tend to occur more frequently in women (female-to-male ratio, 9:1).\textsuperscript{6} Hepatic cysts do not generally impair the liver or other organ function; however, mechanical compression of the biliary tract, vessels, and gastrointestinal tract causes liver disfunction or passage disorder of blood supply and intestine. While not specific, patient complaints caused by growth and compression of hepatic cysts include abdominal discomfort, pain, distention and dietary symptoms such as nausea, vomiting, a feeling of fullness and early satiety.\textsuperscript{9, 10}

Complications of simple cysts include infection,\textsuperscript{11-13} spontaneous hemorrhage,\textsuperscript{14, 15} rupture into peritoneal cavity,\textsuperscript{8, 16} or external compression of biliary tree or major vessels.\textsuperscript{7, 17}

Patients with intracystic bleeding usually complain of sudden and severe right upper quadrant and shoulder pain.\textsuperscript{18} Intracystic bleeding resolves on its own, and pain gradually resolves in a few days.

The etiology of intracystic hemorrhage remains unclear; however, three hypotheses have been proposed.\textsuperscript{19}

I. High intracystic pressure causes necrosis and sloughing of the cyst’s epithelial lining, and injures the fragile blood capillaries in the cystic wall.\textsuperscript{20}

II. Rapid enlargement of hepatic cyst causes rupture of vessels, hemangioma and vascular malformation on the cystic wall or near the cyst.\textsuperscript{21}

III. Traumatic direct external pressure causes injury to the cyst wall or the vessels near the cyst.\textsuperscript{22}

Spontaneous rupture of hepatocellular carcinoma has occurred occasionally; however, spontaneous rupture appears to be a rare complication of nonparasitic hepatic cysts.\textsuperscript{23-25} Salemis et al.\textsuperscript{8} described an extremely rare case of spontaneous rupture of a large hepatic cyst with clinical manifestations of acute abdomen, and suggested that prophylactic treatment should be considered in symptomatic large non-parasitic hepatic cysts with a considerable risk of serious complications.
Complications of the vessel compression are relatively rare; however, if they develop, they are severe. Long et al.\(^6\) reported a case of acute liver failure in which enlarged hepatic cyst obstructed hepatic venous flow and caused Budd-Chiari syndrome. Taguchi et al.\(^{26}\) demonstrated a case of a large, free floating inferior vena cava thrombus caused by an enlarged solitary hepatic cyst.

Simple hepatic cysts are thought to be congenital exclusions of hyperplastic bile duct that lack communication with biliary duct\(^5,27\). However, simple hepatic cysts reportedly communicate with the biliary tree in rare case\(^{28,29}\).

Conversely, simple liver cysts have also been reported to occasionally disappear spontaneously without symptoms\(^{30,31}\).

**Diagnosis**

The majority of simple hepatic cysts are detected incidentally, and they tend to follow a benign course. Laboratory findings are predominantly normal and generally nondiagnostic. However, there may be an elevation in liver enzymes, most commonly with elevation in alkaline phosphatase and gamma-glutamyl trasferase\(^8,9\). These findings are commonly due to the anatomical location of the cyst in the hilar region which can influence biliary tree or major vessels.

US is the most useful and noninvasive diagnostic modality for diagnosis of simple hepatic cyst, which typically shows a saccular, homogenous, anechoic, and fluid-filled lesion with thin-walled smooth margins and posterior acoustic enhancement (Fig.1A). Simple hepatic cysts can be generally differentiated from abscesses, malignancies, hemangiomas and hamartomas on US alone.

CT demonstrates a saccular, smooth, well-demarcated and fluid-filled lesion with water attenuation within cystic lesion and no internal structure. Enhanced CT is negative for enhanced internal structure of cystic lesion with contrast (Fig.1B). Similarly, MRI demonstrates a homogeneous, well-defined and spherical lesion with high signal intensity on T2-weighted images (Fig.1C), and low signal intensity on T1-weighted images without contrast enhancement.

Differential diagnosis with cystic lesion of the liver is often difficult. Differential diagnosis includes malignancy such as biliary cystadenocarcinoma, cystic metastases from primary cystic tumors, and cystic
necrosis of large solid neoplasms. Differential diagnosis excluding neoplasm includes PLD and hydatid cysts resulting from infection by tapeworm of either Echinococcus granulosus or Echinococcus multilocularis.  

Cysts with irregular walls, intracystic septations, calcifications or daughter cysts on US screening should be checked with enhanced CT or MRI for differential diagnosis of cystic neoplasm or hydatid cysts. It is reported that cystadenomas constitute up to 1-5% of total hepatic cystic lesions, and up to 10% of cysts measuring more than 4cm. Cystadenoma has the potential for malignant transformation into cystadenocarcinoma due to the fact that surgical sample for most of cystadenocarcinoma also co-exist as a component of cystadenoma. A malignant transformation rate for cystadenoma of 5-30 % has been reported, and biliary cystadenocarcinoma accounts for 0.41% of malignant hepatic epithelial tumors.

Cystadenoma is classically characterized by imaging as a multilocular, low-density and thick-walled cystic mass with mural nodules and internal septum. However, Labib et al. reported no significant difference in average cyst size and radiological features in differential diagnosis between simple hepatic cyst and cystadenoma. They also reported that patients with cystadenoma were more likely to have a single cyst than simple hepatic cyst on imaging. With current imaging, differentiating between cystic neoplasm and simple hepatic cyst is challenging. In recent papers, cystadenomas have been described as synonymous with Mucinous cystic neoplasms (MCN). WHO redefines cystadenoma as a mucinous cystic neoplasm (MCN) or intraductal papillary neoplasm of the bile duct (IPN-B) depending on the presence of ovarian stroma and bile duct communication, respectively.

Differentiation of simple hepatic cyst is more difficult if the internal fluid contains blood. Hemorrhagic hepatic cysts may also appear nodular with septations on US and weighted MRI, due to intracystic blood clots. Internal bleed in simple hepatic cyst tend to have a heterogenous appearance and be mistaken for complex lesion such as abscess, cystoadenoma, cystadenocarcinoma, or hydatid cysts. Aspiration of intracystic fluid for cytology is not recommended for the diagnose of simple hepatic cysts. However, if aspiration of hepatic cyst is performed for treatment, the screening for intracystic tumor marker concentrations, cytology and bacterial culture can be evaluated.

Marnerite and Alan studied CEA and CA19-9 levels in cystic lesions, and found elevated CEA (>600 µg/L) in fluid from biliary cystadenoma, cystadenocarcinoma, and pseudocystic metastatic carcinoma. However, increased CA19-9 and CEA concentration of internal fluid may also be detected in patients with
simple hepatic cysts. Fuks et al.\textsuperscript{46} reported that intracystic fluid concentrations of CEA and CA19-9 in patients with simple hepatic cysts were greater than the maximum serum reference values in 7% and 88%, respectively. They also show that the cut-off values for differentiating between simple hepatic cyst and mucinous cystic lesion were 30 ng/ml for CEA and 15 000 units/ml for CA19-9\textsuperscript{46}. However, due to lack of specificities and accuracies of intracystic CEA and CA19-9 levels in differentiating patients with simple hepatic cyst from cystic neoplasm, conventional screening of cystic fluid tumor markers is unhelpful for differential diagnosis. In a recent report, high intracystic concentrations of Tumor-associated glycoprotein (TAG-72) was detected in cystic neoplasms, making TAG-72 a promising tool for the differential diagnosis of simple hepatic cyst and cystic neoplasm\textsuperscript{33,46}.

Serum level of CA19-9 is also reported not to be useful for differential diagnosis\textsuperscript{47}. CEA and CA19-9 are expressed by the epithelial cells of normal biliary tract. Therefore, serum CEA and CA19-9 levels cannot be correlated with malignant potential\textsuperscript{33}.

Aspiration cytology is rarely helpful and does not provide adequate information. Microbiological analysis is of value only in rare cases when the lesion is hydatid in origin\textsuperscript{33,39,46}. The preoperative intracystic aspiration cytology and fine-needle biopsy for mural nodules or papillary projections are not recommended because of subsequent development of peritoneal or pleural dissemination in the case of malignancy\textsuperscript{33}.

Management of simple hepatic cyst

A lack of randomized controlled trials and long-term follow-up for the management of simple hepatic cyst make it difficult to establish evidenced-based recommendations with strong support from the literature\textsuperscript{5}.

Asymptomatic simple hepatic cyst encountered incidentally by abdominal imaging does not require treatment or follow-up\textsuperscript{5,48}. Likewise, simple hepatic cyst found incidentally during abdominal surgery should be managed with observation\textsuperscript{28}.

For symptomatic simple hepatic cysts, treatment is indicated. The most feasible treatment is percutaneous aspiration; however, this does not yield permanent therapeutic benefit. Ultrasonographic-guided percutaneous aspiration is particularly effective for the immediate palliation of symptoms of large hepatic cyst. However, this treatment is associated with invariable recurrence as the aspirated hepatic cyst fills up again within several days. Percutaneous aspiration is also performed as a good therapeutic test to confirm
whether abdominal symptoms are caused by hepatic cyst. If abdominal symptoms are not improved by aspiration, other causes of abdominal pain should be investigated\textsuperscript{28,49}.

To improve the effect of percutaneous management and achieve permanent ablation, aspiration of intracystic fluid followed by the instillation of sclerosing agents into the cyst is reasonable to reduce cystic volume and destroy the inner cyst epithelium. Systematic review demonstrated that percutaneous aspiration and sclerotherapy for symptomatic hepatic cysts yield an excellent outcome with symptoms persisting in less than 4\% of patients, and complication and recurrence rates each being $<1\%$\textsuperscript{50}. The most commonly applied sclerosing agent is ethanol\textsuperscript{1}. However, ethanolamine oleate\textsuperscript{36}, polidocanol\textsuperscript{51}, minocycline hydrochloride\textsuperscript{52,53}, and bleomycin\textsuperscript{54} were reported as sclerosing agents. Yoshida et al.\textsuperscript{53} demonstrated that sclerotherapy with minocycline hydrochloride yielded hepatic cyst regression without recurrence.

Surgical options, including open or laparoscopic fenestration, and hepatic resection provide long-term relief in up to 90\% of symptomatic hepatic cyst patients\textsuperscript{4,55}. After fenestration of hepatic cyst was first reported by Lin et al.\textsuperscript{56} in 1968, ‘deroofing’ or ‘marsupialization’ are used as a synonymous terms. Regardless of which term is used, the principle of treatment is to remove the roof of the hepatic cyst as a part of the liver surface, and allow it to drain freely into the peritoneal cavity. The fluid produced on the wall is reabsorbed by the peritoneum\textsuperscript{57}.

Since Fabiani et al.\textsuperscript{58} introduced laparoscopic fenestration of hepatic cysts in 1991, the approach has been widespread with most surgeons adopting laparoscopic fenestration as the preferred therapeutic option because of its success rates and the reduction in morbidity and length hospital stay compared with open procedures\textsuperscript{32,59}. The American College of Gastroenterology (ACG) clinical guidelines\textsuperscript{5} recommend that symptomatic simple hepatic cysts should be managed by laparoscopic fenestration rather than percutaneous aspiration and sclerotherapy. ACG clinical guidelines also note that percutaneous procedures may be appropriate for patients who are not candidates for surgery\textsuperscript{5}. The anatomical suitability of hepatic cysts to laparoscopic deroofing is dependent on operator experience and confidence. Careful mapping of the liver cysts with three-dimensional CT may be useful in evaluating the feasibility of laparoscopic surgery.

However, for hepatic cysts which are very large, or in locations where laparoscopic access may make complete excision of the cyst wall difficult, open fenestration is probably prudent\textsuperscript{32}. Reported recurrence rates, including repeated asymptomatic cysts, vary from 0 to 36\% following
laparoscopic fenestration. The main reason for the recurrence of cysts following fenestration is reconstitution of the cyst with the adjacent organ or diaphragm forming part of the cystic wall. For the prevention of hepatic cyst recurrence, wide fenestration of hepatic cyst, omental transposition flap or electrocoagulator ablation of remnant hepatic cyst epithelium have been introduced (Fig. 2A, 2B). Total excision or lobe resection also have reported recurrence rates of zero.

Despite technological advances in imaging modalities, the presence of the cystobiliary communication remains difficult to demonstrate preoperatively. In the case of biliary communication with hepatic cyst, ligation or running-suture to disrupt biliary communication within the hepatic cyst should be attempted. Incomplete separation between biliary tree and cyst will cause postoperative biloma or biliary peritonitis. Roux-en Y cystoenterostomy has been reported as a treatment for cystobiliary communication; however, this is associated with high risk of sepsis and ascending cholangitis. Tocchi et al. reported a case of repeated cholangitis after cystoenterostomy required hepatectomy.

In situations where an underlying diagnosis of hepatic cystic lesion is uncertain, surgical intervention is important to allow histological examination, particularly for exclusion of hepatic neoplasm. However, in cases of suspected neoplasms, complete surgical excision of cystic lesion without spillage of intracystic fluid is required. Procedures such as complete excision of the hepatic cyst, segmentectomy or lobectomy are associated with high risk of morbidity and mortality compared with fenestration. Due to increased morbidity, hepatic resection should be reserved for recurrence after deroofing procedure, diffuse hepatic involvement, or multiple hepatic cysts.

Liver transplantation is not indicated for patients with simple hepatic cysts. However in patients with Gigot’s type III polycystic liver disease showing diffuse liver enlargement and small cysts not suitable for deroofing or resection, a detailed evaluation for liver transplantation should be conducted to balance against the risk of operation, quality of life, and possible benefits of a combined renal implant with polycystic kidney disease.

Conclusion

Effective management of simple hepatic cyst requires differentiation from neoplasm and infection, and selection of a reliable treatment for symptomatic simple hepatic cyst that reduces recurrence.
Figure legend

1. 
   A. US reveals an anechoic and fluid-filled saccular lesion with thin-walled smooth margins and posterior acoustic enhancement.
   B. CT demonstrates a round, smooth, well-demarcated and fluid-filled lesion without internal structure.
   C. MRI shows a homogeneous, well-defined and spherical lesion with high signal intensity on T2-weighted images.

2. Intraoperative findings
   A: A large and fluid-filled simple hepatic cyst prior to laparoscopic fenestration.
   B: Wide fenestration and electrocoagulator ablation of remnant hepatic cyst epithelium.
Reference

1. Wijnands TF, Görtjes AP, Gevers TJ, et al.: Efficacy and Safety of Aspiration Sclerotherapy of Simple Hepatic Cysts: A Systematic Review. AJR Am J Roentgenol 2017; 208: 201-207.

2. Drenth JP, Chrispijn M, Nagorney DM, Kamath PS, Torres VE: Medical and surgical treatment options for polycystic liver disease. Hepatology 2010; 52: 2223-2230.

3. Sanfelippo PM, Beahrs OH, Weiland LH: Cystic disease of the liver. Ann Surg 1974; 179: 922-925.

4. Reid-Lombardo KM, Khan S, Sclabas G: Hepatic cysts and liver abscess. Surg Clin North Am 2010; 90: 679-697.

5. Marrero JA, Ahn J, Rajender Reddy K, Gastroenterology ACo: ACG clinical guideline: the diagnosis and management of focal liver lesions. Am J Gastroenterol 2014; 109: 1328-1347; quiz 1348.

6. Bahirwani R, Reddy KR: Review article: the evaluation of solitary liver masses. Aliment Pharmacol Ther 2008; 28: 953-965.

7. Long J, Vaughan-Williams H, Moorhouse J, Sethi H, Kumar N: Acute Budd-Chiari syndrome due to a simple liver cyst. Ann R Coll Surg Engl 2014; 96: 109E-111E.

8. Salemis NS, Georgoulis E, Gourgiotis S, Tsohataridis E: Spontaneous rupture of a giant non parasitic hepatic cyst presenting as an acute surgical abdomen. Ann Hepatol 2007; 6: 190-193.

9. Lantinga MA, Gevers TJ, Drenth JP: Evaluation of hepatic cystic lesions. World J Gastroenterol 2013; 19: 3543-3554.

10. Mavilia MG, Pakala T, Molina M, Wu GY: Differentiating Cystic Liver Lesions: A Review of Imaging Modalities, Diagnosis and Management. J Clin Transl Hepatol 2018; 6: 208-216.

11. Yoshida H, Tajiri T, Mamada Y, et al.: Infected solitary hepatic cyst. J Nippon Med Sch 2003; 70: 515-518.

12. Yoshida H, Onda M, Tajiri T, et al.: Infected hepatic cyst. Hepatogastroenterology 2003; 50: 507-509.

13. Ishii K, Yoshida H, Taniai N, Moneta S, Kawano Y, Tajiri T: Infected hepatic cyst treated with percutaneous transhepatic drainage. J Nippon Med Sch 2009; 76: 160-164.

14. Yoshida H, Onda M, Tajiri T, et al.: Intracystic hemorrhage of a simple hepatic cyst. Hepatogastroenterology 2002; 49: 1095-1097.

15. Kawano Y, Yoshida H, Mamada Y, et al.: Intracystic hemorrhage required no treatment from one of multiple hepatic cysts. J Nippon Med Sch 2011; 78: 312-316.

16. Ueda J, Yoshida H, Taniai N, Mineta S, Kawano Y, Uchida E: A case of spontaneous rupture of a simple hepatic cyst. J Nippon Med Sch 2010; 77: 181-185.
17. Kaneya Y, Yoshida H, Matsutani T, et al.: Biliary obstruction due to a huge simple hepatic cyst treated with laparoscopic resection. J Nippon Med Sch 2011; 78: 105-109.

18. Kitajima Y, Okayama Y, Hirai M, et al.: Intracystic hemorrhage of a simple liver cyst mimicking a biliary cystadenocarcinoma. J Gastroenterol 2003; 38: 190-193.

19. Fong ZV, Wolf AM, Doria C, Berger AC, Rosato EL, Palazzo F: Hemorrhagic hepatic cyst: report of a case and review of the literature with emphasis on clinical approach and management. J Gastrointest Surg 2012; 16: 1782-1789.

20. GAVISER D: Solitary nonparasitic cysts of the liver. Minn Med 1953; 36: 831-836; passim.

21. Hanazaki K, Wakabayashi M, Mori H, et al.: Hemorrhage into a simple liver cyst: diagnostic implications of a recent case. J Gastroenterol 1997; 32: 848-851.

22. Hagiwara A, Inoue Y, Shutoh T, Kinoshita H, Wakasa K: Haemorrhagic hepatic cyst: a differential diagnosis of cystic tumour. Br J Radiol 2001; 74: 270-272.

23. Yoshida H, Mamada Y, Taniai N, et al.: Long-term results of elective hepatectomy for the treatment of ruptured hepatocellular carcinoma. J Hepatobiliary Pancreat Surg 2008; 15: 178-182.

24. Yoshida H, Mamada Y, Taniai N, Uchida E: Spontaneous ruptured hepatocellular carcinoma. Hepatol Res 2016; 46: 13-21.

25. Yoshida H, Onda M, Tajiri T, et al.: Treatment of spontaneous ruptured hepatocellular carcinoma. Hepatogastroenterology 1999; 46: 2451-2453.

26. Taguchi E, Nakanishi N, Nakao K, Sakamoto T: Inferior Vena Cava Thrombi Caused by Enlarged, Solitary Hepatic Cyst. Circ J 2018; 82: 604-605.

27. Ammori BJ, Jenkins BL, Lim PC, Prasad KR, Pollard SG, Lodge JP: Surgical strategy for cystic diseases of the liver in a western hepatobiliary center. World J Surg 2002; 26: 462-469.

28. Cowles RA, Mulholland MW: Solitary hepatic cysts. J Am Coll Surg 2000; 191: 311-321.

29. Yamada T, Furukawa K, Yokoi K, Mamada Y, Kanazawa Y, Tajiri T: Liver cyst with biliary communication successfully treated with laparoscopic deroofing: a case report. J Nippon Med Sch 2009; 76: 103-108.

30. Yoshida H, Onda M, Tajiri T, et al.: Spontaneous disappearance of a hepatic cyst. J Nippon Med Sch 2001; 68: 58-60.

31. Arai H, Nagamine T, Suzuki H, et al.: Simple liver cyst with spontaneous regression. J Gastroenterol 2002; 37: 755-757.

32. Garcea G, Pattenden CJ, Stephenson J, Dennison AR, Berry DP: Nine-year single-center experience with nonparastic liver cysts: diagnosis and management. Dig Dis Sci 2007; 52: 185-191.
33. Fragulidis GP, Vezakis AI, Konstantinidis CG, et al.: Diagnostic and Therapeutic Challenges of Intrahepatic Biliary Cystadenoma and Cystadenocarcinoma: A Report of 10 Cases and Review of the Literature. Int Surg 2015; 100: 1212-1219.

34. Läuffer JM, Baer HU, Maurer CA, Stoupis C, Zimmerman A, Büchler MW: Biliary cystadenocarcinoma of the liver: the need for complete resection. Eur J Cancer 1998; 34: 1845-1851.

35. Nakajima T, Sugano I, Matsuzaki O, et al.: Biliary cystadenocarcinoma of the liver. A clinicopathologic and histochemical evaluation of nine cases. Cancer 1992; 69: 2426-2432.

36. Yoshida H, Tajiri T, Mamada Y, et al.: Rapidly enlarging hepatobiliary cystadenoma. J Med Ultrason (2001) 2003; 30: 257-262.

37. Takayasu K, Muramatsu Y, Moriyama N, et al.: Imaging diagnosis of bile duct cystadenocarcinoma. Cancer 1988; 61: 941-946.

38. Fiamingo P, Veroux M, Cillo U, Basso S, Buffone A, D'Amico DF: Incidental cystadenoma after laparoscopic treatment of hepatic cysts: which strategy? Surg Laparosc Endosc Percutan Tech 2004; 14: 282-284.

39. Labib PL, Aroori S, Bowles M, Stell D, Briggs C: Differentiating Simple Hepatic Cysts from Mucinous Cystic Neoplasms: Radiological Features, Cyst Fluid Tumour Marker Analysis and Multidisciplinary Team Outcomes. Dig Surg 2017; 34: 36-42.

40. Rawla P, Sunkara T, Muralidharan P, Raj JP: An updated review of cystic hepatic lesions. Clin Exp Hepatol 2019; 5: 22-29.

41. Averbukh LD, Wu DC, Cho WC, Wu GY: Biliary Mucinous Cystadenoma: A Review of the Literature. J Clin Transl Hepatol 2019; 7: 149-153.

42. Tani A, Yoshida H, Mamada Y, Tanai N, Naito Z, Tajiri T: Case of biliary cystadenocarcinoma with intracystic bleeding. J Nippon Med Sch 2008; 75: 293-297.

43. Takahashi G, Yoshida H, Mamada Y, Tanai N, Bando K, Tajiri T: Intracystic hemorrhage of a large simple hepatic cyst. J Nippon Med Sch 2008; 75: 302-305.

44. Pinto MM, Kaye AD: Fine needle aspiration of cystic liver lesions. Cytologic examination and carcinoembryonic antigen assay of cyst contents. Acta Cytol 1989; 33: 852-856.

45. Lin CC, Lin SC, Ko WC, Chang KM, Shih SC: Adenocarcinoma and infection in a solitary hepatic cyst: a case report. World J Gastroenterol 2005; 11: 1881-1883.
46. Fuks D, Voitot H, Paradis V, Belghiti J, Vilgrain V, Farges O: Intracystic concentrations of tumour markers for the diagnosis of cystic liver lesions. Br J Surg 2014; 101: 408-416.

47. Choi HK, Lee JK, Lee KH, et al.: Differential diagnosis for intrahepatic biliary cystadenoma and hepatic simple cyst: significance of cystic fluid analysis and radiologic findings. J Clin Gastroenterol 2010; 44: 289-293.

48. Doty JE, Tompkins RK: Management of cystic disease of the liver. Surg Clin North Am 1989; 69: 285-295.

49. Saini S, Mueller PR, Ferrucci JT, Simeone JF, Wittenberg J, Butch RJ: Percutaneous aspiration of hepatic cysts does not provide definitive therapy. AJR Am J Roentgenol 1983; 141: 559-560.

50. Furumaya A, van Rosmalen BV, de Graeff JJ, et al.: Systematic review on percutaneous aspiration and sclerotherapy versus surgery in symptomatic simple hepatic cysts. HPB (Oxford) 2020.

51. Spârchez Z, Radu P, Zaharie F, Al Hajjar N, Sparchez M: Percutaneous treatment of symptomatic non-parasitic hepatic cysts. Initial experience with single-session sclerotherapy with polidocanol. Med Ultrason 2014; 16: 222-228.

52. Yoshida H, Egami K, Onda M, Tajiri T, Uchida E: Treatment of symptomatic hepatic cyst by injection of minocycline hydrochloride. J Hepatobiliary Pancreat Surg 1996; 3: 491-494.

53. Yoshida H, Onda M, Tajiri T, et al.: Long-term results of multiple minocycline hydrochloride injections for the treatment of symptomatic solitary hepatic cyst. J Gastroenterol Hepatol 2003; 18: 595-598.

54. Souftas VD, Kosmidou M, Karanikas M, Souftas D, Menexes G, Prassopoulos P: Symptomatic abdominal simple cysts: is percutaneous sclerotherapy with hypertonic saline and bleomycin a treatment option? Gastroenterol Res Pract 2015; 2015: 489363.

55. Gall TM, Oniscu GC, Madhavan K, Parks RW, Garden OJ: Surgical management and longterm follow-up of non-parasitic hepatic cysts. HPB (Oxford) 2009; 11: 235-241.

56. Lin TY, Chen CC, Wang SM: Treatment of non-parasitic cystic disease of the liver: a new approach to therapy with polycystic liver. Ann Surg 1968; 168: 921-927.

57. Moorthy K, Mihsin N, Houghton PW: The management of simple hepatic cysts: sclerotherapy or laparoscopic fenestration. Ann R Coll Surg Engl 2001; 83: 409-414.

58. Fabiani P, Katkhouda N, Iovine L, Mouiel J: Laparoscopic fenestration of biliary cysts. Surg Laparosc Endosc 1991; 1: 162-165.

59. Krähenbühl L, Baer HU, Renzulli P, Z’graggen K, Frei E, Büchler MW: Laparoscopic management of nonparasitic symptom-producing solitary hepatic cysts. J Am Coll Surg 1996; 183: 493-498.
60. Tagaya N, Nemoto T, Kubota K: Long-term results of laparoscopic unroofing of symptomatic solitary nonparasitic hepatic cysts. Surg Laparosc Endosc Percutan Tech 2003; 13: 76-79.

61. Emmermann A, Zornig C, Lloyd DM, Peiper M, Bloechle C, Broelsch CE: Laparoscopic treatment of nonparasitic cysts of the liver with omental transposition flap. Surg Endosc 1997; 11: 734-736.

62. Masatsugu T, Shimizu S, Noshiro H, et al.: Liver cyst with biliary communication successfully treated with laparoscopic deroofing: a case report. JSLS 2003; 7: 249-252.

63. Jain SK, Vindal A, Basra BK, Kaza RC: Cystojejunostomy for non-parasitic hepatic cyst with biliary communication. Singapore Med J 2010; 51: e27-29.

64. Longmire WP, Mandiola SA, Gordon HE: Congenital cystic disease of the liver and biliary system. Ann Surg 1971; 174: 711-726.

65. Tocchi A, Mazzoni G, Costa G, et al.: Symptomatic nonparasitic hepatic cysts: options for and results of surgical management. Arch Surg 2002; 137: 154-158.

66. Kaul V, Friedenberg F, Rothstein KD: Hepatic Cysts. Curr Treat Options Gastroenterol 2000; 3: 439-444.
Fig. 1A
Fig. 1B
Fig. 1C
Fig. 2A
Fig. 2B