

Gastric heterotopia together with squamous metaplasia in the gallbladder

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Summary

Heterotopic gastric mucosa in the gallbladder is extremely unusual. In this study, we aimed to report a case of gastric heterotopia together with squamous metaplasia in the gallbladder of a 47-year-old female patient who experienced an intensive abdominal pain. He was admitted to the hospital for clinical treatment without any improvement. Ultrasonography showed a stone located in the gallbladder neck and dilatation of intrahepatic bile ducts, both hepatic ducts and common hepatic duct. Laparoscopic cholecystectomy was performed. In the microscopical examination, the epithelium of the gallbladder revealed an unspecified chronic cholecystitis. Besides, at the level of the gallbladder body, a heterotopic gastric mucosa contain chief, parietal and mucosal cells with cystic glands and squamous metaplasia was found. Actually the patient is in long-time follow-up, asymptomatic. We also review 96 other reports of HGM in the gallbladder in the international medical literature from 1934. As heterotopic tissue may promote carcinogenesis of the gallbladder, close attention should be paid to any occurrence of such lesions in this anatomical region. 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; intestinal metaplasia; precancerous lesion.

Heterotopía gástrica y metaplasia escamosa en la vesícula biliar

Resumen

La heterotopía de la mucosa gástrica (HGM) en vesícula biliar es extremadamente rara. En este estudio, reportamos un caso de heterotopía gástrica junto con metaplasia escamosa en vesícula biliar de un paciente femenino de 47 años que experimentó un dolor abdominal intenso. Lo admitieron al hospital para el tratamiento clínico sin ninguna mejoría. Ultrasonografía demostró un cálculo situado en el cuello de la vesícula y dilatación de conductos biliares intrahepáticos, los conductos hepáticos y conducto hepático común. Se realizó la colecistectomía por vía laparoscópica. En el exámen microscópico el epitelio reveló una colecistitis crónica inespecífica. Además, en el nivel del cuerpo de la vesícula biliar fue hallada una mucosa gástrica heterotópica con células principales, parietales, células mucosas con las glándulas enquistadas y metaplasia escamosa. El paciente está en el seguimiento a largo plazo, asintomático. Revisamos 96 informes de HGM en vesícula biliar en la literatura médica internacional a partir de 1934. El tejido heterotópico puede promover la carcinogénesis de la vesícula biliar; por lo cual se debe prestar atención a cualquier ocurrencia de tales lesiones en esta región anatómica. La colecistectomía laparoscópica puede ser inevitable para los pacientes afectados por la mucosa gástrica heterotópica actualmente y todo cuidado debe ser tomado cuando se hace un diagnóstico por secciones congeladas intraoperatorias.

Palabras Claves: mucosa gástrica heterotópica; vesícula biliar; metaplasia intestinal; lesión precancerosa.

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Heterotopia (or ectopia) is defined as the occurrence of normal tissue in an abnormal location. Heterotopic gastric mucosa is rather common th-

roughout the gastrointestinal tract, from the tongue to the rectum.^{1,2} However, heterotopia in the gallbladder is unusual; cases of heterotopia in the gallbladder reported to date have included gastric mucosa,³ liver,⁴ pancreas⁵ and adrenal gland,⁶ but no case of squamous metaplasia.

Comparing to the gastrointestinal tract, reports of heterotopic gastric mucosa in the gallbladder are extremely unusual. Heterotopic gastric mucosa, as well as squamous metaplasia in the gallbladder, may be one of the causes of gallbladder cancer.⁷ The first case of heterotopic gastric mucosa was reported by Egyedi,³ in 1934. We found 96 reports of heterotopic gastric mucosa in the gallbladder since 1934 in the international medical literature, and this is the second one in the South America.

Case report

A 47 year old woman presented to our hospital with chief complaint of intensive abdominal pain, without any improvement after clinical treatment. There was no history of trauma and no relevant family history. Hematologic and biochemical investigations showed a hemoglobin of 10,6 g/dl, leucocytosis of 16.400 g/dl; total bilirrubina 0,8 mg/dl; indirect bilirrubina 0,6 mg/dl; direct bilirrubina 0,2 mg/dl; ALT (alanine transaminase) 7 U/l e AST (aspartate aminotransferase) 19 U/l.

Ultrasonography showed a stone located in the gallbladder neck and dilatation of intrahepatic bile ducts, both hepatic ducts and common hepatic duct, but without any sign of thickness wall or signs of cholecystitis. Cholecystectomy was carried out for cholelithiasis. Laparoscopic cholecystectomy was performed with extraction of the gallbladder in a bag. Postoperative course was uneventful.

The specimen was 13 cm long and 5 cm large. Macroscopically, the gallbladder looked large, with thin walls, involved in adiposity tissue and with irregular epithelium in the body (figure 1). Histologically, the epithelium of the gallbladder revealed an unspecified chronic cholecystitis. Besides, at the level of the gallbladder body, a heterotopic gastric mucosa contain chief, parietal and mucosal cells with cystic glands and squamous metaplasia was found (figure. 2,3,4).

These findings were consistent with the diagnosis of gastric heterotopia of the gallbladder, without any sign of malignancy or ulceration. The *Helicobacter pylori* test was negative.

Figure 1. Gallbladder macroscopi.



Figure 2. Gallbladder epitellium with heterotopic gastric mucosa contain presence of fundic glands with both parietal and chief cells as well as pyloric glands (HE100x).

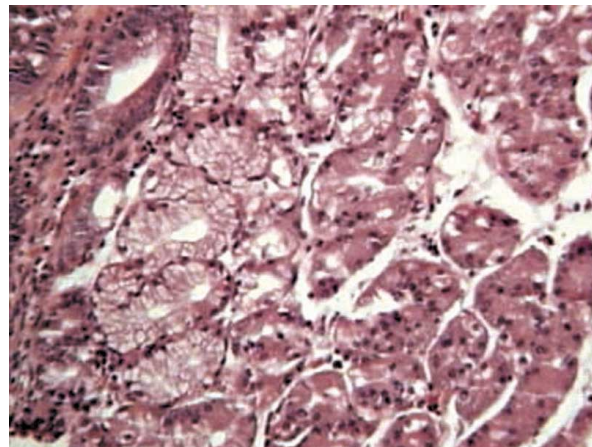


Figure 3. Gallbladder epitellium with heterotopic gastric mucosa type Antro-pyloro (HE 100x).

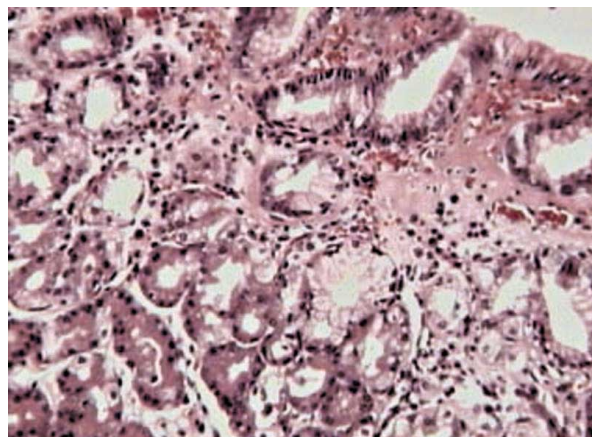
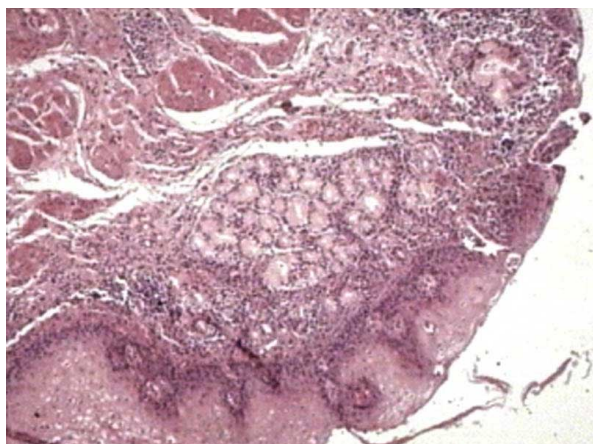


Figure 4. Gallbladder epithelium with squamous metaplasia and heterotopic gastric mucosa (HE 32x).



Discussion

The first case of heterotopic gastric mucosa in the gallbladder was reported by Egyedi,³ in 1934. Since then has been reported in various organs and sites in the gastrointestinal tract, including the tongue,¹ esophagus, epiglottis, small bowel, vermiform appendix, rectum² and gallbladder.³⁻¹⁴ A survey of the world literature revealed 96 reports, including the present case.

The incidence in men is about 20% higher than in women. The average age at discovery was 34 years, ranging from 3 to 78 years. Heterotopic gastric mucosa in the biliary tract often is discovered incidentally, but it may cause symptoms from gallbladder obstruction, inflammation, or perforation. Clinical symptoms are generally colic-type upper quadrant abdominal pain, abdominal discomfort, nausea, and vomiting or sometimes symptoms with biliary obstruction and jaundice. Under 25 years of age, clinical symptoms are generally acute and relatively short and ectopic gastric mucosa tends to be the only pathological finding. In older patients, it may be with chronic cholecystitis and cholelithiasis, and seems to be incidental. In gastric heterotopia, hemorrhage and inflammation may occur because of peptic ulceration. The gallbladder may be normal, multilobulated, or consist of nodular or polypoid lesions protruding into the lumen, and localized diffuse thickening of the bladder wall may be present. It is often situated in the neck or, as in our case, at the body of the gallbladder. The characteristic feature of heterotopic gastric mucosa is the his-

tological presence of fundic glands with both parietal and chief cells as well as pyloric glands, and most investigators have reported that heterotopic gastric mucosa involves all of these components (fundic type). APUD cells have been demonstrated in some cases, either thyroid tissue and pancreatic tissue. In three cases there was peptic ulceration of the wall of the gallbladder. This low frequency of mucosal ulceration has been attributed to the ability of the alkaline contents of the bile to neutralize acidic contents.

In this case there was only abdominal pain without any discomfort, nausea or vomiting. Squamous metaplasia has not been reported in any one of gallbladders with heterotopic gastric mucosa. In our case, there was an ectopic gastric mucosa with body type epithelium in the gallbladder. Furthermore, there was an association between heterotopic gastric mucosa and squamous metaplasia.

There are three hypotheses regarding the etiology of heterotopic gastric mucosa: 1) developmental anomaly, 2) heterotopic differentiation, and 3) metaplastic differentiation.⁸ 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 may result from congenitally displaced tissue.^{9,10}

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, Stein¹¹ and Matsumine et al.¹² 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. No case squamous metaplasia in the gallbladder has been re-

ported at the international literature.

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. 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. 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. Ishii et al.¹³ 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.¹²

In conclusion, surgeons must be aware of heterotopic gastric mucosa of the gallbladder, especially in young patients with cholecystitis and cholelithiasis with abdominal pain as chief complaint. As heterotopic tissue may promote carcinogenesis of the gallbladder, close attention should be paid to any occurrence of such lesions in this anatomical region.

References

1. Melato M, Ferlito A. Heterotopic gastric mucosa of the tongue and oesophagus. *J Otorhinolaryngol Relat Spec* 1975;37:244-254.
2. Jordan FT, Mazzea RJ, Soiederer MH. Heterotopic gastric mucosa of the rectum: a rare cause of rectal bleeding. *Arch Surg* 1983;118:878-880.
3. Egedi L. Case of polypus of gallbladder containing aberrant gastric mucous membrane (in Hungarian). *Gyogyaszat (Gyogyastat)* 1934;74:596-599.
4. Boyle L, Gallivan MVE, Chun B, et al. Heterotopia of gastric mucosa and liver involving the gallbladder. Report of two cases with literature review. *Arch Pathol Lab Med* 1992;116:138-142.
5. Mutschmann PN. Aberrant pancreatic tissue in the gallbladder wall. *Am J Surg* 1946;72:282-283.
6. Busuttill A. Ectopic adrenal within the gallbladder wall. *J Pathol* 1974;113:231-233.
7. Xeroptamos N, Skopelitou AS, Batsis C, et al. Heterotopic gastric mucosa together with intestinal metaplasia and moderate dysplasia in the gallbladder: report of two clinically unusual cases with literature review. *Gut* 2001;48:719-723.
8. Hamazaki K, Fujiwara T. Heterotopic gastric mucosa in the gallbladder. *J Gastroenterol* 2000;35:376-381.
9. Murakami M, Tsutsumi Y. Aberrant pancreatic tissue accompanied by heterotopic gastric mucosa in the gallbladder. *Pathology International*; 49:580-582.
10. Kalman PG, Stone RM, Phillips MJ. Heterotopic gastric tissue of the bile duct. *Surgery* 1981;89:384-386.
11. Stein AA. The surgically resected gallbladder: a morphologic evaluation. *Arch Surg* 1961;82:556-561.
12. Matsumine T, Kubota Y, Yamamoto I, et al. A histopathological study of the gallbladder carcinoma with special reference to intestinal metaplasia (double-nalization) of the cholecystic mucosa (in Japanese). *Nippon Rinshyo Geka Gakkai Zasshi (J Jpn Soc Clin Surg)* 1978;39:927-934.
13. Ishii Y, Ohmori K, Suzuki M, et al. Heterotopic gastric mucosa in the wall of the gallbladder: a case report and review of the literature (in Japanese). *Nippon Geka Gakkai Zasshi (J Jpn Surg Soc)* 1985;86:868-876.
14. Sciume C, Geraci G, Pisello E, Li Volsi E, Facella T, Modica G. Heterotopic gastric mucosa in the gallbladder: case report and literature review. *Ann Ital Chir.* 2005;76:93-97.