Radiology

Tumefactive Gallbladder Sludge at US: Prevalence and Clinical Importance[1]

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Purpose: To evaluate the prevalence of tumefactive sludge of the gallbladder detected at ultrasonography (US) and to assess whether any clinical and imaging differences exist between benign and malignant tumefactive sludge.

Materials and Methods: The institutional review board approved this retrospective study. The requirement for informed consent was waived. The study included a cohort (n = 6898) of patients with gallbladder sludge drawn from all adults (n = 115 178) who underwent abdominal US between March 2001 and March 2015. Tumefactive sludge was identified according to the following US findings: *(a)* nonmovable mass-like lesion and *(b)* absence of posterior acoustic shadowing at B-mode US and vascularity at color Doppler US. Follow-up examinations were arranged to ascertain whether the results showed true sludge or gallbladder cancer. Risk factors for malignant tumefactive sludge based on clinical and US characteristics were identified with multivariate logistic regression analysis.

Results: The prevalence of gallbladder and tumefactive sludge at abdominal US during the observation period was 6.0% (6898 of 115 178) and 0.1% (135 of 115 178), respectively. Twenty-eight (20.7%) patients were lost to follow-up. Of the 107 with tumefactive sludge, 15 (14%) were confirmed to have malignant tumefactive sludge. The risk factors for malignant tumefactive sludge were old age (odds ratio [OR], 1.06; P = .035), female sex (OR, 5.48; P = .014), and absence of hyperechoic spots within the sludge (OR, 6.78; P = .008).

Conclusion: Although the prevalence of tumefactive sludge at US was rare, a considerable proportion of patients had a malignancy. Careful follow-up is essential, especially for older patients, women, and those with an absence of hyperechoic spots at US.

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Ultrasonography (US) has a primary role in the imaging of gallbladder diseases including polyps, cholelithiasis, and sludge (1). Although gallbladder polyps and gallstones are relatively common, with a prevalence of 3%–7% and 10%, respectively, at abdominal US, biliary sludge is quite rare in asymptomatic healthy adults (2,3), with a reported prevalence of 0.18%–0.27% (4,5). However, its incidence can be higher in specific clinical situations such as pregnancy (6), total parenteral nutrition (7), rapid weight loss (8), and prolonged fasting in the intensive care unit (9).

Biliary sludge is usually found incidentally at US and is easily diagnosed. It typically appears as low-level echoes that layer in the dependent portion of the gallbladder, without acoustic shadowing or internal vascularity. In addition, it tends to move slowly with changes in patient position because of a higher specific gravity (10). In comparison, tumefactive biliary sludge does not form a fluid level, but rather appears as a polypoid mass that does not move with change in position, mimicking gallbladder cancer (11).

The clinical relevance of gallbladder sludge has been well established, as has its association with colicky pain, cholecystitis, cholangitis, and acute pancreatitis. The epidemiology, prevalence, and clinical importance of tumefactive sludge, however, remain unclear (11–13). In clinical practice, when tumefactive sludge is incidentally detected at US examination, observation, short-term follow-up with US, or further evaluation with additional imaging modalities usually is performed. This may include contrast material–enhanced US, computed tomography (CT), and magnetic resonance (MR) imaging (1,2). However, no clinical guidelines have been published regarding the treatment of patients with tumefactive sludge seen at US, and to our knowledge, no study exists regarding the rate of malignancy in patients found to have tumefactive sludge at US. Thus, we aimed to evaluate the prevalence of tumefactive sludge and its association with gallbladder malignancy. In addition, we assessed for the existence of clinical and imaging differences between benign and malignant tumefactive sludge.

Advances in Knowledge

- The prevalence of gallbladder and tumefactive sludge at abdominal US was 6.0% (6898 of 115 178; 95% confidence interval [CI]: 5.9%, 6.1%) and 0.1% (135 of 115 178; 95% CI: 0.08%, 0.12%), respectively.
- Patients with tumefactive sludge did not have any specific well-known predisposing factors for gallbladder sludge, such as pregnancy, total parenteral nutrition, or intensive care unit setting.
- Of the 107 patients with tumefactive sludge who underwent follow-up, 15 (14%) were confirmed to have malignant tumefactive sludge (gallbladder cancer).
- Old age (odds ratio [OR], 1.06; *P* = .035), female sex (OR, 5.48; *P* = .014), and absence of hyperechoic spots at US (OR, 6.78; *P* = .008) were independent risk factors for malignant tumefactive sludge at multivariate analysis.

Materials and Methods

Subjects

In this retrospective cohort study, we included patients found to have gallbladder sludge at US at a single tertiary academic hospital, Samsung Medical Center, Sungkyunkwan University, Seoul, Korea. The institutional review board granted approval for the study and waived the requirement for informed consent. Patients were identified through a search of our electronic medical records system. In the database search we identified 358 387 consecutive studies in 115 178 patients aged 18 years or older who underwent abdominal US between March 1, 2001, and March 1, 2015. The initial search for "gallbladder sludge" isolated 9308 studies in 6898 patients by using US reports. Then, patients were extracted by using the following keywords: "tumefactive sludge," "tumor like sludge," "mass-like sludge," "tumor" and "sludge" in same sentence, and "mass" and "sludge" in the same sentence (13). For each patient, the first US examination that met the search criteria was taken as the index US study. Then, all reports and US images from the initial index study to the most recent US examination were extracted from the database in the second search and were manually reviewed by two abdominal radiologists (S.H.K. and T.W.K., with 20 and 12 years of experience in abdominal imaging, respectively). A consensus was reached to minimize the classification error according to the following definition of tumefactive sludge: *(a)* a nonmovable mass-like lesion during US examination, *(b)* absence of posterior acoustic shadowing at B-mode US, and *(c)* absence of internal vascularity at

Implication for Patient Care

- In patients with tumefactive sludge at US, careful follow-up is essential because a considerable proportion of patients had a malignancy, especially older patients, women, and those with an absence of hyperechoic spots at US.

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Abbreviations:
CI = confidence interval
OR = odds ratio

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Conflicts of interest are listed at the end of this article.

color Doppler US (10,14). Reasons for exclusion of 53 patients who did not meet the definition of tumefactive sludge at manual image review representing interpretive errors were as follows: nonmass-like lesion (*n* = 29), movability during US examination (*n* = 18), and internal vascularity (*n* = 6) (Appendix E1 [online]). Ten patients without US images and two patients with improper Doppler studies were also excluded. All US images were reviewed by using our picture archiving and communication system (Centricity; GE Healthcare, Chicago, Ill) workstation. These search processes yielded records for 135 patients. Among them, 28 were subsequently excluded because they were lost to follow-up. Finally, 107 patients who underwent follow-up for tumefactive sludge were included in our final cohort. The detailed selection process is described in Figure 1.

Classification of Tumefactive Sludge

Our final cohort was divided into two groups, benign tumefactive sludge (true gallbladder sludge) or malignant tumefactive sludge (gallbladder cancer). The confirmation occurred after histopathologic analysis of a surgical specimen or serial imaging follow-up. At imaging follow-up, a lesion was termed benign if it met at least one of the following criteria: *(a)* lesion with interval regression in size or disappearance at follow-up US, *(b)* high-density lesion at nonenhanced CT or T1 high-signal-intensity lesion at MR imaging without enhancement after administration of contrast material (13), or *(c)* no change in size 24 months after index US.

Figure 1

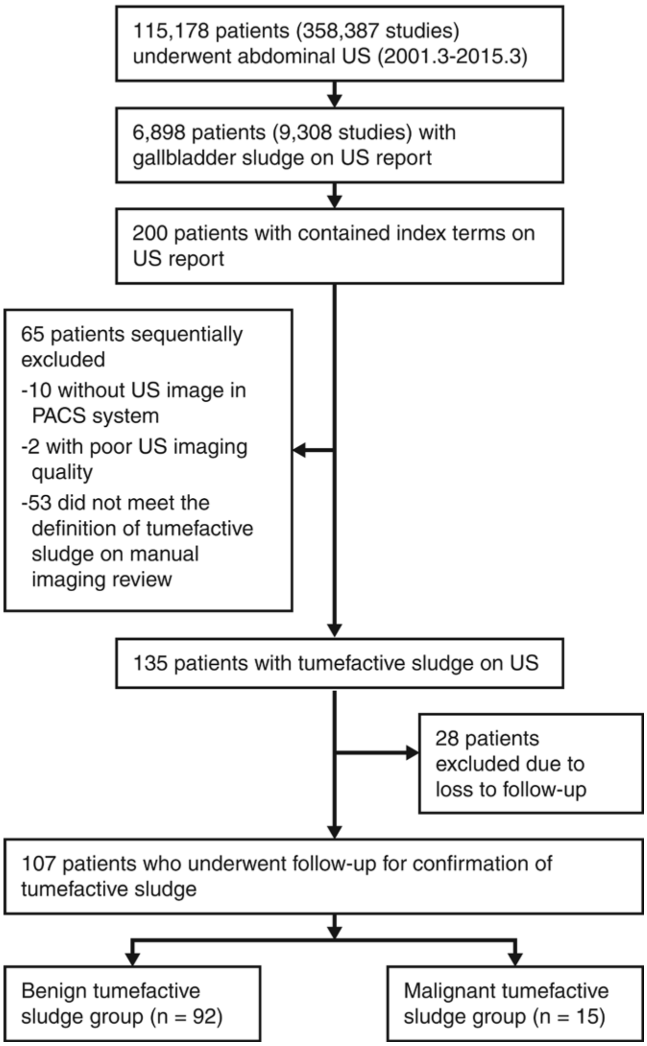


Figure 1: Flow diagram shows patient selection for study. Index terms included "tumefactive sludge," "tumor-like sludge," "mass-like sludge," "tumor" and "sludge" in same sentence, and "mass" and "sludge" in same sentence. For each patient, first US examination meeting search criteria was taken as index US study. *PACS* = picture archiving and communication system.

US Examination

The US examinations were performed by using one of the following US systems: RS80A (Samsung Medison, Seoul, Korea), iU22 (Philips Medical Systems, Bothell, Wash), LOGIQ E9 (GE Healthcare, Waukesha, Wis), Acuson Sequoia 512 or model 128XP (Siemens Medical Solutions, Mountain View, Calif), HDI UM-9 or -3000 or -5000 (Advanced Technology Laboratories, Bothell, Wash). In general, our transabdominal US examination protocol was as follows: *(a)* All patients were asked to fast for at least 6 hours before US examination. *(b)* They underwent a B-mode and Doppler US examination with a convex-array transducer with or without a linear high-megahertz transducer. *(c)* The routine checklist for abdominal US included the liver, gallbladder, bile duct, pancreas, spleen, and pelvic cavity for evaluation of ascites, with or without both kidneys (according to the diagnostic test order). *(d)* Supine, left or right lateral decubitus, and semierect positions were used during examination. *(e)* Harmonic imaging was used for gallbladder examination. *(f)* To rule out the possibility of true gallbladder cancer, short-term follow-up with US, or additional work-up with contrast-enhanced CT or MR imaging, was recommended if tumefactive sludge was seen at US.

US Image Analysis

Two radiologists (Y.K.K. and M.K., with 18 and 6 years of experience in abdominal imaging, respectively) analyzed the US images retrospectively in consensus by using the picture archiving and communications system. Both reviewers were blinded to the radiologic reports and histopathologic diagnoses at the time of image evaluation. The following imaging variables for tumefactive sludge were evaluated on the basis of previous US studies for the gallbladder (15–17): *(a)* multiplicity (single or multiple), *(b)* location, *(c)* maximal diameter of tumefactive sludge, *(d)* height-to-width ratio on the transverse plane, *(e)* shape (pedunculated or sessile), *(f)* internal echo level of tumefactive sludge (grades 1, 2, and 3), *(g)* internal echo pattern (homogeneous or heterogeneous), *(h)* margin (well defined or ill defined), *(i)* surface pattern (smooth, granular or lobular, irregular), *(j)* presence or absence of hyperechoic spots, *(k)* presence or absence of adjacent gallbladder wall thickening, and (l) presence or absence of coexistent gallstones. Height was defined as the maximum vertical distance from the base of the inner layer of the gallbladder wall to the top of the lesion. Width was defined as the length parallel to the gallbladder wall to the base of the lesion. A pedunculated shape was defined as the maximum diameter of a lesion that was larger than the base of the lesion (16). The internal echo level of tumefactive sludge was classified as grade 1, 2, or 3 according to the following criteria: grade 1, lower echogenicity than that of the adjacent liver parenchyma; grade 2, higher echogenicity than that in the adjacent liver parenchyma but lower echogenicity than that of the outer wall of the gallbladder; and grade 3, higher echogenicity than the outer wall of the gallbladder. Smooth surface was defined as a surface without lumps or holes; whereas a granular or lobular surface had a scalloped appearance, and an irregular surface was defined as any other surface pattern not included in the preceding two criteria. Hyperechoic spots indicated partial aggregates of multiple tiny echogenic foci within tumefactive sludge (17). Adjacent gallbladder wall thickening was defined as a transverse wall measurement greater than 3 mm adjacent to the lesion and perpendicular to the sonographic beam (15). If the patient had multiple lesions, we analyzed the imaging findings of the largest lesion.

Table 1

Baseline Clinical Characteristics of Study Patients

Parameter	Benign Tumefactive Sludge (*n* = 92)	Malignant Tumefactive Sludge (*n* = 15)	*P* Value
Age at index study (y)*	57.6 ± 13.0 (19–86)	62.8 ± 11.2 (45–80)	.749
No. of women	37 (40)	11 (73)	.017
All symptoms	26 (28)	6 (40)	.373
Abdominal pain	18 (69)	3 (50)	
Abdominal discomfort	5 (19)	1 (17)	
Others	3 (12)	2 (33)	
Location of sludge in gallbladder			.416
Neck	20 (22)	5 (33)	
Body	46 (50)	5 (33)	
Fundus	26 (28)	5 (33)	
Location of patient at diagnosis			.145
Outpatient	67 (73)	8 (53)	
Inpatient	21 (23)	5 (33)	
Emergency department	4 (4)	2 (13)	
Method of further workup			.333
Follow-up with US	12 (13)	0 (0)	
Contrast-enhanced US	0 (0)	0 (0)	
CT	37 (40)	5 (33)	
MR imaging	5 (5)	1 (7)	
Surgical resection	38 (41)	9 (60)	
TNM staging for gallbladder cancer†	. . .		. . .
Tumor staging			
T1		3 (33)	
T2		4 (44)	
T3		2 (22)	
Nodal staging			
N0		6 (67)	
N1		3 (33)	
N2		0 (0)	

Note.—Unless otherwise indicated, data are number of patients, with percentage in parentheses.

* Data are means ± standard deviations, with the range in parentheses.

† In the malignant tumefactive sludge group, six patients had unresectable gallbladder cancers.

Review of Clinical Information

The presence of symptoms, location at diagnosis, predisposing factors such as pregnancy, total parenteral nutrition, or admission to an intensive care unit as part of hospitalization (18), the time interval between initial US and follow-up imaging or surgery, and the type of follow-up imaging modalities used for confirmation were reviewed. All of these review processes were performed by one author (K.M.J.). In addition, histopathologic findings from resected specimens including histologic type and TNM classification for staging were analyzed by one pathologist specializing in gallbladder pathology (S.Y.H.) according to the American Joint Committee on Cancer staging system (19).

Statistical Analysis

A comparison of clinical and imaging characteristics was performed in both groups by using the Mann-Whitney test for continuous variables and the Fisher

Figure 2

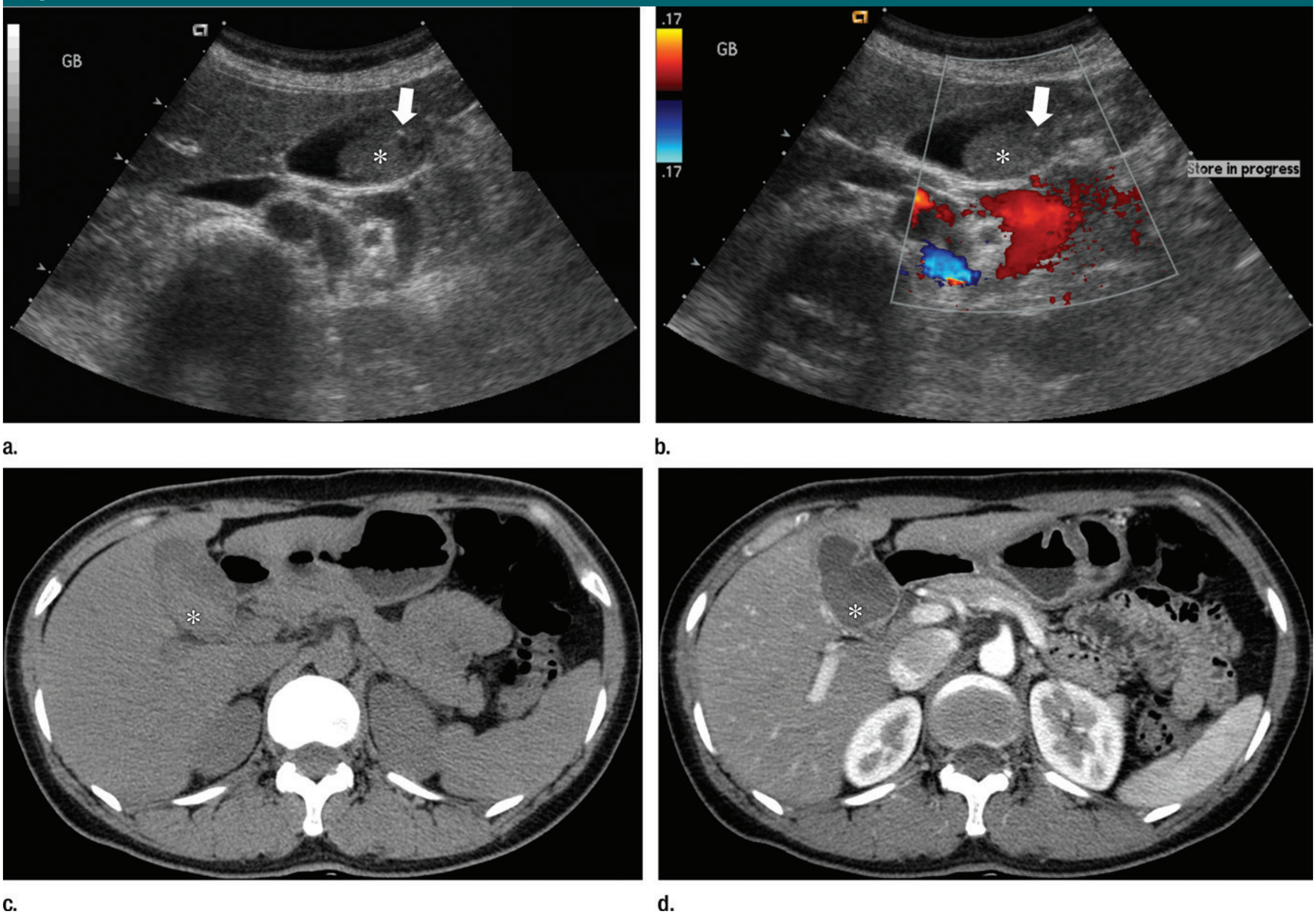


Figure 2: Images in a 58-year-old-man with benign tumefactive sludge. **(a)** On B-mode US image, 2.3-cm echogenic mass without movability is located in body of gallbladder (*). Arrow indicates hyperechoic spot in tumefactive sludge. **(b)** On color Doppler US image, lesion (*) does not have internal vascularity. **(c)** Unenhanced axial CT image shows hyperintense lesion in gallbladder (*) compared with adjacent liver. **(d)** After administration of contrast material, axial CT image shows absence of enhancement of corresponding lesion (*). It was confirmed as sludge with chronic cholecystitis at laparoscopic cholecystectomy.

exact test for categorical variables. The prevalence of gallbladder sludge and tumefactive sludge was calculated. The clinical and imaging parameters were analyzed for possible risk factors for malignant tumefactive sludge by using univariate and multivariate logistic regression analyses. The variables with *P* values of .2 or less at univariate analyses were entered into the final multivariate model to examine the significance of the differences in risk factors for malignant tumefactive sludge after adjustment for other risk factors. We checked the multicollinearity problem by computing the variance inflation factor, and the values were less than 5. For each parameter, an odds ratio (OR) for malignant to benign tumefactive sludge was provided, with a 95% confidence interval (CI). Results were considered statistically significant when a *P* value was less than .05. All statistical analyses were performed with commercially available statistical software (SAS version 9.3; SAS Institute, Cary, NC).

Results

Prevalence and Baseline Characteristics

The prevalence of gallbladder sludge and tumefactive sludge at abdominal US during the observation period was 6.0% (6898 of 115 178 [95% CI: 5.9%, 6.1%]) and 0.1% (135 of 115 178 [95% CI: 0.08%, 0.12%]), respectively. Among the gallbladder sludge, the frequency of the tumefactive sludge was 2.0% (135 of 6898). Of the 107 patients (59 men, 48 women; mean age, 58.3 years; range, 19–86 years) who underwent follow-up, 15 (14%) were confirmed to have malignant tumefactive sludge. With regard to the clinical characteristics, patients with malignant tumefactive sludge were significantly more likely to be women (*P* = .017). However, the two groups showed no significant differences in other baseline characteristics (Table 1). None of the patients with tumefactive sludge had known predisposing factors for gallbladder sludge such as

Figure 3

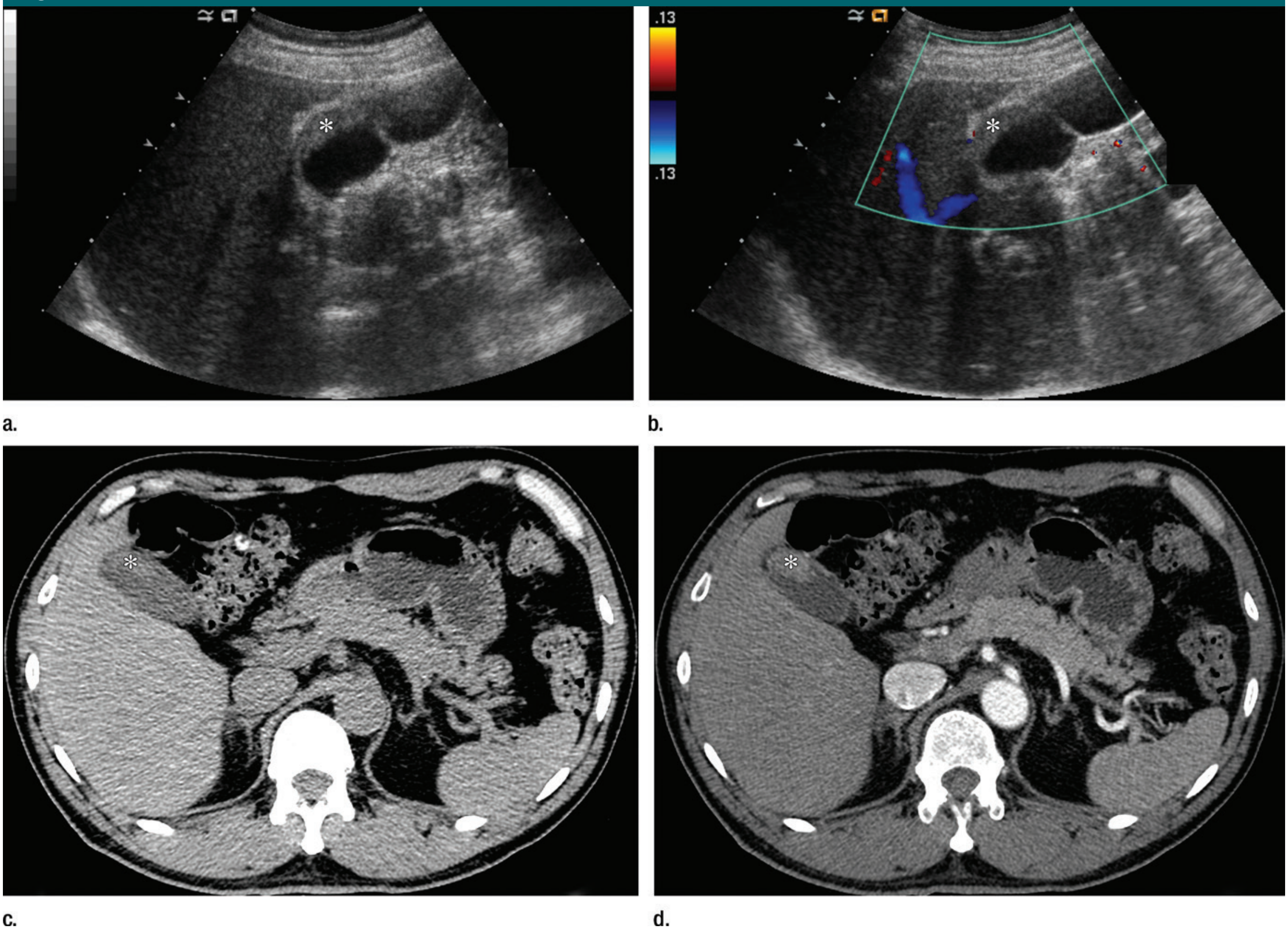


Figure 3: Images in a 63-year-old-woman with operable malignant tumefactive sludge. **(a)** On B-mode US image, a 2.8-cm echogenic mass without movability is located in body to fundus of gallbladder (*). **(b)** On color Doppler US image, lesion (*) does not have internal vascularity. **(c)** Axial unenhanced CT image shows iso- to hypointense lesion in gallbladder (*) compared with adjacent liver. **(d)** On arterial phase axial CT image, lesion is highly enhancing (*) and is confirmed to be gallbladder cancer at radical cholecystectomy.

pregnancy, total parenteral nutrition, or admission to an intensive care unit.

US Analysis

Among US imaging features of tumefactive sludge, those with benign tumefactive sludge had higher rates of hyperechoic spots within the gallbladder lesion than did those in the malignant tumefactive sludge group (59.8% vs 20.0%; *P* = .004) (Figs 2, 3). The mean size of the lesions was 2.93 cm (range, 0.8–9 cm) in the group with benign tumefactive sludge and 3.20 cm (range, 1.5–6 cm) in the group with malignant tumefactive sludge, without a significant difference (*P* = .175). According to the size criteria of 1 cm, most benign tumefactive sludge (92.3%, 85 of 92) and all malignant tumefactive sludge were larger than 1 cm. The other investigated variables were not significantly different between the groups (Table 2).

Clinical Follow-up

The diagnosis of benign tumefactive sludge (*n* = 92) was established by using the following clinical-pathologic results: *(a)* absence of malignancy in surgical specimen (*n* = 38), *(b)* further workup with contrast-enhanced CT (*n* = 37) or MR imaging studies (*n* = 5), *(c)* a lesion with interval regression in size or disappearance at follow-up US (*n* = 9), *(d)* no change in size at least 24 months after US (*n* = 3). The median interval between index US and the next imaging study was 17 days (range, 0–241 days). For the group with malignant tumefactive sludge (*n* = 15), nine patients underwent radical cholecystectomy. The median interval between index US and surgery was 20 days (range, 6–60 days). In terms of the American Joint Committee on Cancer TNM staging of the malignant tumefactive sludge (gallbladder cancer), three (33%) patients had T1 tumors, four (44%) had T2 tumors, and two (22%) had T3 tumors. The histopathologic analysis revealed adenocarcinoma in eight (89%) patients and adenosquamous carcinoma in one (11%) patient. The remaining six patients had unresectable gallbladder cancers with or without lymph node involvement and hepatic metastasis at further workup with CT or MR imaging studies (Fig 4).

Risk Factor Analysis for Malignant Tumefactive Sludge

Univariate analysis showed that female sex (OR, 4.09 [95% CI: 1.21, 13.82]; *P* = .024) and absence of hyperechoic spots at US (OR, 5.95 [95% CI: 1.57, 22.53]; *P* = .009) were associated with increased risk of malignancy (Table 3). At multivariate analysis, the risk of malignant tumefactive sludge was significantly higher in older patients (OR, 1.06 [95% CI: 1.00, 1.12]; *P* = .035), women (OR, 5.48 [95% CI: 1.42, 21.16]; *P* = .014), and those with an absence of hyperechoic spots at US (OR, 6.78 [95% CI: 1.64, 28.15]; *P* = .008).

Table 2

US Imaging Findings of Patients in Both Groups

Parameter	Benign Tumefactive Sludge (*n* = 92)	Malignant Tumefactive Sludge (*n* = 15)	*P* Value
Multiplicity			.675
Single	82 (89)	13 (87)	
Multiple	10 (11)	2 (13)	
Maximal diameter (cm)*	2.93 ± 1.64 (0.7–9.0)	3.20 ± 1.17 (1.5–6.2)	.175
Height-to-width ratio*	0.60 ± 0.38 (0.20–2.64)	0.65 ± 0.33 (0.26–1.59)	.282
Shape			.545
Pedunculated	29 (31)	3 (20)	
Sessile	63 (68)	12 (80)	
Level of internal echogenicity			.644
Grade 1	30 (33)	6 (40)	
Grade 2	47 (51)	8 (53)	
Grade 3	15 (16)	1 (7)	
Internal echo pattern			.346
Homogeneous	27 (29)	2 (13)	
Heterogeneous	65 (71)	13 (87)	
Margin			.512
Well defined	69 (75)	13 (87)	
Ill defined	23 (25)	2 (13)	
Surface pattern			.264
Smooth	28 (30)	3 (20)	
Granular or lobular	33 (36)	9 (60)	
Irregular	31 (34)	3 (20)	
Presence of hyperechoic spots			.004
Yes	55 (60)	3 (20)	
No	37 (40)	12 (80)	
Presence of adjacent gall bladder wall thickening			.611
Yes	7 (8)	2 (13)	
No	85 (92)	13 (87)	
Presence of coexistent gallstone			.133
Yes	37 (40.2)	3 (20.0)	
No	55 (59.8)	12 (80.0)	

Note.—Unless otherwise indicated, data are number of patients, with percentage in parentheses.

* Data are means ± standard deviation, with the range in parentheses.

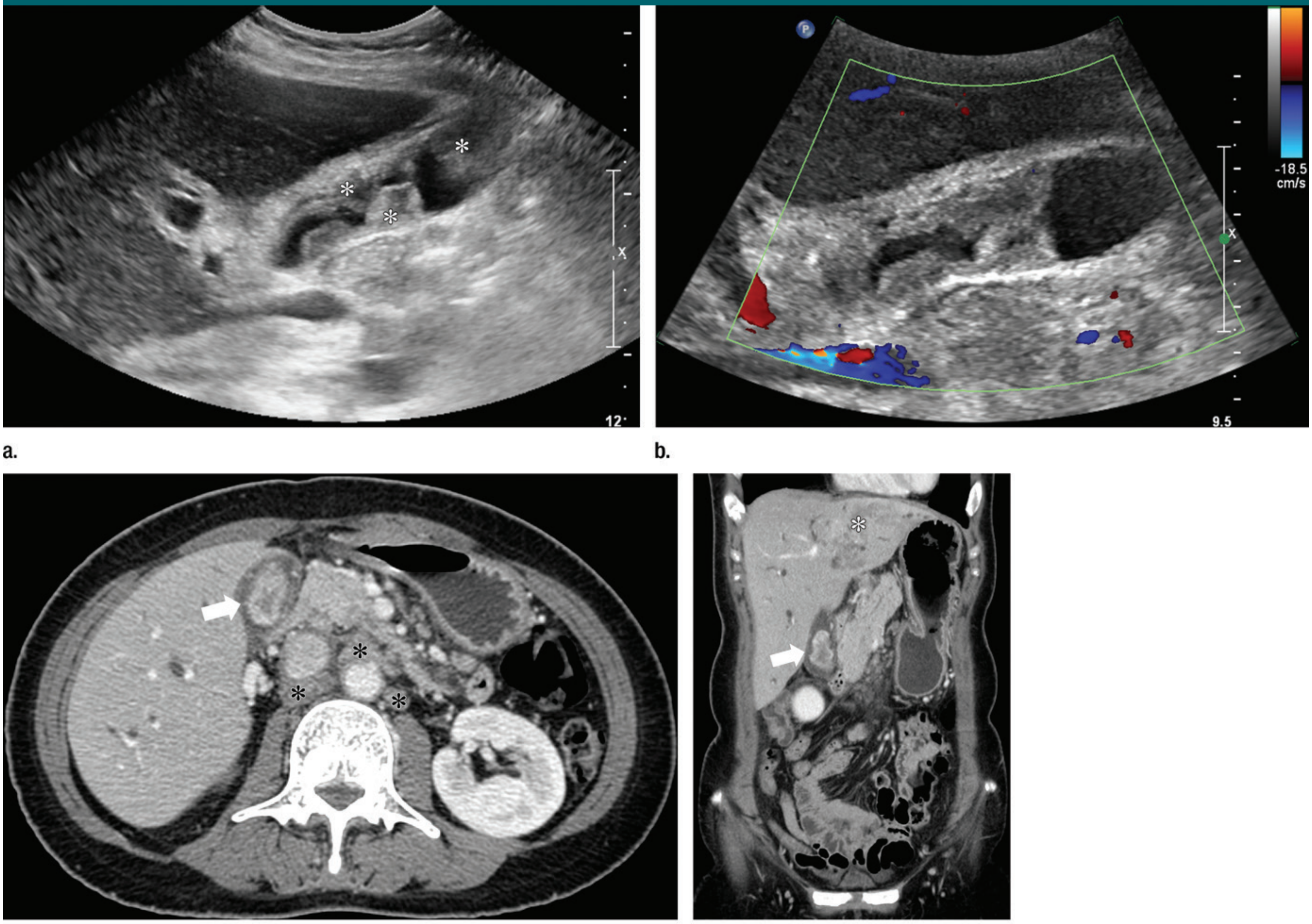
Discussion

We found that the prevalence of gallbladder sludge and tumefective sludge differed markedly. In addition, patients with tumefactive sludge did not have any specific well-known predisposing factors for gallbladder sludge, such as pregnancy, total parenteral nutrition, and intensive care unit setting (6–9). A previous study (18) reported that gallbladder sludge was causally associated with biliary colic in less than 10% of patients. In comparison, we found the incidence of symptomatic abdominal pain at the time of US examination was as high as 20% among our patients with tumefactive sludge. On the basis of these results, although gallbladder sludge and tumefactive sludge could be considered part of the wide spectrum of cholelithiasis, they may be somewhat different in terms of clinical characteristics.

Tumefactive sludge appears as the absence of blood flow in the mass on color Doppler US, because it is composed of a suspension of cholesterol monohydrate crystals or calcium bilirubinate granules embedded in mucus (13,18). These properties are important imaging clues to differentiate tumefactive sludge from mass-forming or polypoid gallbladder cancer, since gallbladder cancer usually demonstrates blood flow with low resistance arterial waveforms at power and color Doppler US (14). Similarly, a previous study (20) reported that the specificity of color Doppler signal patterns for the diagnosis of gallbladder cancer, at 62.5%, was sufficiently high. However, although all patients with tumefactive sludge in our cohort did not show internal vascularity at color Doppler US according to the definition of the inclusion criteria, 14% of these patients had gallbladder cancer. Thus, color Doppler US has its limitations for differential diagnosis between benign and malignant tumefactive sludge.

With regard to other criteria at US, according to the treatment algorithm for polypoid lesion in the gallbladder (2), the risk of gallbladder cancer primarily depends on the size of the lesion. Incidentally detected gallbladder polyps measuring less than 5 mm do

Figure 4



a. b. c. d.

Figure 4: Images in a 45-year-old-woman with inoperable malignant tumefactive sludge. **(a)** On B-mode US image, multiple heterogeneous echogenic masses without movability are located in body to fundus of gallbladder (*). **(b)** On color Doppler US image, these lesions do not have internal vascularity. Follow-up **(c)** axial and **(d)** coronal CT images show irregular thickening gallbladder inner wall with prominent enhancement (arrow). There are multiple metastatic lymph nodes in the retroperitoneum (*, **c**) and hepatic metastasis in left lobe (*, **d**). The patient underwent palliative chemotherapy for advanced gallbladder cancer.

not require additional follow-up, while a diameter of larger than 10 mm indicates a need for surgery due to risk of malignancy (21,22). A previous study (23) reported that approximately 30% of polyps measuring 11–20 mm in diameter were cholesterol polyps after cholecystectomy and 92% (85 of 92) of patients with benign tumefactive sludge in our study had a polypoid mass larger than 10 mm. Therefore, additional predictive factors are needed to differentiate malignant from benign tumefactive sludge beyond the size criteria because of the difference in clinical treatment. In our study, old age and female sex were significant risk factors for malignant tumefactive sludge at multivariate analysis. These risks are similar to that of gallbladder cancer. In general, the risk of gallbladder cancer can increase with age. In addition, sex differences exist with geographic variances, generally being unfavorable for women (24). In a prior study (25), 29% of patients with polypoid lesions of the gallbladder did not show focal lesions at histopathologic analysis after cholecystectomy. Some of them may be cases of tumefactive sludge that mimic polypoid masses at US.

On the basis of our multivariate analysis, lack of hyperechoic spots within the tumefactive sludge was a significant risk factor for malignancy, along with old age and female sex. Gallbladder sludge is typically associated with cholelithiasis, and evolution to calcium bilirubinate stones has been described (18). Therefore, hyperechoic spots at US may represent microlithiasis (26) and could be helpful for differentiation of benign from malignant tumefactive sludge. However, in our study, some patients with malignant tumefactive sludge (20%) had hyperechoic spots at US, and authors of previous studies

Table 3

Risk Factor Analysis for Malignant Tumefactive Sludge in Gallbladder

	Univariate Analysis		Multivariate Analysis	
Parameter	OR	*P* Value	OR	*P* Value
Age	1.03 (0.99, 1.08)	.146	1.06 (1.00,1.12)	.035
Female vs male sex	4.09 (1.21, 13.82)	.024	5.48 (1.42,21.16)	.014
Symptomatic tumefactive sludge	1.69 (0.55, 5.23)	.361	. . .	. . .
Location of patient		.235	. . .	. . .
Outpatient	1*	. . .		
Inpatient	1.99 (0.59, 6.76)	.970		
Emergency department	4.19 (0.66, 26.61)	.238		
Maximal diameter	1.11 (0.80, 1.53)	.533	. . .	. . .
Height to width radio	1.41 (0.38, 5.21)	.606	. . .	. . .
Sessile vs pedunculated shape	1.84 (0.48, 7.03)	.372	. . .	. . .
Internal echogenicity		.621	. . .	. . .
Grade 1	1*	. . .		
Grade 2	0.85 (0.27, 2.70)	.569		
Grade 3	0.33 (0.04, 3.03)	.343		
Heterogeneous vs homogeneous internal echo pattern	2.70 (0.57, 12.78)	.211	. . .	. . .
Ill-defined vs well-defined margin	0.46 (0.10, 2.20)	.332	. . .	. . .
Surface pattern		.223	. . .	. . .
Smooth	1*	. . .		
Granular or lobular	2.55 (0.63, 10.33)	.084		
Irregular	0.90 (0.17, 4.85)	.418		
Absence of hyperechoic spots	5.95 (1.57, 22.53)	.009	6.78 (1.64,28.15)	.008
Adjacent gallbladder wall thickening	1.87 (0.35, 9.99)	.465	. . .	. . .
Coexistent gallstone	0.37 (0.10, 1.41)	.145	0.33 (0.07,1.57)	.163

Note.—Data in parentheses are 95% CIs.

* Reference category.

reported that adenocarcinoma with the accumulation of foamy cells underneath cancerous epithelium may also manifest similarly as hyperechoic spots at US (27). Thus, diagnosis for tumefactive sludge should be based on a combination of clinical results and those of other imaging modalities.

Because our study showed relatively high proportions of malignancy in patients (14%) with tumefactive sludge at US, follow-up imaging with contrast-enhanced US, contrast-enhanced CT, or MR imaging should be performed. In our study, a large number of patients were lost to follow-up without confirmation of tumefactive sludge. By applying the rate of malignancy in our patients known to have tumefactive sludge, we can assume that some of the patients lost to follow-up may have had undiagnosed gallbladder cancer.

There were several limitations in our study. First, there was the possibility of selection bias related to the retrospective design. Second, the US equipment and radiologists involved were variable and not standardized because our study cases spanned a period of 14 years. This may have had an influence on the degree of heterogeneity in our cohort of patients with tumefactive sludge. Third, although most of the lesions in the group with benign tumefactive sludge were larger than 1 cm and were confirmed as the absence of polyps at follow-up CT and MR imaging or surgical specimen results, gallbladder polyps could mimic tumefactive sludge in some of patients with benign small tumefactive sludge. Fourth, due to the small number of patients with malignant tumefactive sludge (n = 15) in the final study cohort, the multivariate logistic regression analysis was subject to the problems associated with multicollinearity.

In conclusion, although tumefactive sludge at abdominal US is rare in clinical practice, a considerable proportion of patients may have a malignancy. Thus, careful follow-up and further imaging evaluation should be performed in patients with tumefactive sludge at US, especially in older patients, women, and those with an absence of hyperechoic spots at US.

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