

Heterotopic gastric mucosa in the gallbladder: case report and literature review



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Introduction

Heterotopia (or ectopia) is defined as the occurrence of normal tissue in an abnormal location. Heterotopic gastric mucosa (HGM) is rather common throughout the gastrointestinal tract, from the tongue (1) to the rectum (2). However, heterotopias in the gallbladder is unusual; cases of heterotopia in the gallbladder reported to date have included gastric mucosa, liver (3) pancreas (4) and adrenal gland (5). Comparing to the gastrointestinal tract, reports of HGM in the gallbladder are rare: we found 95 cases of HGM in the gallbladder in the international literature and we report on a new case of HGM of gallbladder appearing as a polypoid lesion. We also review the past literature from the clinicopathological standpoint.

Case report

A 43-year-old caucasian man presented with a 3-year history of intermittent post-prandial right upper quadrant abdominal pain occasionally radiated to the scapula. This was aggravated by fatty foods and had recently become more frequent. He had been history of chronic anxiety syndrome, well controlled with pharmacological treatment.

Riassunto

MUCOSA GASTRICA ETEROTOPICA IN COLECISTI: CASE REPORT E REVISIONE DELLA LETTERATURA

Introduzione: riportiamo un caso di mucosa gastrica eterotopica (MGE) nel colletto della colecisti e la confrontiamo con gli altri 95 casi di MGE riportati in letteratura internazionale a partire dal 1977.

Obiettivo: valutare il migliore trattamento della MGE in colecisti attraverso l'analisi della letteratura, confrontata con la nostra iniziale esperienza.

Materiali e metodi: un uomo di 43 anni, recentemente affetto da coliche biliari, giungeva al nostro ambulatorio per essere valutato e sottoporsi successivamente a colecistectomia videolaparoscopica (CVL). La ecografia dell'addome rivelava un polipo a larga base d'impianto nel colletto della colecisti (2.5 cm di diametro), associata a microlitiasi.

Risultati: è stata eseguita la CVL, senza difficoltà tecniche. Il pezzo operatorio recava una lesione polipoide di 2.5x1.7x0.5 cm nel contesto di una microlitiasi della colecisti. Istologicamente, il polipo era costituito da ghiandole gastriche di tipo fundico, localizzate solo nella mucosa della colecisti. La mucosa circostante era costituita da epitelio normale senza alterazioni metaplastiche. La scintigrafia postoperatoria total body con tecnezio 99m-pertecnato non ha dimostrato altre isole di eterotopia gastrica. Attualmente il paziente gode di buona salute ed è asintomatico.

Conclusioni: a causa della estrema difficoltà a porre diagnosi definitive e per la possibilità, seppur infrequente, che la lesione evolva in senso neoplastico, secondo noi la CVL è inevitabile in soggetti in cui ci sia un polipo della colecisti; un ausilio al corretto trattamento chirurgico può essere fatto grazie all'uso dell'esame estemporaneo intraoperatorio.

Parole chiave: Mucosa gastrica eterotopica, colecisti, lesioni polipoidi.

Abstract

Introduction: we report on a case of heterotopic gastric mucosa in the neck of the gallbladder and we also review 95 other reports of HGM in the gallbladder in the international medical literature from 1977.

Aim: to evaluate the gold standard treatment in heterotopic gastric mucosa of the gallbladder by the analysis of literature, compared with our anecdotal experience.

Patient and method: a 43-year-old man, who was recently symptomatic, visited our hospital to submit to laparoscopic cholecystectomy for cholelithiasis. Ultrasonography revealed a broad-based polypoid lesion in the gallbladder (2.5 cm in diameter in the neck of the gallbladder), with multiple gallstones.

Results: standard laparoscopic cholecystectomy was performed. The specimen revealed a 2.5 x 1.7 x 0.5 cm polypoid lesion with deep in the body, with many gallstones in the gallbladder. Histologically, the polypoid lesion consisted of gastric fundic glands located only in the mucosa of the gallbladder. The surrounding mucosa consisted of almost normal epithelium without any metaplastic changes. Postoperative technetium 99m-perchnetate scintigraphy demonstrated no evidence of gastric heterotopia elsewhere in the body. Actually the patient is in long-time follow-up, asymptomatic.

Conclusions: for its extreme difficult to make a conclusive diagnosis and thereby rule out the possibility of cancer, it appears that laparoscopic cholecystectomy may be unavoidable for patients affected by heterotopic gastric mucosa at the present time and care must be taken when a diagnosis is made based on intraoperative frozen sections.

Key words: Heterotopic gastric mucosa, gallbladder, polypoid lesion.

Physical examination revealed no unusual findings, except a phimosis.

The results of laboratory tests, including peripheral blood count, serum protein, liver function test and renal function test were all within the normal ranges, except for mild leucocytosis. US showed a broad-based echogenic polypoid mass, 2.5 cm in maximum diameter, located in the neck of the gallbladder and many little hyperechogenic gallstones.

Laparoscopic cholecystectomy was performed, without any complications and intraoperative cholangiography was normal.

At the macroscopic examination, the specimen consisted of a gallbladder measuring 8.1x2.0x1.2 cm, with a pink, glistening serosa. A broad-based polypoid lesion,

2.5x1.7x0.5 cm in size, was confirmed in the neck of the gallbladder and many little gallstones were found.

At 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. The diagnosis, therefore, was "heterotopic gastric mucosa of the gallbladder involving only the mucosa layer". The remaining gallbladder was histologically unremarkable and no other abnormalities were identified.

The patient's postoperative course was uneventful and he was discharged on the second day after surgery. Technetium 99m perchnetate scintigraphy was performed after 3 months, when he was an outpatient, and there was no evidence of gastric heterotopia elsewhere in the body.

The patient is actually in one year follow-up and he is asymptomatic (Table I).

Discussion

Heterotopia, from the Greek "heteros" (different) and topos ("location" or "localization") is defined as the occurrence of normal tissue in abnormal location; synonymously, the term "choristoma", from the greek "choristos" (separated) has also been used.

The first case of HGM in the gallbladder was reported in Hungary in 1934 (6). In Japan, 19 cases have been reported to the present, since the first case reported by Tomita in 1977 (7); 29 cases of HGM had been reported in other countries up to 1996 in a review of the literature by Leymann (8), 45 cases in Europe by Xeropotamos (9) and Vallera (10), with other sporadic case reports (11, 12).

Heterotopic gastric tissue has been found at sites throughout the entire gastrointestinal tract. This has included in the biliary system the gallbladder, cystic duct, common hepatic duct, common bile duct, and the ampulla of Vater (13). Other heterotopic tissues have been found in tongue, oesophagus, epiglottis, small intestine, vermiform appendix, rectum, liver, adrenals, thyroid, and pancreas, (3, 5, 9, 14) but gastric heterotopia is the most common variant. In the biliary tree, gastric heterotopia

Table I – REVIEW OF LITERATURE COMPARED WITH OUR EXPERIENCE

	Literature review*	Our case report
Male – female ratio	1.02:1	Male
Average age at discovery (yrs)	38.5	43
Clinical presentation (most frequent)	Upper abdominal pain	Right hypocondralgia
Incidence of gallstones	35%	Microolithiasis
Site (most frequent)	Neck	Neck
Location in the wall (most frequent)	Mucosa layer	Mucosa layer
Size (range in cm)	0.55 - 2.03	2.5

*Literature review: 7, 8, 9, 10, 11, 12.

typically consists of fundic-type mucosa containing both parietal and chief cells. It differs from metaplasia, which, in the gallbladder, is characterized by intestinal or pyloric-type epithelium found in association with cholelithiasis, congenital anomalies, or tumors (15).

It is well established that there is a strong association between gallbladder carcinoma, premalignant epithelial or metaplastic inflammatory lesions and cholelithiasis (9); however, pyloric type metaplasia has less relationship with the bases of carcinogenesis than with those of intestinal metaplasia (16).

Pseudopyloric or pyloric gland metaplastic epithelium in the gallbladder is most common, being found in 66-84% of cholecystectomy specimens, while intestinal metaplastic epithelium has been reported in 12-52% of gallbladders and it is frequently associated with pyloric metaplasia (9).

Macroscopically, HGM in gallbladder may appear polypoid, nodular, or flat, and these lesions are a rare cause of acalculous biliary tract disease (12).

According to international literature, the male-to-female ratio is 1.02:1 and the average age at discovery was 38.5 years, ranging from 6 to 77 years.

Symptoms of upper abdominal pain were observed in 59.3% of the patients (right abdominal pain, often associated with colicky pain). 34.6% of patients had no symptoms. The incidence of gallstones was 35% and the symptoms were related to cholelithiasis in 33.3% of patients. The pain is produced by intermittent obstruction of cystic duct by the polyp itself (ball-valve), located at the neck of the gallbladder, as the heterotopic gastric mucosa is often situated in the neck of gallbladder (7), or by peptic ulceration of the gallbladder or to chronic cholecistitis (10). The latter presentation is characteristic of the older patients, while in the pediatric age the presentation is generally that of an acute cholecistitis or recurrent acute pancreatitis or perforation, hemorrhage (10-11) or hematemesis (30).

In the reports we reviewed, gastric heterotopia in the gallbladder was found in the following locations: 46% in the neck, 27% in the body, 23% in the fundus, and 4% in the cystic duct. Heterotopic tissue was located in the mucosa of the gallbladder in 47% of patients, in the submucosa in 27%, in the subserosa in 11%, and in the whole wall in 15%.

Macroscopically, all but 1 patient was reported to show polypoid lesions, and the dimension ranged in size from 0.55 to 2.03 cm. The mean size of the lesions (89% of patients) was more than 1.0 cm.

In these patients, it is 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 hyperechogenic (17-19) and hypoechoic (20) lesions were reported. On CT, heterotopic gastric mucosal tissue was usually reported to have a tendency to be faintly enhanced by contrast.

From the viewpoint of diagnostic imaging, there appear to be no characteristic findings of HGM in the gallbladder to differentiate it from other usual polyps, such as cholesterol polyps, adenomyomatosis, adenoma, and adenocarcinoma.

Histologically, in general, HGM 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 (15, 21). Ishii (22) reported a rare case of HGM involving the pyloric gland alone, which is called pyloric-type. To date, no cases of HGM in the gallbladder originating from metaplasia had been reported. There are three hypotheses regarding the etiology of HGM: (1) developmental anomaly, (2) heterotopic differentiation, and (3) metaplastic differentiation (23). 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, HGM may result from congenitally displaced tissue (19, 24) or heterotopic differentiation within the primitive gallbladder (10). 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 (25) and Matsumine (26) 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 HGM; 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 (15) contained fundic type gastric epithelium; therefore, it is not difficult to differentiate metaplasia from HGM in the gallbladder according to the presence or absence of fundic glands. Care must be taken when a diagnosis is made based on intraoperative frozen sections. Incorrect diagnosis may result from ignorance of the possible existence of the heterotopia, which is quite rare (27).

Thus, it is necessary for the pathologist to be aware of the possibility of HGM 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 HGM 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 (28-30), 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. Many Authors (22) suggested that HGM may have the potential for carcinogenesis, as a polyp, but so far no cases of malignant changes have been reported: the presence of polyps is a predisposing factor for carcinoma of the gallbladder. Recent evidence suggests that polyps larger than 10 mm in diameter have the greatest malignant potential. If diagnosed in asymptomatic patients, even in the absence of gallstones, removal of the gallbladder is recommended. Small polyps (less than 10 mm in diameter) need only be removed if they are producing symptoms or are associated with gallstones (31).

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 (26). We believe that further investigations of the molecular biology of gallbladder precancerous lesions should be undertaken to better understand its pathogenesis.

As for the treatment of HGM in the gallbladder, a condition essentially caused by a benign tumor, close follow-up may be sufficient (17, 19), but some potentially important complications must also be considered when we deal with HGM in gallbladder, including ulceration of the gallbladder and possible malignant changes (7). However, because it is extremely difficult to make a conclusive diagnosis and thereby rule out the possibility of cancer, it appears that laparoscopic cholecystectomy may be unavoidable for these patients at the present time and care must be taken when a diagnosis is made based on intraoperative frozen sections.

After surgery, the follow up is based on ^{99m}Techne- tium scintigraphy, doted of high diagnostic accuracy and specificity (32).

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