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CASE REPORT

Gastric gastrointestinal stromal tumor with predominant cystic formation diagnosed by endoscopic ultrasound-fine needle aspiration

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Abstract
A 69-year-old woman who had no symptoms was found to have an intraperitoneal tumor on abdominal ultrasonography in a medical checkup. Thereafter, she was referred to our hospital for a further detailed examination. Contrast-enhanced computed tomography revealed a thin-walled cystic tumor with a diameter of 8 cm and with a hypervascular solid masses in the cystic wall, along with intraperitoneal multiple nodules. The cystic tumor was contiguous with the stomach wall. For solid mass of cystic lesions, endoscopic ultrasound-fine needle aspiration was performed transgastrically with a 25-gauge Franseen needle. Pathologically, the cells in the tumor were spindle shaped with atypical nucleus and were positive for c-kit, CD34, and smooth muscle actin. The tumor was diagnosed as gastrointestinal stromal tumor (GIST). With the diagnosis of gastric GIST with peritoneal dissemination, imatinib chemotherapy was initiated.

Keywords Endoscopic ultrasound-fine needle aspiration · Gastrointestinal stromal tumor · Predominant cystic formation

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal tract and most frequently arise from the stomach [1]. Typically, GISTs appear as solid masses. Although GISTs with some cystic components are occasionally found, GISTs with predominant cystic formation are very rare [2–11]. Hemorrhage or tumor necrosis is considered to be an important factor involved in the mechanism of cystic space formation in GIST [12]. In previous reports, most cases of GISTs with predominant cystic formation were diagnosed by surgical resection. Here, we report a case of gastric GIST with predominant cystic formation diagnosed by endoscopic ultrasound-fine needle aspiration (EUS-FNA). EUS-FNA is less invasive for patients compared with surgical resection or laparoscopic biopsy and allowed for the early initiation of imatinib chemotherapy.

Case presentation

A 69-year-old woman who had no symptoms was found to have an intraperitoneal tumor on abdominal ultrasonography in a medical checkup. Thereafter, she was referred to our hospital for a further detailed examination. Laboratory examinations revealed no abnormal findings other than a slightly increase in the levels of serum potassium (Table 1). Contrast-enhanced computed tomography revealed a thin-walled cystic tumor with hypervascular solid masses in the cystic wall and intraperitoneal multiple nodules in contact with the peritoneum. The diameter of the tumor was found to be 8 cm. The cystic tumor was contiguous with the stomach wall (Fig. 1). On magnetic resonance imaging, the solid masses in the cystic lesion had low signal intensity on T1-weighted imaging, high signal intensity on T2-weighted imaging, high signal intensity on diffusion-weighted imaging, and low signal intensity on apparent diffusion coefficient imaging (Fig. 2). Endoscopic ultrasound (EUS) revealed that the mass was a thin-walled cyst with some solid masses and

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Table 1 Laboratory data

WBC	4,900/μL	TP	6.7 g/dL	ALP	315 IU/L
RBC	435×10^4/μL	Alb	4.3 g/dL	γGTP	14 IU/L
Hb	13.2 g/dL	BUN	8.1 mg/dL	T.Bil	0.71 mg/dL
Hct	40.7%	Cre	0.62 mg/dL	CK	83 IU/L
MCV	93.6 fl	Na	141 mEq/L	CRP	0.04 mg/dL
MCH	30.3 pg	K	5.4 mEq/L	PT	132%
MCHC	32.4 g/dl	Amy	57 mg/dL	APTT	28.3 s
Plt	27.2×10^4 /μL	AST	18 IU/L	CEA	3.1 ng/mL
		ALT	15 IU/L	CA19-9	8.8 U/mL
		LDH	213 IU/L	sIL-2R	103 U/mL

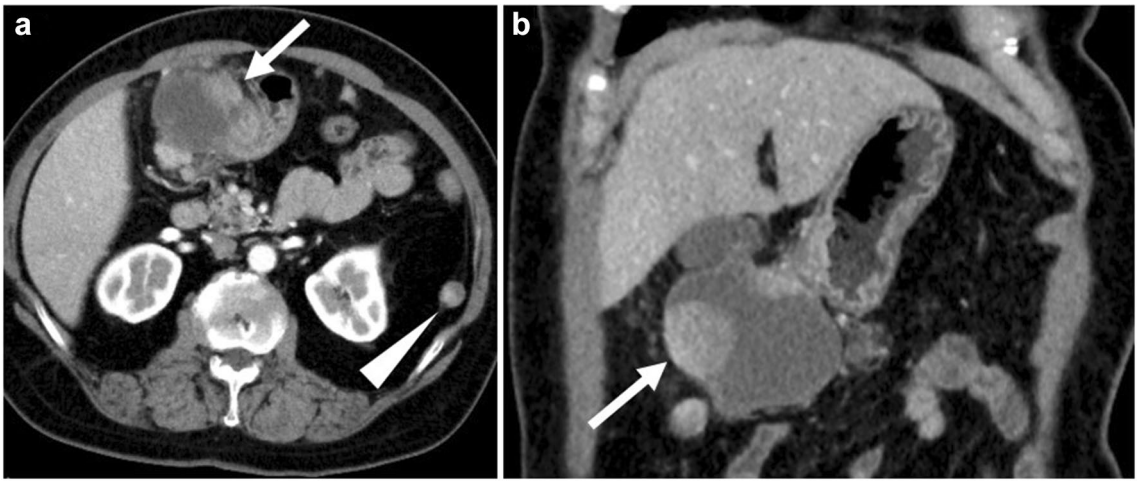

Fig. 1 Contrast-enhanced computed tomography revealed a thin-walled cystic tumor with hypervascular solid masses in the cystic wall (arrow) and intraperitoneal multiple nodules (arrowhead), and the cystic tumor was contiguous with the stomach wall. The diameter of the tumor was 8 cm. **a** Axial image and **b** Coronal image

septum. Considering the malignant tumor with peritoneal dissemination, we decided to conduct EUS-FNA to confirm the pathological diagnosis. For solid mass of cystic lesions, EUS-FNA was performed transgastrically with a 25-gauge Franseen needle (Fig. 3). Since a nodule component was present directly under the scope, puncture could be performed without breaking the cyst. Pathologically, the cells in the tumor were spindle shaped, and hematoxylin and eosin staining revealed cells with atypical nucleus. Immunostaining revealed that the cells were positive for c-kit, CD34, and smooth muscle actin and negative for S-100 protein. Pathologically, the tumor was diagnosed as GIST. The Ki-67 labeling index was 21% (Fig. 4), and the mitotic count was 4/22 per high-power fields (HPFs). With the diagnosis of gastric GIST with peritoneal dissemination, imatinb administration was initiated 15 days after EUS-FNA. Imatinib (400 mg/day) was administered for 6 months, and the size of the tumor remained almost unchanged.

Discussion

GISTs are the most common tumors of mesenchymal neoplasms and originate from the interstitial cells of Cajal [13, 14]. The interstitial cells of Cajal are morphologically characterized by a spindle- or stellate-shaped body. Histologically, GISTs vary from spindle-cell tumors to epithelioid and pleomorphic tumors, and 95% of GISTs express kit (CD117) and 70% express CD34 [15]. Most GISTs originate from the stomach (60%) followed by the small intestine (30%) and the colon (5%) [16].

Cystic components are macroscopically identified in less than 50% of GISTs [17]. However, gastric GISTs

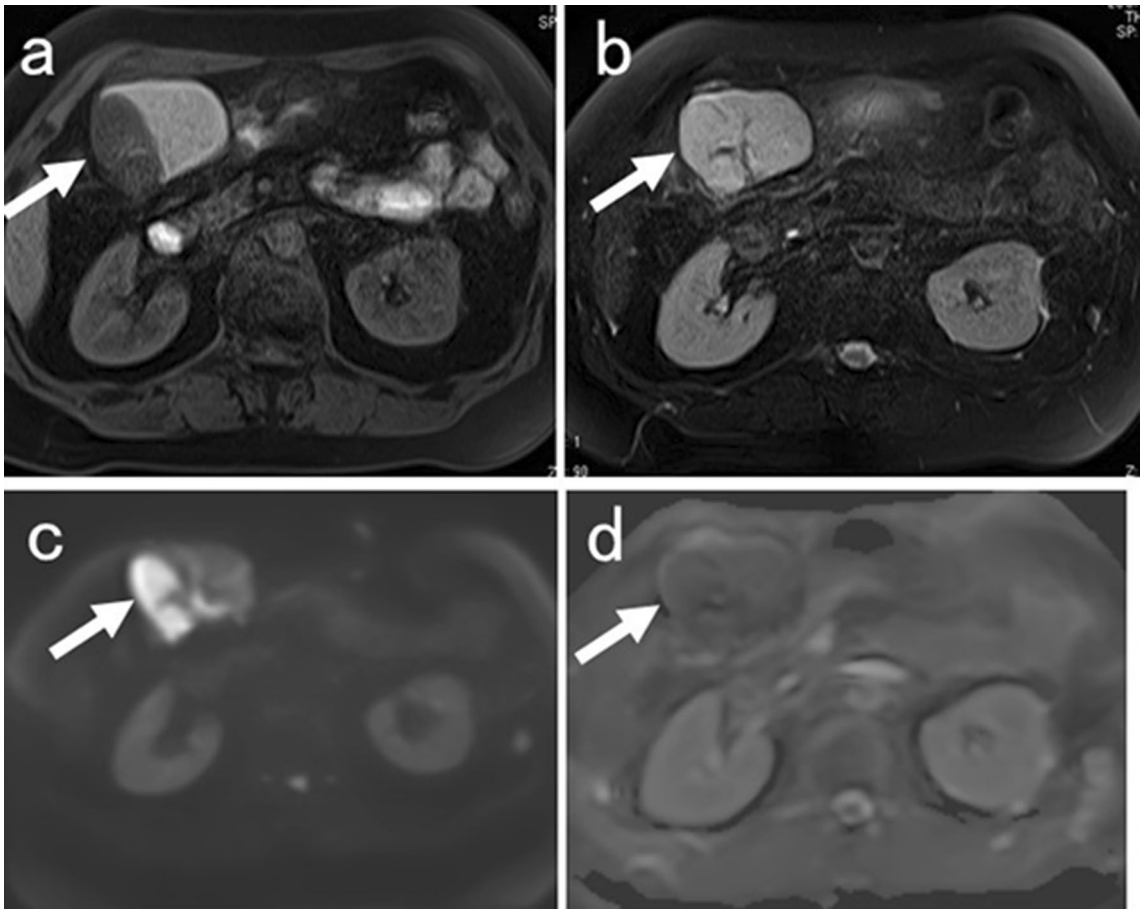

Fig. 2 On magnetic resonance imaging, the solid mass (arrow) in the cystic lesion had low signal intensity on T1-weighted imaging (**a**), high signal intensity on T2-weighted imaging (**c**), high signal intensity on diffusion-weighted imaging (**c**), and low signal intensity on apparent diffusion coefficient imaging (**d**)

with predominant cystic formation are very rare. EUS has been reported to be a useful modality for diagnosing cystic components of GISTs [7]. Table 2 presents a summary of cases of gastric GIST with predominant cystic formation including our present case [2–11]. In previously reported cases that developed predominant cystic changes, many of them were cases involving large-sized GISTs. In some cases, they were misdiagnosed as cystic tumors derived from other organs. In our case, before EUS-FNA, as differential diagnosis of gastric submucosal tumor with cystic formation, neuroendocrine neoplasm, metastatic tumor and GIST were considered. And it was not possible to make a diagnosis only with image findings. Most cases were diagnosed by surgical resection, and there were no other reports of cases diagnosed with EUS-FNA, except our case. Many patients who underwent surgical resection received imatinib after surgery. If tumor necrosis contributes to cystic formation, the Ki-67 index or the mitotic index may be involved in the formation of cysts. In previous reports, there were a few cases where both the Ki-67 index and the mitotic index were listed and the values varied from case to case. The Ki-67 index of our case was the highest compared with previously reported cases. Cystic changes of GIST are considered to be formed by degeneration, necrosis, and bleeding [18]. If the tumor is highly proliferative, it seems to be easy to cause necrosis and form a cyst. However, since factors such as bleeding are also involved, it cannot be explained only by the proliferating ability.

GISTs with dominant cystic components are often difficult to diagnose only by radiological imaging [19], and EUS-FNA is a useful diagnostic tool. The size of the tissue obtained by EUS-FNA is usually small. Moreover, one study reported that EUS-FNA did not reliably reflect the proliferation of GIST, and alternative parameters should be validated for a pre-surgical prognostic classification [20].

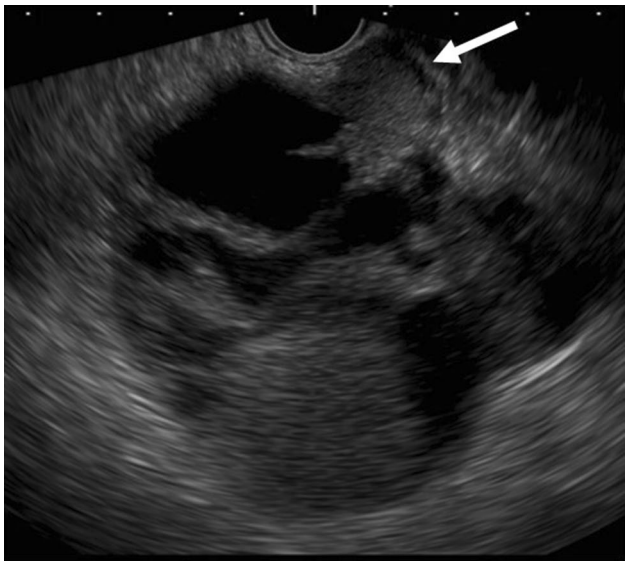

Fig. 3 In endoscopic ultrasound, the mass was a thin-walled cyst with some solid masses and septum. For solid mass (arrow) of cystic lesion, endoscopic ultrasound-fine needle aspiration (EUS-FNA) was performed transgastrically with a 25-gauge Franseen needle

The Fletcher's or Miettinen's GIST risk classifications require counting the number of mitosis at 50 HPFs [21, 22]. In the present case, 50 HPFs could not be secured because the obtained samples by EUS-FNA of 25-gauge needle were small. The EUS-FNA sample is often inadequate for the risk classification of GIST, and there is also a risk of leakage of cyst contents or needle tract seeding by EUS-FNA. However, the leakage of cyst contents can be technically prevented, and the occurrence of needle tract seeding is very rare. In addition, EUS-FNA is less invasive compared with surgical resection or laparoscopic biopsy. Thus, for cases with peritoneal dissemination, such as our present case, EUS-FNA is very useful for the early initiation of chemotherapy.

In conclusion, we reported a case of gastric GIST with predominant cystic formation diagnosed by EUS-FNA. For intraperitoneal cystic lesions that are continuous with the stomach, the possibility of gastric GIST needs to be considered. EUS-FNA is less invasive for patients compared with surgical resection or laparoscopic biopsy and allows for the early initiation of chemotherapy.

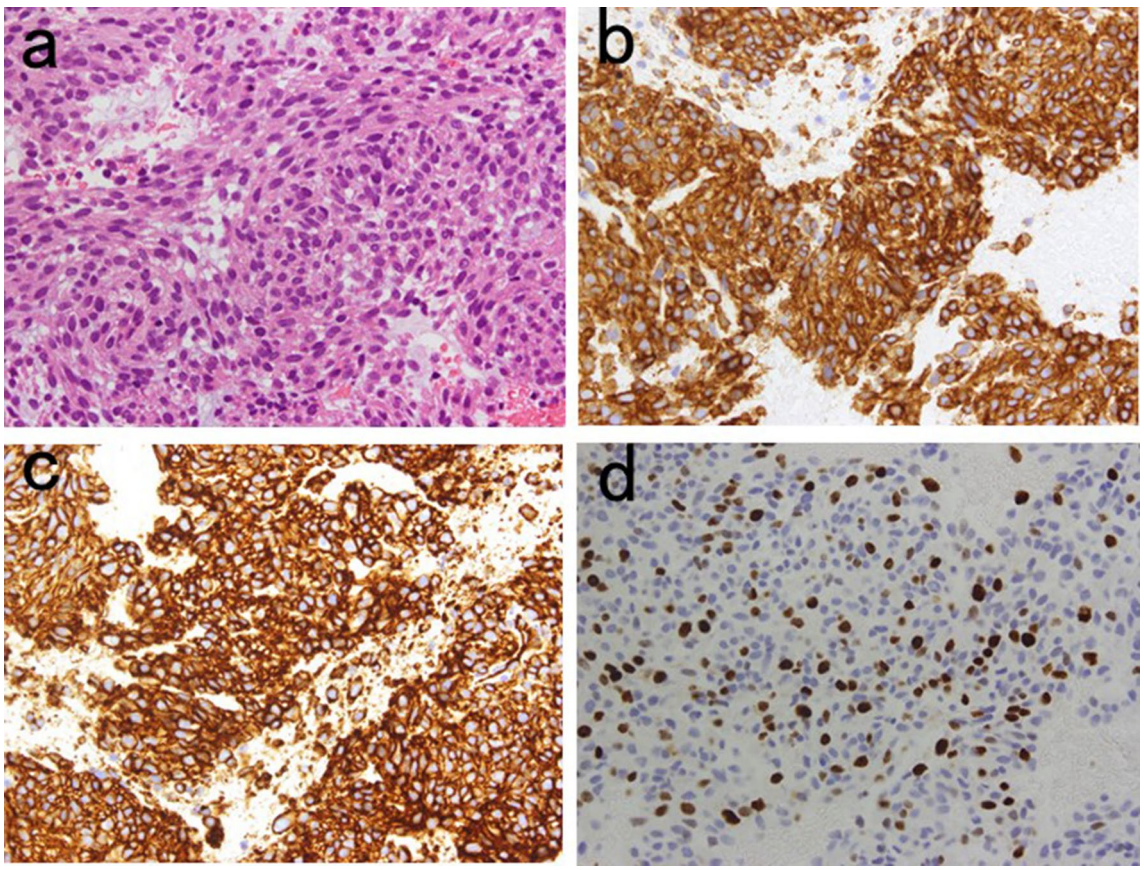

Fig. 4 Histopathological findings of biopsy specimens. Cells in the tumor were spindle shaped with atypical nucleus (hematoxylin and eosin staining). c-kit was diffusely positive and CD34 was also diffusely positive upon immunostaining. Pathologically, the tumor was diagnosed with gastrointestinal stromal tumor. The Ki-67 labeling index was 21%. **a** Hematoxylin and eosin stain (×200), **b** c-kit stain (×200), **c** CD34 stain (×200), and **d** Ki-67 stain (×200)

Table 2 Summary of cases of gastric gastrointestinal stromal tumor with predominant cystic formation including our present case

Published year	Author	Age (years)	Sex	Size (cm)	Diagnostic method	Ki-67 index or MIB-1 index	Mitotic index	Treatment	Journal	Reference number
2006	Park	11	Woman	10	Surgical resection	N.D.	N.D.	Surgical resection and chemotherapy	*Pediatr Radiol*	[2]
2007	Osada	74	Man	12	Endoscopic biopsy	18% (biopsy specimens)	N.D.	Surgical resection and chemotherapy	*World J Gastroenterol*	[3]
2008	Cruz	37	Man	32	Surgical resection	N.D.	10/50 HPFs	Surgical resection and chemotherapy	*World J Surg Oncol*	[4]
2011	Yu	81	Woman	6	Surgical resection	N.D.	4/50 HPFs	Surgical resection	*World J Surg Oncol*	[5]
2014	Zhu	78	Man	17	Surgical resection	N.D.	> 10/50 HPFs	Surgical resection	*Oncol Lett*	[6]
2015	Okano	79	Man	6	Surgical resection	< 10%	< 5/50 HPFs	Surgical resection	*Clin J Gastroenterol*	[7]
2016	Hamza	74	Woman	6.6	Laparoscopic biopsy	4%	1/50 HPFs	Surgical resection and chemotherapy	*BMJ Case Rep*	[8]
2016	Sun	75	Man	13	Surgical resection	N.D.	< 5/50 HPFs	Surgical resection and chemotherapy	*Oncol Lett*	[9]
2017	Wang	74	Woman	15	Surgical resection	5%	10/50 HPFs	Surgical resection	*World J Surg Oncol*	[10]
2018	Okagawa	72	Man	5.7	Surgical resection	N.D.	2/50 HPFs	Surgical resection	*Mol Clin Oncol*	[11]
	Our present case	69	Woman	8	EUS-FNA	21%	4/22 HPFs	Chemotherapy		

N.D. not described, *HPF* high-power field, *EUS-FNA* endoscopic ultrasound-fine needle aspiration

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

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