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Case report

Heterotopic gastric mucosa in the gallbladder

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Abstract: We report on a case of heterotopic gastric mucosa in the body of the gallbladder. A 39-year-old man, who was asymptomatic, visited our hospital because of a polypoid lesion in the gallbladder, discovered during a routine health screening. Ultrasonography (US) revealed a broad-based polypoid lesion 1.7 cm in diameter in the body of the gallbladder, which was free of gallstones. The gallbladder mass was faintly enhanced by helical computed tomography. Laparoscopic cholecystectomy was performed because of the possibility of malignancy. The specimen revealed a 1.7 × 1.3 cm polypoid lesion with deep delle in the body, with no gallstones in the gallbladder. Intraoperative frozen examination yielded a diagnosis of hyperplastic polyp of the gallbladder. Histologically, the polypoid lesion consisted of gastric fundic glands located in the whole wall of the gallbladder. The surrounding mucosa consisted of almost normal epithelium without any metaplastic changes. Postoperative technetium 99m-pertechnetate scintigraphy demonstrated no evidence of gastric heterotopia elsewhere in the body. We also review 18 other reports of heterotopic gastric mucosa in the gallbladder in the Japanese medical literature.

Key words: heterotopic gastric mucosa, gallbladder, polypoid lesion

Introduction

Heterotopia (or ectopia) is defined as the occurrence of normal tissue in an abnormal location. Heterotopic gastric mucosa is rather common throughout the gastrointestinal tract, from the tongue[1] to the rectum.[2] However, heterotopia in the gallbladder is unusual; cases of heterotopia in the gallbladder reported to date have included gastric mucosa,[3] liver,[4] pancreas,[5] and adrenal gland.[6]

Comparing to the gastrointestinal tract, reports of heterotopic gastric mucosa in the gallbladder are extremely rare. The first case of heterotopic gastric mucosa in the gallbladder was reported by Egyedi[3] in 1934. The first Japanese report was that of Tomita et al.[7] in 1977. We found 18 reports of heterotopic gastric mucosa in the gallbladder in the Japanese literature. We report on a new case of heterotopic gastric mucosa in the gallbladder appearing as a polypoid lesion. We also review the past literature from the clinicopathological standpoint.

Case report

History and physical examination. A 39-year-old Japanese man visited our hospital in March 1999, after the discovery of a polypoid lesion in the gallbladder by ultrasound (US) examination during a health screening. He had been asymptomatic and had no history of illness. Physical examination revealed no unusual findings.

Laboratory data. The results of laboratory tests, including peripheral blood count, serum protein, liver function test, renal function test, and fasting blood sugar (FBS), were all within the normal ranges, except for mild leucocytosis. Tumor markers were negative (Table 1). Results of urinalysis were also normal.

Ultrasonography (US). US showed a broad-based echogenic polypoid mass, 1.7 × 1.3 cm in size, located in the body of the gallbladder (Fig. 1).

Helical computed tomography (CT). Helical CT showed a slightly enhanced mass in the body of the gallbladder (Fig. 2).

Drip infusion cholangiogram CT (DIC-CT). A filling defect of the mass with a deep delle was seen in the body of the gallbladder (Fig. 3).

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Table 1. Laboratory data on admission

WBC	11200/mm^3	BUN	16.8 mg/dl
RBC	467 × 10^4/mm^3	Creatinine	0.8 mg/dl
Hb	14.5 g/dl	UA	6.1 mg/dl
Hct	43.1%	Na	140 mEq/l
Plt	24.5 × 10^4/mm^3	K	4.0 mEq/l
CRP	0.18 mg/dl	Cl	108 mEq/l
TP	6.6 g/dl	FBS	91 mg/dl
Alb	4.5 g/dl		
AST	15 IU/l	HBsAg	(−)
ALT	15 IU/l	HCVAb	(−)
T. Bil	0.59 mg/dl		
D. Bil	0.16 mg/dl	CEA	1.6 ng/ml
Alp	194 IU/l	CA19-9	1 U/ml
LDH	314 IU/l		
γ-GTP	32 IU/l		

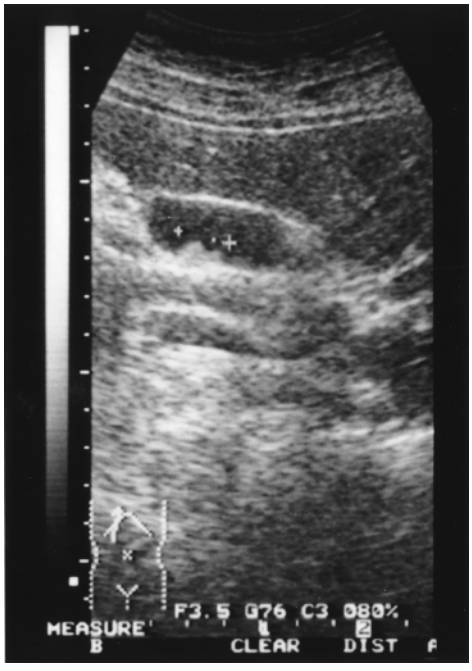


Fig. 1. Ultrasonography shows an echogenic Yamada type-1 polyp in the body of the gallbladder

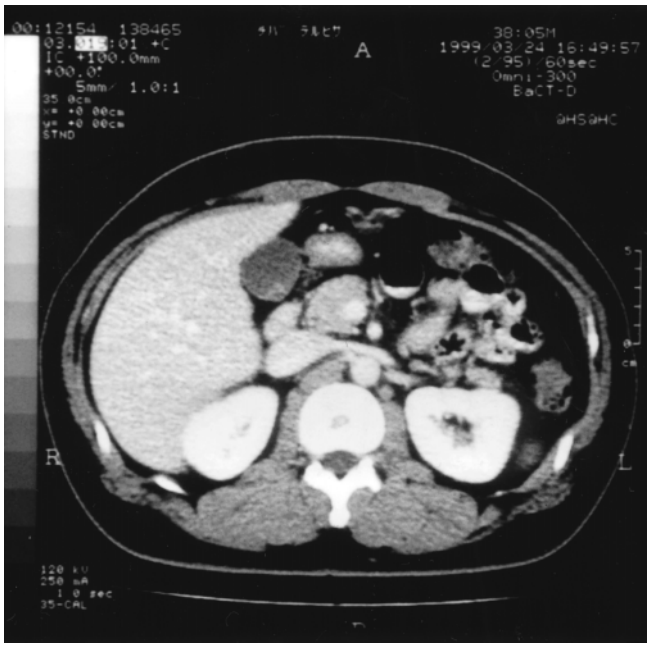


Fig. 2. Computed tomography (CT) scan shows a mass, which is faintly enhanced by iopamidol, in the body of the gallbladder

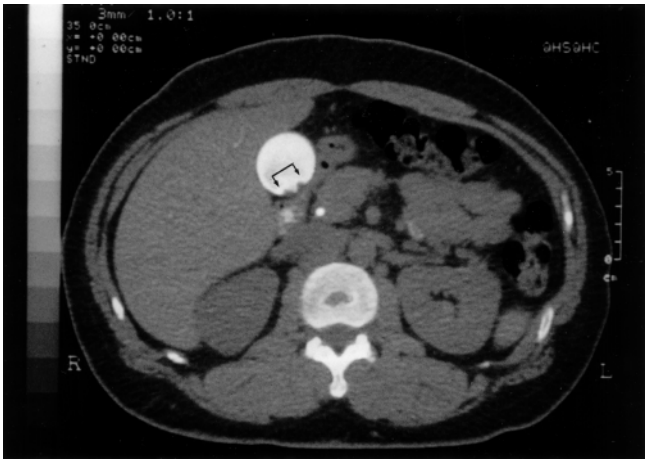


Fig. 3. Drip infusion cholangiogram-CT shows a broad-based mass with a deep central delle (*arrows*) in the body of the gallbladder

Surgery. Because the possibility of cancer in the gallbladder could not be ruled out despite the above examinations, laparoscopic cholecystectomy was performed, on April 8 1999. The polypoid lesion in the body of the gallbladder was diagnosed as a hyperplastic polyp on intraoperative frozen examination.

Gross findings of the resected specimen. A broad-based polypoid lesion, 1.7 × 1.3 cm in size, was found in the body of the gallbladder. A deep delle was located at the center of mass. Gallstones were not found (Fig. 4).

Histopathological examination. The polypoid lesion consisted of mucous glands, similar to gastric fundic glands, composed of parietal cells and chief cells. Neither goblet cells nor Paneth cells were observed in the lesion (Fig. 5a). The diagnosis, therefore, was heterotopic gastric mucosa of the gallbladder involving the whole wall (Fig. 5b). The remaining gallbladder was histologically unremarkable and no gallstones were identified (Fig. 5c).

Postoperative course. The patient's postoperative course was uneventful and he was discharged on the

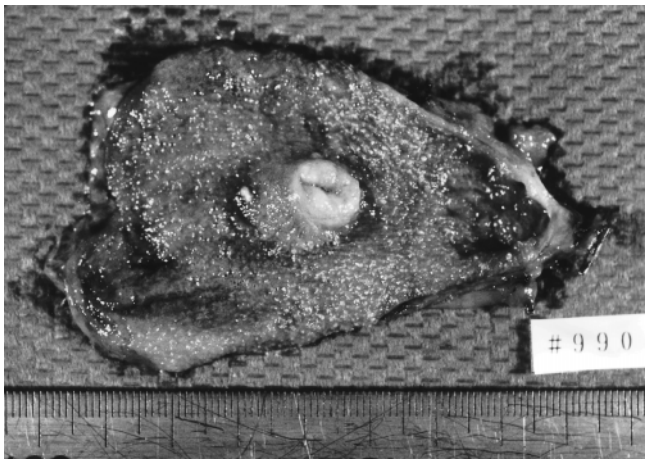
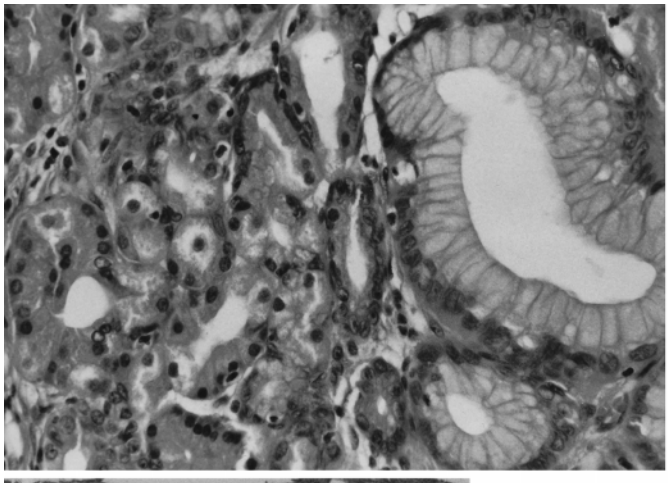


Fig. 4. Macroscopic appearance of the gallbladder, containing a polypoid lesion, 1.7 × 1.3 cm in size, in the body of the gallbladder

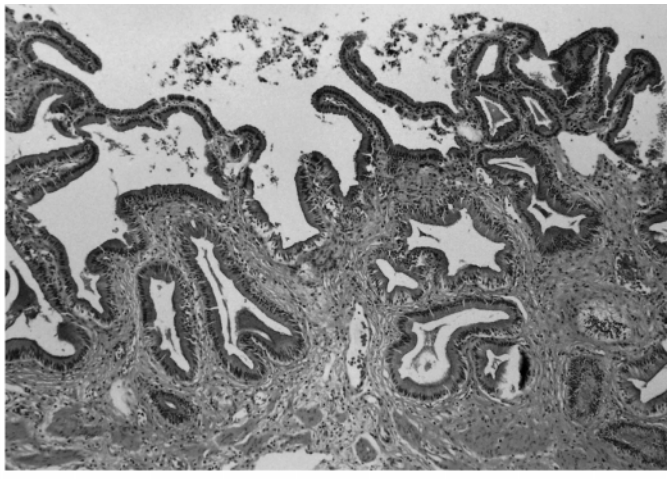
third day after surgery. Technetium 99m pertechnetate scintigraphy was performed when he was an outpatient, and there was no evidence of gastric heterotopia elsewhere in the body.

Discussion

The first case of heterotopic gastric mucosa in the gallbladder was reported by Egyedi[3] in 1934. In Japan, 18 cases of heterotopic gastric mucosa, including that in the present patient, have been reported to the present,[8–24] since the first case reported by Tomita et al.[7] in 1977, while according to a review of the literature by Leymann et al.,[25] 29 cases of heterotopic gastric mucosa in the gallbladder had been reported in other countries up to 1996.



a



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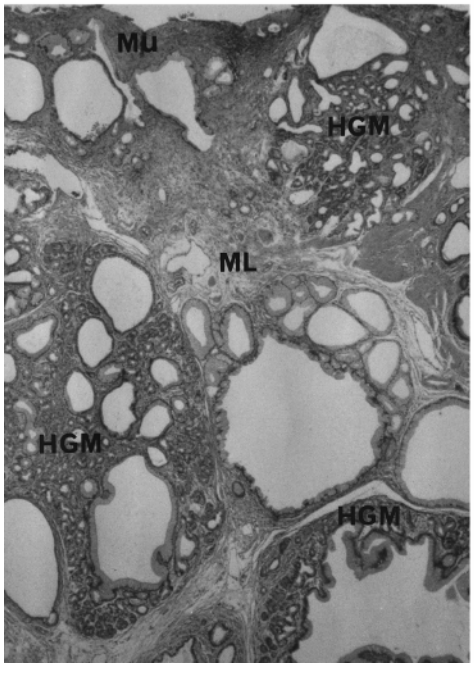

b

Fig. 5a–c. Histological appearance of heterotopic gastric mucosa in the gallbladder. **a** Some glands are gastric fundic type, composed of chief cells and parietal cells. **b** The heterotopic gastric tissues were located in the whole wall of the gallbladder. *Mu*, mucosa of the gallbladder; *ML*, muscle layer of the gallbladder; *HGM*, heterotopic gastric mucosal tissue. **c** Other areas of the remaining gallbladder show normal mucosa. **a** H&E, ×20; **b** H&E, ×10; **c** H&E, ×4

Table 2. Findings in 19 patients with heterotopic gastric mucosa in the gallbladder reported in Japan

Patient no.	Author	Year	Age (years)	Sex	Site	Location in the wall	Size (cm)	Chief complaint	Stone
1.	Tomita[7]	1977	22	F	N	Whole wall	1.0	Rt. hypochondralgia	−
2.	Shimizu[8]	1984	44	M	F	Subserosa	1.7	Unclear	−
3.	Yoshikawa[9]	1985	30	F	N	Submucosa	1.5	Upper abdominal pain	+
4.	Ishii[10]	1985	58	F	F	Subserosa	1.5	Rt. hypochondralgia	−
5.	Sasaki[11]	1987	23	M	N	Mucosa	1.5	No symptoms	−
6.	Ninomiya[12]	1987	55	F	N	Mucosa	2.5	Upper abdominal pain	+
7.	Ohyama[13]	1987	28	M	Unclear	Unclear	0.8	Unclear	+
8.	Yamamoto[14]	1989	44	M	B	Mucosa	1.0	Unclear	−
9.	Yamagiwa[15]	1990	47	M	N	Mucosa	1.0	Lt. Back pain	+
10.	Murakami[16]	1990	44	M	B	Mucosa	1.0	No symptoms	−
11.	Hachiya[17]	1991	22	M	B	Unclear	1.0	Rt. hypochondralgia	−
12.	Matsuda[18]	1993	51	M	N	Mucosa	0.7	No symptoms	−
13.	Uchiyama[19]	1995	23	M	F	Mucosa	1.5	No symptoms	−
14.	Kurumiya[20]	1995	59	M	CD	Submucosa	2.0	Nausea	−
15.	Nagasaka[21]	1996	26	M	N	Whole wall	2.0	Upper abdominal pain	+
16.	Nakasone[22]	1998	58	F	N	Submucosa	1.5	No symptoms	−
17.	Wakiyama[23]	1998	25	F	Unclear	Submucosa	Unclear	Epigastralgia	+
18.	Sawada[24]	1999	50	F	B	Submucosa	1.0	No symptoms	−
19.	Present patient	1999	39	M	B	Whole wall	1.7	No symptoms	−

N, neck; B, body; F, fundus; CD, cystic duct; Rt., right; Lt., left

The clinicopathologic features of the Japanese patients are summarized in Table 2. The male-to-female ratio is 12:7, (therefore, the incidence in men is about twice that in women). The average age at discovery was 39 years, ranging from 22 to 59 years. Symptoms of upper abdominal pain were observed in 7 of the 16 patients (excluding unclearly mentioned 3 patients), and in 5 of these patients, the symptoms were thought to be related to cholelithiasis. Seven patients had no symptoms. The incidence of gallstones was 32% (in 6 of 19 patients). Heterotopic gastric mucosa in the gallbladder was found in the following locations: 47% in the neck, 29% in the body, 18% in the fundus, and 6% in the cystic duct. Heterotopic tissue was located in the mucosa of the gallbladder in 7 of 17 patients (excluding unclearly mentioned 2 patients) (41%), in the submucosa in 5 (29%), in the subserosa in 2 (12%), and in the whole wall in 3 (18%). Macroscopically, all but 1 patient was reported to show polypid lesions, and the lesions ranged in size from 0.7 to 2.5 cm. The size of the lesions in 16 of the 18 previously reported patients (89%) was more than 1.0 cm.

The most frequent symptom reported was upper right abdominal pain, often associated with colic pain. However, it appears that this pain was produced by gallbladder stones in most patients. In the patients without gallstones, the pain may have been produced by intermittent obstruction of the cystic duct by the polyp itself, located at the neck of the gallbladder, as the heterotopic gastric mucosa is often situated in the neck of gallbladder. In the present patient, the absence of symptoms may have been due to the location of the polypoid lesion in the body of the gallbladder. Seven patients, including the present one, had no symptoms. As US examinations become more and more common in routine physical examinations, we can expect to see the discovery of more asymptomatic patients.

In the present patient, it was necessary to differentiate this lesion from other possible lesions of the gallbladder, including inflammatory polyp, cholesterol polyp, adenomyomatosis, adenomatous polyp, and cancer of the gallbladder.

Regarding US findings, both hyperechogeneic[16,17,19,24] and hypoechogenic[18] lesions were reported. On CT, heterotopic gastric mucosal tissue was usually reported to have a tendency to be faintly enhanced by iopamidol.[18] From the viewpoint of diagnostic imaging, there appear to be no characteristic findings of heterotopic gastric mucosa in the gallbladder to differentiate it from other usual polyps, such as cholesterol polyps, adenomyomatosis, adenoma, and adenocarcinoma.

Macroscopically, all except one of the cases of heterotopic gastric mucosa in the gallbladder reported in Japan were of the Yamada classification type I or type III, and delle were sometimes observed.[14,16,18] The size of the polyps in all patients reported was less than 2.5 cm, and the most common location was in the neck of the gallbladder. The incidence of gallstones was low (32%).

Histologically, in general, heterotopic gastric mucosa consists of fundic and pyloric glands, and demonstrates no metaplastic changes. In contrast, metaplastic polyps usually consist of mucous glands and often contain Paneth and goblet cells, but never fundic glands.[14,26] Ishii et al.[10] reported a rare case of heterotopic gastric

mucosa involving the pyloric gland alone, which is called pyloric-type. The pyloric-type accounted for only 2 of the 18 cases of heterotopic gastric mucosa in the gallbladder reported in the Japanese literature.[10,23] In these 2 patients, there were no metaplastic changes in the remaining mucosa of the gallbladder. To date, no cases of heterotopic gastric mucosa in the gallbladder originating from metaplasia had been reported.

There are three hypotheses regarding the etiology of heterotopic gastric mucosa: (1) developmental anomaly, (2) heterotopic differentiation, and (3) metaplastic differentiation.[27] Embryologically, the epithelium of the mucous membrane of the respiratory system, esophagus, stomach, and superior part of the upper half of the duodenum, together with the parenchyma of the liver and pancreas, all arise from the endoderm of the primitive foregut. The liver, bile duct, and pancreas arise from the endodermal lining at the junction of the embryonic foregut and midgut. This endodermal lining forms the mucosal lining and also the secretory cells of the liver, pancreas, and other associated gastrointestinal glands. Considering the common origin of these structures from the primitive foregut, which is lined by multipotential cells capable of differentiation along several lines, heterotopic gastric mucosa may result from congenitally displaced tissue.[24,28] Metaplasia, on the other hand, is a change of one type of differentiated tissue into another type. This change is induced by chronic inflammation and may represent an adaptive substitution of cells by other cell types that are better able to withstand an adverse environment. Actually, Stein[29] and Matsumine et al.[30] reported that metaplasia, involving components of the pyloric gland, was often found in gallbladder with chronic inflammation. Metaplastic polyps have some features in common with heterotopic gastric mucosa; namely, a polypoid configuration and the presence of goblet cells, Paneth cells, and tall columnar mucinous cells. None of the intestinal metaplasias of the gallbladder reported by Saavedra et al.[26] contained fundic type gastric epithelium; therefore, it is not difficult to differentiate metaplasia from heterotopic gastric mucosa in the gallbladder according to the presence or absence of fundic glands.

Regarding our patient, in whom fundic gland was found and metaplasia was not observed, it seems reasonable to assume that heterotopic gastric mucosa in the gallbladder was the result of heterotopic differentiation or developmental anomaly.

Care must be taken when a diagnosis is made based on intraoperative frozen sections, as we did in our patient. Nagasaka et al.[21] reported an experience similar to ours. In addition, in a patient with intercalation of glandular structures between bundles of smooth muscle, the diagnosis of adenocarcinoma was rendered.[31] Incorrect diagnosis may result from ignorance of the possible existence of the heterotopia, which is quite rare. Thus, it is necessary for the pathologist to be aware of the possibility of heterotopic gastric mucosa in the biliary tract in order to avoid confusing this condition with hyperplastic polyp or adenocarcinoma of the gallbladder.

Some potentially important complications must also be considered when we deal with heterotopic gastric mucosa in the gallbladder, including ulceration of the gallbladder and possible malignant changes. Although a few cases of mucosal ulceration have been reported in the English-language literature,[32–34] no cases of mucosal ulceration have been reported in Japan. This low frequency of mucosal ulceration has been attributed to the ability of the alkaline contents of the bile to neutralize acidic contents. Ishii et al.[10] suggested that heterotopic gastric mucosa may have the potential for carcinogenesis, but so far no cases of malignant changes have been reported.

As mentioned above, gastric mucosa in the gallbladder can occur as a result not only of congenital causes but also as a result of metaplasia. Metaplasia is well known as one of the most important factors in carcinogenesis, and therefore attention should be paid to gastric mucosa in the gallbladder resulting from metaplasia.[30]

As for the treatment of heterotopic gastric mucosa in the gallbladder, a condition essentially caused by a benign tumor, close follow-up may be sufficient.[16,24] However, because it is extremely difficult to make a conclusive diagnosis and thereby rule out the possibility of cancer, it appears that cholecystectomy may be unavoidable for these patients at the present time.

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