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CASE REPORT

Successful aspiration and ethanol sclerosis of a large, symptomatic, simple liver cyst: Case presentation and review of the literature

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Abstract

Simple liver cysts are congenital with a prevalence of 2.5%-4.25%. Imaging, whether by US, CT or MRI, is accurate in distinguishing simple cysts from other etiologies, including parasitic, neoplastic, duct-related, and traumatic cysts. Symptomatic simple liver cysts are rare, and the true frequency of symptoms is not known. Symptomatic simple liver cysts are predominantly large (> 4 cm), right-sided, and more common in women and older patients. The vast majority of simple hepatic cysts require no treatment or follow-up, though large cysts (> 4 cm) may be followed initially with serial imaging to ensure stability. Attribution of symptoms to a large simple cyst should be undertaken with caution, after alternative diagnoses have been excluded. Aspiration may be performed to test whether symptoms are due to the cyst; however, cyst recurrence should be expected. Limited experience with both laparoscopic deroofing and aspiration, followed by instillation of a sclerosing agent has demonstrated promising results for the treatment of symptomatic cysts. Here, we describe a patient with a large, symptomatic, simple liver cyst who experienced complete resolution of symptoms following cyst drainage and alcohol ablation, and we present a comprehensive review of the literature.

Key words: Simple hepatic cyst; Alcohol sclerosis; Laparoscopic deroofing

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INTRODUCTION

Liver cysts are classified as true or false, depending on the presence of an epithelial lining[1]. True cysts include congenital cysts (simple cysts and polycystic liver disease), parasitic (hydatid) cysts caused by *Echinococcus granulosis* and *multilocularis* tapeworms, neoplastic cysts (including cystadenoma, cystadenocarcinoma, cystic sarcoma, squamous cell carcinoma, and metastatic ovarian, pancreatic, colon, renal and neuroendocrine cancers), and biliary duct-related cysts (Caroli's disease, bile duct duplication, and peribiliary cysts)[1]. False cysts may be caused by spontaneous intrahepatic hemorrhage, post-traumatic hematoma, or intrahepatic biloma[1].

The pathogenesis of liver cysts is not clear. Simple liver cysts are congenital[2]. They are lined by cuboidal epithelium and originate from the abnormal development of intrahepatic ducts *in utero*. They are generally stable in size over time, but may slowly enlarge and occasionally become symptomatic due to mass effect, rupture, hemorrhage, or infection[3]. However, an enlarging cyst should prompt consideration of diagnosis other than simple cysts. Although simple cysts are generally solitary, more than one cyst may be present ("several solitary"), even in the absence of polycystic liver disease, as is the case with the patient described below.

We report herein a case of a patient with a large, symptomatic, simple hepatic cyst with resolution of symptoms immediately after therapy. In addition, we present a comprehensive literature review of diagnosis and treatment options of symptomatic hepatic cysts.

CASE REPORT

A 59-year-old African-American woman was referred to the Division of Gastroenterology at the University of Pennsylvania for evaluation of abdominal pain for 2 years. The patient described frequent, intermittent epigastric pain and bloating not associated with meals or bowel movements. Typically, pain would last for one-half hour before spontaneously resolving. She had twice presented to the emergency room with abdominal pain

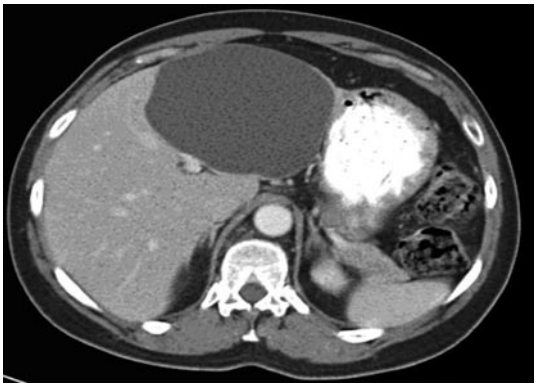

Figure 1 Enhanced abdominal CT scan showing large, simple hepatic cyst.

and was discharged without definitive diagnosis. She also complained of early satiety and occasional nausea without weight loss.

The patient was taking daily fiber supplements and had regular, daily bowel movements. Reflux symptoms were well controlled with esomeprazole. Hypertension was treated with metoprolol and amlodipine. Other chronic medications were progesterone and estrogen. She denied non-steroidal anti-inflammatory drug usage. Physical examination was unremarkable.

Laboratory evaluation showed normal liver-associated enzymes, metabolic panel, complete blood count, and urinalysis. Screening colonoscopy, performed two years prior to presentation, revealed internal hemorrhoids and melanosis. Upon presentation, she underwent double contrast upper gastrointestinal examination, which suggested antral gastritis and a hiatal hernia. On subsequent upper gastrointestinal endoscopy, the mucosa appeared normal, and a medium-sized hiatal hernia was present. Treatment with a proton pump inhibitor, fiber, and hyoscyamine failed to improve symptoms by six months.

The patient underwent abdominal CT scan with intravenous and oral contrast, which showed a large (7.7 cm) hepatic cyst in the lateral segment of the left lobe, as well as several other smaller cysts (Figure 1). Gallstones without gallbladder wall thickening or pericholecystic fluid were also visualized. On ultrasonography, tenderness was elicited specifically over the site of the cyst, which measured 10.3 cm in its longest dimension.

After several months of expectant management, the patient was referred to interventional radiology for drainage of the large hepatic cyst. Under ultrasonographic guidance, an 8-gauge French catheter was placed into the cyst, serous non-bilious fluid was aspirated, and the catheter was placed to gravity drainage. One week later, after drainage had ceased, the patient underwent ethanol sclerosis. At 4 mo follow-up, the patient was completely symptom-free. Follow-up ultrasound showed complete cyst resolution.

DISCUSSION

Previous studies, based on autopsy and surgical series, estimated a very low prevalence of simple non-parasitic hepatic cysts (0.14%-0.17%)[4]. More recently, among patients referred for abdominal ultrasonography, the prevalence of simple hepatic cysts has been reported 2.5%-4.65%[5,6]. Liver cysts have been recognized increasingly as the routine use of imaging studies becomes more widespread. Hepatic cysts may be more common in women[5] and in patients older than 40 years[6]. Symptoms, though quite rare, may be related to the space-occupying effect of large cysts[7] and may be more common in right-sided cysts[8]. Symptoms may include abdominal discomfort, chronic right upper quadrant or epigastric abdominal pain, early satiety, dyspnea, increasing abdominal girth, nausea, and vomiting[7,9]. Sanfelippo *et al*[4] reported that among 15 symptomatic patients with solitary non-parastic liver cysts, abdominal mass was present in 54%, hepatomegaly in 40%, abdominal pain in 33% and jaundice in 9% patients.

Table 1 Rare complications of simple liver cysts

Obstructive jaundice
Infection
Intracystic haemorrhage
Spontaneous rupture
Inferior vena cava obstruction
Neoplastic transformation
Primary squamous cell carcinoma
Cystadenocarcinoma
Adenosquamous carcinoma
Adenocarcinoma
Hepatocellular carinoma
Cholangiocarcinoma

Although the natural history of simple hepatic cysts is not well known, complications appear to be quite rare (Table 1). Obstructive jaundice caused by solitary non-parasitic liver cyst is rare[11-15], and such cysts are usually large and located centrally in the liver, causing compression of the hepatic hilum[13]. However, sometimes even small hepatic cysts (3 cm in diameter) may cause common bile duct stenosis and intrahepatic biliary dilatation[15].

Liver cysts may also cause obstruction of the inferior vena cava, which may lead to massive edema of the legs[16,17] and scrotum[16]. Infections of simple hepatic cysts with *Klebsiella pneumoniae*[18] and *Escherichia coli*[19], presenting with acute onset of right upper quadrant abdominal pain, diarrhea, and fever have also been reported. Other documented complications include intracystic haemorrhage[19-23] and spontaneous rupture[23]. Neoplasms arising from solitary non-parasitic liver cysts, including primary squamous cell carcinoma[24-26], cystadenocarcinoma, adenosquamous carcinoma, adenocarcinoma, hepatocellular carinoma, and cholangio carcinoma[27-29], have been reported, but appear to be very rare. A possible association with Peutz-Jeghers syndrome has also been suggested[30].

Imaging modalities (ultrasound, CT, and MRI) are highly accurate for diagnosing simple cysts (Table 2). Large differences in echogenicity between hepatic parenchyma and cyst fluid allow for easy recognition of simple cysts by ultrasound[31]. The ultrasonographic appearance of simple cyst is characterized by well-defined, echo-free lesions with

Table 2 Radiologic features of simple hepatic cysts

Features supporting diagnosis of a simple cyst	Features not supporting diagnosis of a simple cyst
Anechoic lesion	Echoic lesion
Thin wall	Thick wall
Absence of septations	Presence of septations
No peripheral enhancement on CT/MRI	Peripheral enhancement on CT/MRI
Homogeneous appearance	Heterogeneity within the cyst
	Hydatid sand
	Presence of daughter cysts
	Heavy wall calcifications

Table 3 Alternative explanations for symptoms in patients with simple hepatic cysts

Diagnosis
Biliary colic
Gastroesophageal reflux
Peptic ulcer
Non-ulcer dyspepsia
Irritable bowel syndrome
Chronic pancreatitis
Abdominal wall pain syndrome

good through transmission and an imperceptible wall[3,32]. The presence of acoustic enhancement results from relative lack of absorption and reflection of sound by cyst fluid, as compared with hepatic parenchyma[32]. On CT scan, simple cysts appear as well-demarcated, water-density sacs, which do not demonstrate peripheral enhancement after intravenous contrast [3]. The presence of septations suggests that a cyst is not simple. Occasionally, large simple cysts may have "septations" due to hemorrhage. MRI shows simple cysts as hypointense lesions on T1-weighted and hyperintense on T2-weighted images[32,33]. Simple cysts differ from cavernous hemangiomas in that they are more hypointense on T1-weighted and of equal hyperintensity on T2-weighted images[33]. Radiologic characteristics which would argue against a cyst being simple include a thick wall, peripheral enhancement on CT or MRI, heterogeneity within the cyst, and an increase in size over time. Hepatic cysts should be differentiated from hepatic abscesses, hematomas, necrotic metastases, an intrahepatic gallbladder, biliary cystadenoma, and echinococcal (hydatid) cysts[32].

Radiologic imaging can accurately identify hydatid cysts, with an accuracy of 96% in one series[34]. Presence of hydatid sand, internal sepatations, daughter cysts, and heavy wall calcifications argue for *Echinococcus granulosis* infection, instead of a simple cyst. Epidemiologic features and serology in combination with radiologic imaging generally lead to the correct diagnosis non-invasively.

Distinction between cystic and solid hepatic lesions can be made accurately by ultrasonography, though CT or MR imaging may be more sensitive for the detection of focal hepatic masses[35]. The presence of any peripheral enhancement or thick-walled component suggests the possibility of hepatic abscess or neoplasm[32]. Small hepatic lesions with diameter < 1 cm are difficult to classify[36]. Such lesions should be differentiated from benign cysts, hepatic metastases with central necrosis, and microabscesses[36]. In order to differentiate small cysts from small metastases, follow-up imaging may be considered in selected cases[36].

The vast majority of simple hepatic cysts require no treatment. Large cysts (diameter of 4 cm or more) can be followed for stability with repeated imaging[37]. If the cyst remains unchanged for 2 years, further monitoring may be discontinued[37]. Symptomatic or enlarging cysts require consideration of alternative diagnoses, including cystadenoma, cystadenocarcinoma, and hepatic metastases. It should be stressed that attribution of symptoms to simple cysts should be undertaken with caution after excluding alternative diagnoses. Epigastric or right upper quadrant abdominal pain provoked by eating may indicate biliary colic, if gallstones are present. A successful trial of acid suppression therapy points to gastroesophageal reflux disease. Selected patients may undergo upper gastrointestinal endoscopy to diagnose erosive esophagitis or peptic ulcer disease. Esophageal pH monitoring can confirm the diagnosis of gastroesophageal reflux. If symptoms fluctuate in concert with changes in stool frequency or form, a diagnosis of irritable bowel syndrome should be suspected. Finally, a diagnosis of non-ulcer dyspepsia may be entertained in patients with unremarkable upper gastrointestinal endoscopy who have continued prominent upper abdominal pain, possibly in association with nausea and vomiting (Table 3). If the preceding diagnoses can be confidently excluded, then treatment of a large, symptomatic hepatic cyst may be undertaken. Treatment options include needle aspiration with or without injection of sclerosing solution, internal drainage with cystojejunostomy, wide deroofing, and different degrees of liver resection[37].

Percutaneous US- or CT-guided needle aspiration of hepatic cysts is associated with high recurrence rates (78%-100%)[38,39]. Several small case series have demonstrated efficacy for the performance of US- or CT-guided needle aspiration of hepatic cysts combined with alcohol injection[40-44]. Because US-guided aspiration with ethanol sclerosis is generally safe, effective, and relatively non-invasive, it may be a first-line treatment for selected symptomatic congenital hepatic cysts, especially in patients with high surgical risk or polycystic liver disease[15]. The 95%, 96% and 99% alcohol solutions are equally safe and effective[15,42,45]. Enough alcohol should be instilled to replace 25% of the aspirated cyst fluid volume[46]. For larger cysts (> 400 mL), multiple alcohol injections in the same sitting have been proposed[46]. Alcohol fixes the cells lining the cyst cavity, disabling their ability to secrete fluid and promote cyst enlargement[46]. Recurrence may occur if alcohol does not come in contact with all cells lining the cyst cavity[46] and may be more common in uncooperative patients[47]. Combinations of percutaneous aspiration with other sclerosing substances, such as iophendylate (pantopaque)[48], tetracycline chloride[49-52], doxycycline[52], minocycline chloride[53-56], and hypertonic saline solution[8] have also achieved good outcomes.

Several recent series have demonstrated good results for laparoscopic deroofing procedures. Widest possible excision of the cystic wall and concomitant argon beam

Table 4 Comparison of treatment options for symptomatic simple liver cysts

Treatment options	Advantages	Disadvantages
Observation alone	- Because most cysts are asymptomatic, intervention is unlikely to be helpful and may be harmful	- Only effective cyst treatment can prove whether symptoms are related to the cyst
US-guided aspiration	- Simple procedure - May be used as a diagnostic test to assess whether symptoms are related to the cyst	- High recurrence rate
US-guided aspiration with sclerotherapy	- Relatively non-invasive - Complications are rare - Effective - Possible in poor surgical candidates	- Less effective for uncooperative patients - Can not be performed if cyst communicates with biliary tree
Laparoscopic unroofing	- Technically feasible and effective in > 80% cases - Improved results with extensive fenestration and argon beam coagulation or electrocoagulation - Low recurrence rate (0%-20%) - Visualization of cyst interior (exclude other diagnoses)	- More invasive - Morbidity in up to 25% - Less effective for cysts which are superior, posterior, or deep within hepatic parenchyma - Less effective if prior surgery has been attempted
Laparotomy (resection, fenestration, or excision)	- Effective - Allows treatment of laparoscopically inaccessible cysts - Useful for cysts with complications - May perform cystojejunostomy at time of laparotomy for cysts with biliary communication	- Most invasive - Larger scars - Longer hospital stays compare to laparoscopy - Significant post-surgical morbidity

coagulation or electrocoagulation may improve the durability of results[57-61]. Recurrence has ranged from 0% to 20% with morbidity in 0% to 25%[57-60,62]. In one series, laparoscopic fenestration of simple hepatic cysts was found to be technically feasible in 90% with symptomatic relief in 95% during 38.5 mo follow-up[61]. Careful selection of patients who have not previously undergone surgical treatment and have large, symptomatic, superficial, and anterior cysts may improve outcomes[63]. US- or CT-guided cyst aspiration can be performed prior to laparoscopic fenestration in selected cases to assess whether symptoms are truly referable to the cyst[63]. Reported complications associated with laparoscopic deroofing include wound infection, bile leak, chest infection, subphrenic hematoma, and prolonged post-procedure drainage[37]. In selected cases, an open surgical procedure (fenestration, excision, or resection) may be preferred, despite longer recovery times and larger surgical scar, because of cyst location, surgeon expertise, or the presence of complicating factors[8,39,61,63,64].

Laparoscopic deroofing and cyst aspiration, followed by sclerosis, are both reasonable approaches for the majority of symptomatic simple liver cysts (Table 4)[64]. Whereas sclerosis may be less invasive and associated with lower rates of complications, laparoscopy is effective and provides the opportunity to directly examine the cyst interior to rule out etiologies other than a simple hepatic cyst[64,65].

It is important to rule out biliary communication before sclerosing a cyst, as irreversible sclerosing cholangitis has been reported as a complication[7,16,46,52,66]. The presence of cystobiliary communication may be established by endoscopic retrograde cholangiography or aspiration of bile-stained cystic fluid and is often treated by open cystojejunostomy[39], although the cystobiliary communication may be closed laparoscopically[67].

In summary, we present the case of a large, symptomatic simple hepatic cyst. We established that the cyst was the cause of symptoms only after systematically excluding alternative diagnoses through testing and empiric therapy. The usual standard of care for patients with large, simple hepatic cysts is observation, but our case demonstrates that large cysts can occasionally be responsible for symptoms. In selected cases, symptoms may respond to cyst treatment. Our treatment approach was ultrasound-guided aspiration and ethanol sclerotherapy. We believe that aspiration alone is associated with unacceptably high rates of recurrence. In our patient, excellent symptomatic and radiologic responses were achieved. In the case of cyst recurrence laparoscopic deroofing may be considered, though complications may occur in up to 25% of cases.

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