



# Imaging findings of hemorrhagic hepatic cysts with enhancing mural nodules

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## Abstract

**Purpose** This study aimed to evaluate the clinical and radiological findings of hemorrhagic hepatic cysts with enhancing mural nodules.

**Methods** The radiology databases of five facilities were retrospectively searched for reports indicating hemorrhagic hepatic cysts or hepatic cystic tumors. Cases of hemorrhagic hepatic cysts with enhancing mural nodules based on pathological or radiological findings were identified and reviewed.

**Results** We included 14 cases (11 female and 3 male) with a mean patient age of 72.6 years. Up until the enhancing mural nodules were detected, the cysts had decreased in size in all ten cases for which radiological imaging was available for a period of > 3 years previous to detection. Dynamic contrast-enhanced CT or MRI showed focal enhancement in the early phase and progressive centrifugal enhancement in the delayed phase in all 16 mural nodules  $\geq 10$  mm in diameter. Thirteen of 14 MRI assessable enhancing mural nodules  $\geq 10$  mm in diameter showed a hypointense rim with central hyperintensity on T2-weighted imaging. All cases showed calcification of the cyst wall. In the three referred cases, <sup>18</sup>F-fluorodeoxyglucose (FDG) positron emission tomography/CT demonstrated no intense FDG uptake in the enhancing mural nodules. In the four resected cases, histopathology of the enhancing mural nodules revealed neovascularization within an organized hematoma, including extensive dilated vessels and hemangioma-like lesions.

**Conclusions** Features including a decrease in cyst size, a progressive centrifugal enhancing pattern on dynamic contrast-enhanced CT or MRI, a hypointense rim with central hyperintensity on T2-weighted MRI, and cyst wall calcification may indicate a hemorrhagic hepatic cyst.

**Keywords** Hemorrhagic hepatic cyst · Intracystic hemorrhage · Organized hematoma · Cystic liver lesion · Computed tomography · Magnetic resonance imaging

## Introduction

Hepatic simple cysts are the most common benign liver lesions, occurring in 2.5–18% of the population, with their incidence increasing with age [1]. Intracystic hemorrhage is a rare complication of hepatic simple cysts. Hepatic simple cysts are usually easily diagnosed, but hemorrhagic hepatic

cysts often show complicated imaging findings [2]. It is sometimes difficult to differentiate hemorrhagic hepatic cysts from cystic neoplasms, particularly when the former are accompanied by mural nodules that enhance after intravenous contrast medium injection on CT or MRI. It is generally accepted that intrahepatic cysts with mural nodules should be considered suspicious for cystic neoplasms [1, 2]. The occurrence of hemorrhagic hepatic cysts with enhancing mural nodules is rare, and there are several case reports of hepatectomies being performed as a result of its misdiagnosis as cystic neoplasm [3–19]. To avoid unnecessary surgery, it is essential to differentiate between hemorrhagic hepatic cysts and cystic neoplasms. In most of the previously reported cases with enhancing mural nodules, the pathological findings were neovascularization, extensive dilated vessels, and hemangioma-like lesions within organized

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hematomas [3–16]. We suspected that imaging findings of enhancing mural nodules would reflect the pathological findings and could be useful for their diagnosis. This study, therefore, evaluated the clinical and radiological findings of hemorrhagic hepatic cysts with enhancing mural nodules.

## Materials and methods

The radiology databases of five facilities were retrospectively reviewed to identify patients who underwent CT or MRI between January 2000 and November 2017 and whose reports indicated hemorrhagic hepatic cysts or hepatic cystic tumors. Patients who met all of the following criteria were included in the study: (i) cystic lesions with contents showing high intensity on T1-weighted imaging (T1-WI) and high intensity with partial low intensity on T2-weighted imaging (T2-WI), or, in cases of no referable MRI, high density on CT; (ii) enhancing mural nodules were detected by dynamic contrast-enhanced CT or MRI; and (iii) histopathology of the enhancing mural nodules revealed no neoplastic lesion, or, in cases of no histopathological diagnoses, the enhancing mural nodules showed no signs of neoplastic disease after follow-up of  $\geq 2$  years from the first detection.

The medical records were retrospectively reviewed to retrieve information on age, sex, tumor markers, pathological findings, and follow-up data. CT, MRI, and  $^{18}\text{F}$ -fluorodeoxyglucose positron emission tomography (FDG-PET)/CT imaging findings, including images acquired before and after initial detection, were evaluated by a board-certified abdominal radiologist with 9 years of experience. The time

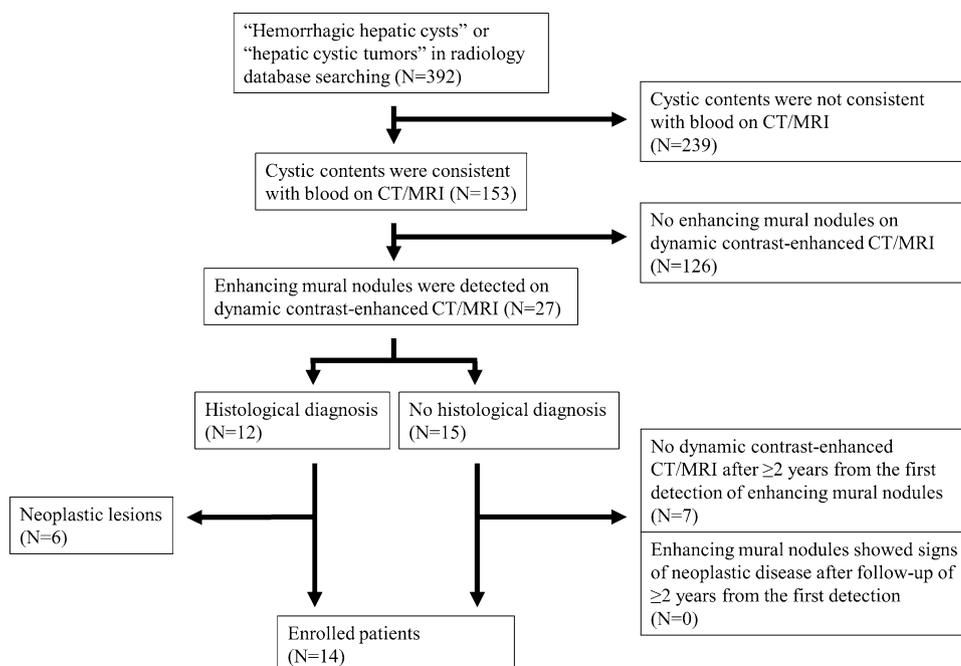
courses of the cysts and mural nodules, the size and number of mural nodules, the enhancement pattern of mural nodules on dynamic contrast-enhanced CT or MRI, and the signal intensity of mural nodules on T1-WI and T2-WI were assessed. In the evaluation of enhancement pattern and signal intensity, only those mural nodules  $\geq 10$  mm in diameter were included, because partial volume effects might have impeded precise evaluation of the enhancement pattern and signal intensity of smaller nodules. In addition, cyst wall calcification was assessed on non-contrast enhanced CT.

## Results

A total of 14 patients (11 female and 3 male) were identified: four underwent surgical resection, two underwent biopsy, and eight were followed up without surgery or biopsy. The preoperative diagnosis of all cases that underwent surgical resection was cystic neoplasm. A flow chart summarizing the study population is presented in Fig. 1.

The clinical and radiological data are summarized in Table 1. The mean age of the 14 patients was 72.6 years (range 53–80 years). Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) were measured as tumor markers in all cases, and  $\alpha$ -fetoprotein (AFP) and protein induced by vitamin K absence or antagonist-II (PIVKA-II) were measured in 11 cases. The tumor marker CA 19-9 was elevated in four patients and CEA was elevated in one, although no patients showed elevated AFP or PIVKA-II. Up until the enhancing mural nodules were initially detected, the cyst size decreased in all ten cases

**Fig. 1** Flow chart of the inclusion criteria applied to the study population



**Table 1** Clinical and radiological data of the 14 cases of hemorrhagic hepatic cysts with enhancing mural nodules

Case no.	Age (yr)/sex	Treatment	Histopathology	Cyst size until initial diagnosis/follow up period (yr)	Number/size of nodules (mm)	Focal enhancement in the early phase with progressive centrifugal enhancement in the delayed phase	Hypointense rim with central hyperintensity on T2-WI	Calcification of cyst wall	FDG uptake	Serum tumor marker (CEA, CA19-9/AFP, PIVKA-II)
1	76/F	Hepatectomy	Organized hemangioma	NA	1/20	+	+	+	Not significant	WNL/WNL
2	76/F	Hepatectomy	Organized hemangioma	Decreased/6	1/19	+	+	+	Not significant	CA19-9 elevated/WNL
3	80/F	Hepatectomy	Organized hemangioma	NA	1/20	+	+	+	NA	WNL/NA
4	73/M	Hepatectomy	Organized hemangioma	NA	1/16	+	+	+	NA	WNL/WNL
5	76/M	Biopsy	Organized hemangioma	NA	5/8, 9, 12, 17, 28	+	+	+	NA	WNL/WNL
6	53/F	Biopsy	No evidence of neoplasm	Decreased/4	1/22	+	+	+	NA	WNL/WNL
7	79/F	Follow-up	NA	Decreased/11	2/2, 12	+	NA	+	NA	WNL/WNL
8	75/F	Follow-up	NA	Decreased/12	3/2, 3, 12	+	NA	+	NA	CA19-9 elevated/WNL
9	76/F	Follow-up	NA	Decreased/5	1/2	NA	NA	+	NA	WNL/WNL
10	69/F	Follow-up	NA	Decreased/7	1/8	NA	NA	+	Not significant	WNL/NA
11	72/F	Follow-up	NA	Decreased/15	2/4, 10	+	-	+	NA	CEA and CA19-9 elevated/NA
12	69/M	Follow-up	NA	Decreased/3	1/10	+	+	+	NA	WNL/WNL
13	71/F	Follow-up	NA	Decreased/3	2/12, 14	+	+	+	NA	WNL/WNL
14	71/F	Follow-up	NA	Decreased/3	2/11, 14	+	+	+	NA	CA19-9 elevated/WNL

Evaluation of enhancement pattern and MRI signal was performed if the enhancing mural nodules were  $\geq 10$  mm in diameter  
 F female, M male, T1-WI T1-weighted MRI, T2-WI T2-weighted MRI, FDG 18F-fluorodeoxyglucose, NA not available, WNL within normal limits

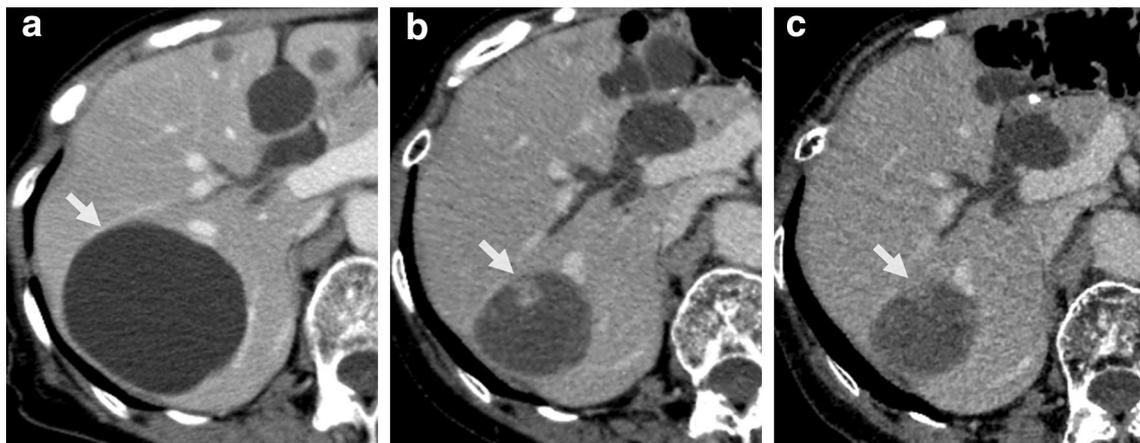
for which data on radiological examinations > 3 years previous were available (Fig. 2). The mean number of enhancing mural nodules per patient was 1.7 (range 1–5), and the mean size of the enhancing mural nodules was 12.0 mm (range 2–28 mm). Dynamic contrast-enhanced CT or MRI showed focal enhancement in the early phase with progressive centrifugal enhancement in the delayed phase in all 16 assessable nodules (Figs. 3a–d, 4b–d). Progressive centrifugal enhancement in the delayed phase was particularly clear in large nodules. On T1-WI, the signal intensity of the enhancing mural nodules was hypointense in 8 of 14 MRI assessable nodules, and hypointense with partial hyperintensity in 6 of 14 nodules. In 13 of 14 MRI assessable nodules, there was a hypointense rim with central hyperintensity on T2-WI (Figs. 3f, 4e). All cases showed calcification of the cyst wall, with this calcification having newly appeared in all 10 cases for which data on radiological examinations obtained > 3 years previously were available. FDG-PET/CT demonstrated no significant FDG uptake in the enhancing mural nodules and cysts in all three referred cases (Figs. 3g, 4g). In the ten cases without surgery, the time courses of the enhancing mural nodules after appearance were: a size decrease in five, no change in two, no change after temporary enlargement in two, and size decrease after temporary enlargement in one. In the four resected cases, histopathology of the enhancing mural nodules revealed neovascularization within an organized hematoma, including extensive dilated vessels and hemangioma-like lesions (Figs. 3h–j). In the two biopsy cases, one revealed an organized hematoma, while the other showed no evidence of neoplasm.

## Discussion

In the present study, we investigated the characteristic findings of hepatic hemorrhagic cysts with enhancing mural nodules. The lesions predominantly occurred in older women. Serum CA19-9 and CEA, which are common markers of liver cystic neoplasms, were elevated in four and one case, respectively. Several previous studies have also reported cases of hemorrhagic hepatic cysts with elevated CA19-9 or CEA [4–6, 8, 15, 19].

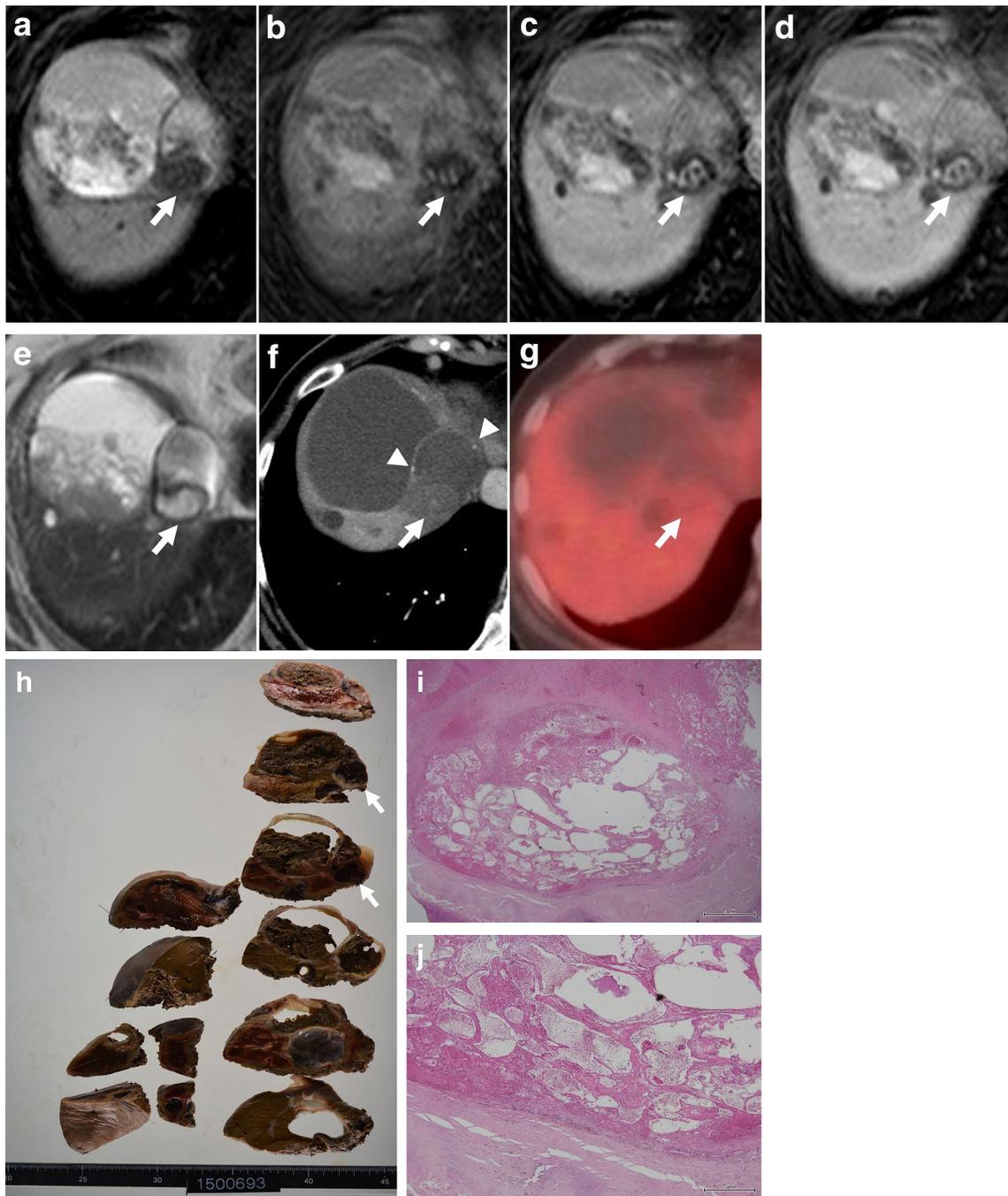
The cyst size presented with a characteristic time course. Generally, spontaneous tumor regression is a rare phenomenon [20], and there is no report of spontaneous regression of hepatic cystic neoplasms. Therefore, a decrease in cyst size may be a specific finding of hemorrhagic hepatic cysts with enhancing mural nodules. We assumed that the decrease in cyst size resulted from the absorption and organization process of the hematoma after intracystic hemorrhage, and that the enhancing mural nodules appeared during this process.

The progressive centrifugal enhancement pattern of the mural nodules is similar to the patterns previously reported [5]. We speculate that this progressive centrifugal enhancement pattern reflects the pathological findings of mural nodules, which are neovascularization within an organized hematoma including extensive dilated vessels and hemangioma-like lesions. Most cases showed a hypointense rim with central hyperintensity on T2-W MRI. We speculate that this central hyperintensity reflects the pathological findings of neovascularization, extensive dilated vessels, and hemangioma-like lesions, and that the hypointense rim reflects the fibrous pseudocapsule or surrounding hemosiderin. In the present study, FDG uptake by the enhancing mural nodules



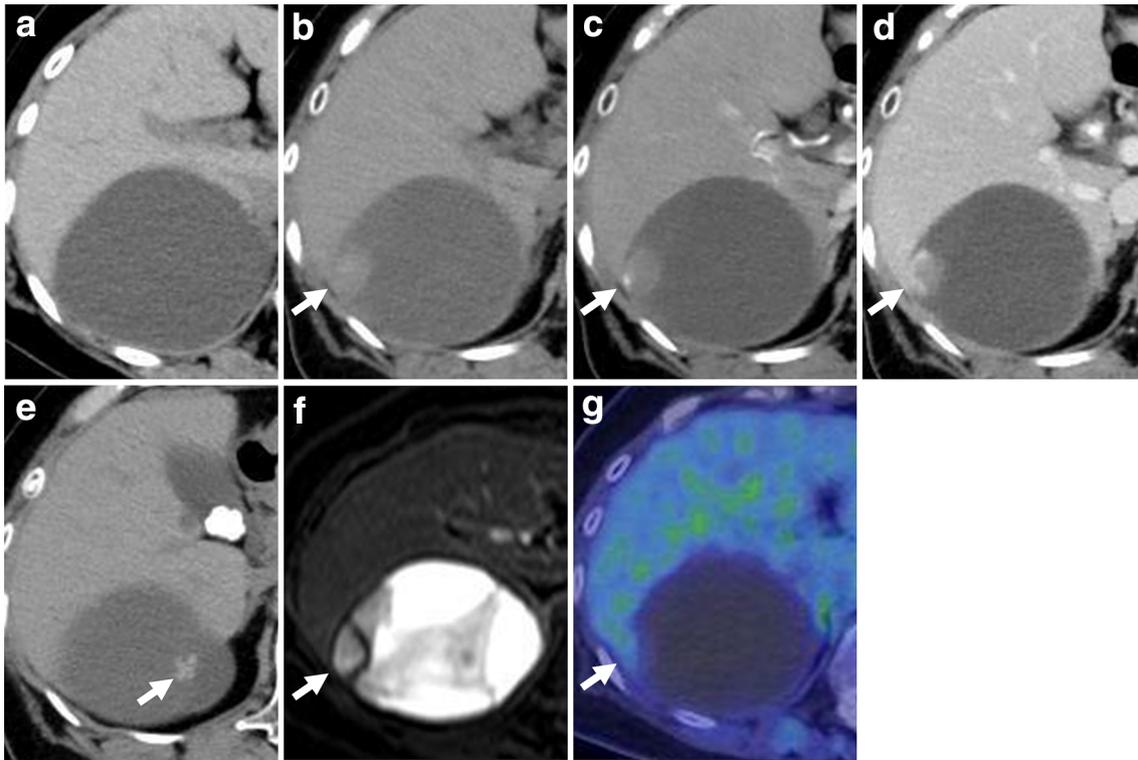
**Fig. 2** CT images of a 75-year-old woman. A simple hepatic cyst was detected on postoperative examination of gastric cancer (a, arrow). Although the cyst had decreased in size 7 years later, a mural nodule that enhanced after intravenous contrast medium had appeared

(b, arrow). Based on the progress and imaging findings, a hemorrhagic hepatic cyst with enhanced mural nodule was suspected, and the lesion was followed up. The hepatic cyst and mural nodule had decreased in size > 3 years later (c, arrow)



**Fig. 3** MR, CT, FDG-PET/CT, specimen, and histological images from a 76-year-old woman. A hepatic cyst with a mural nodule was incidentally detected on ultrasonic examination. MRI showed a cystic lesion with hyperintensity on T1-weighted images (**a**) and hyper- to hypointensity on T2-weighted images (**e**); this suggested a hemorrhagic cyst. The lesion was accompanied by a mural nodule that was hypointense on T1-weighted images (**a**, arrow). Dynamic contrast-enhanced T1-weighted images showed focal enhancement in the early phase (**b**, arrow) with progressive centrifugal enhancement within the mural nodule in the delayed phase (**c**, **d**, arrow). The mural nodule showed a hypointense rim with central hyperintensity on T2-weighted images (**e**, arrow). Contrast-enhanced CT showed focal enhance-

ment in the early phase (**f**, arrow) and calcification of the cyst wall (**f**, arrowhead).  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) positron emission tomography/CT did not demonstrate any intense FDG uptake in the mural nodule (**g**, arrow). Hepatectomy was performed under preoperative diagnosis of cystic neoplasm. Gross specimens of the resected lesion show a cyst with hemorrhagic contents and a mural nodule (**h**, arrows). Histological examination (hematoxylin–eosin stain) revealed that the mural nodule consisted of an organized hematoma with neovascularization, including extensive dilated vessels and a hemangioma-like lesion (**i**, **j**). No evidence of malignancy was seen in the mural nodule or cystic wall



**Fig. 4** CT, MR, and FDG-PET/CT images from a 76-year-old woman. Non-contrast enhanced CT shows a simple hepatic cyst under observation (a). 1 year later, a mural nodule was newly detected on non-contrast enhanced CT (b, arrow), while the cyst had decreased in size. Dynamic contrast-enhanced CT showed focal enhancement in the early phase (c, arrow) with progressive centrifugal enhancement in the mural nodule in the delayed phase (d, arrow). Calcification of the cyst wall can be seen on another slice (e, arrow). The mural

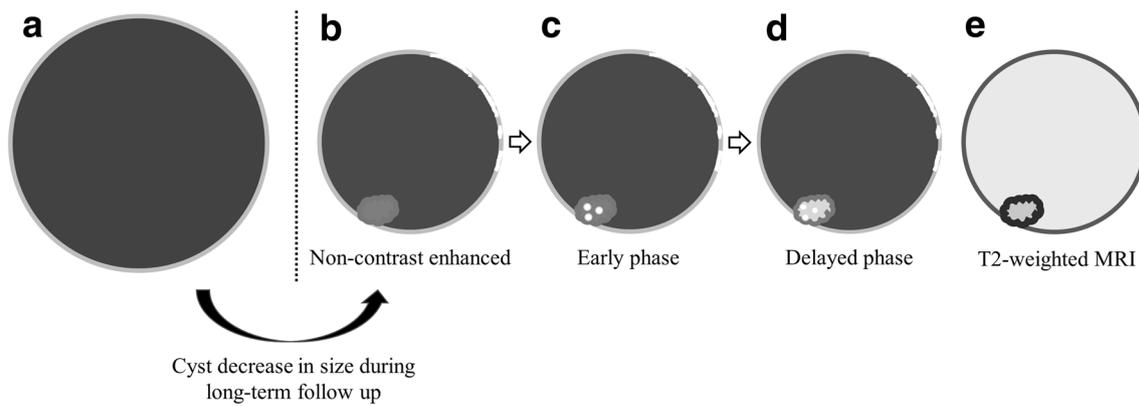
nodule showed a hypointense rim with central hyperintensity on T2-weighted images (f, arrow).  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) positron emission tomography/CT did not demonstrate any intense FDG uptake in the mural nodule (g, arrow). Hepatectomy was performed under preoperative diagnosis of cystic neoplasm, and the histopathology of the mural nodule revealed neovascularization within an organized hematoma

was less than that of hepatic parenchyma. The use of FDG-PET/CT was also reported in two previous cases, and the nodules demonstrated no intense FDG uptake [6, 19]. From the time course of cyst wall calcification, we speculate that the calcification was a reactive change following intracystic bleeding, and that this may be helpful for diagnosis.

The pathogenesis of the enhancing mural nodules is unknown. Previously reported pathological findings of enhancing mural nodules include 16 cases of neovascularization within an organized hematoma (including extensive dilated vessels and hemangioma-like lesions), one case of chronic expanding hematoma, and two cases of cavernous hemangioma [3–19]. In our cases, the histopathology of the enhancing mural nodules revealed neovascularization within an organized hematoma, and we speculate that the enhancing mural nodules appeared when neovascularization occurred during organization of the hematoma after intracystic hemorrhage, as has been previously reported [4]. In the present study, the enhancing mural nodules showed temporary enlargement in three cases. Reports of similar lesions from sites other than the liver include a sinonasal

organized hematoma and a chronic expanding hematoma, with the hematoma increasing in size [21, 22]. Although the pathogenic mechanisms of sinonasal organized hematoma are not fully known, it has been suggested that hemorrhage may repeatedly occur in an organized hematoma, and that this contributes to enlargement of the lesion [21]. We speculate that enhancing mural nodules may enlarge when a similar pathogenic mechanism occurs. Although sinonasal organized hematoma generally increases the overall size of the lesion, the cyst size did not increase in our hepatic lesion cases. Future research is needed to elucidate the pathogenic mechanisms of the enhancing mural nodules. At present, we consider that it is important to recommend follow-up rather than immediate surgical resection if such mural nodules with the characteristic imaging findings are incidentally encountered (Fig. 5).

There are several limitations to our study. First, this study is retrospective in design. Second, the number of patients is small. Third, because the occurrence of hepatic cystic neoplasms is rare, this study could not compare the imaging findings of hepatic cystic neoplasms with hemorrhagic



**Fig. 5** Schematic drawing of the typical imaging findings of a hemorrhagic hepatic cyst with enhancing mural nodules. CT imaging acquired before the appearance of the enhancing mural nodule (a). The cyst shows a decrease in size during long-term follow up until detection of the mural nodule, when calcification of the wall appears

hepatic cysts containing enhancing mural nodules, and further research is needed in this respect. Fourth, we collected data from five different hospitals, with these institutions using different types of CT and MRI scanners and various imaging protocols. Fifth, we included eight cases in which the diagnosis was not confirmed by histopathology. However, in these cases, the patients were monitored for a long time after initial diagnosis and the lesions displayed benign behavior and required no treatment.

## Conclusions

We evaluated the clinical and radiological findings of hemorrhagic hepatic cysts with enhancing mural nodules and found the following features to be indicative of hemorrhagic hepatic cysts: a decrease in cyst size, a progressive centrifugal enhancement pattern on dynamic contrast-enhanced CT or MRI, a hypointense rim with central hyperintensity on T2-WI, and cyst wall calcification.

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(b). The mural nodule shows focal enhancement in the early phase (c) with progressive centrifugal enhancement in the delayed phase (d). The mural nodule shows a hypointense rim with central hyperintensity on T2-weighted images (e)

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required. This article does not contain any studies with animals performed by any of the authors.

**Informed consent** Formal consent was not required for this retrospective study.

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