

Received: 2013.07.12  
Accepted: 2014.06.25  
Published: 2014.09.03

## Pancreatic and gastric heterotopy in the gastrointestinal tract

### Heterotopia trzustkowa i żołądkowa w przewodzie pokarmowym

Jakub Wlaz<sup>1,2</sup>, Agnieszka Mądro<sup>2</sup>, Weronika Kaźmierak<sup>2</sup>, Krzysztof Celiński<sup>2</sup>,  
Maria Słomka<sup>2</sup>

<sup>1</sup> Department of Gastroenterology, The Cardinal Stefan Wyszyński Regional Specialist Hospital, Lublin, Poland

<sup>2</sup> Department of Gastroenterology with Endoscopic Unit, Medical University of Lublin, Poland

#### Summary

Heterotopic or ectopic tissue is a congenital anomaly defined as the presence of the tissue outside its normal location. This tissue is usually discovered incidentally and may be asymptomatic or may present with non-specific gastrointestinal (GI) symptoms. Two types of heterotopic tissues, pancreatic and gastric, predominantly occur in the GI tract. The frequency of ectopic pancreas found in autopsy studies is approximately 0.5%-13.7%. Heterotopic pancreatic tissue can be located anywhere along the GI tract; the most common sites are the stomach (27.5%), duodenum (25.5%), colon (15.9%), esophagus, and Meckel's diverticulum. It has been found in approximately one per 500 surgical procedures involving the upper GI tract. It can also occur in the gallbladder, biliary tract, spleen, liver, omentum, mesentery, lung and pelvis. Likewise, heterotopic gastric mucosa can occur anywhere along the GI tract yet its most common locations are different from those of heterotopic pancreatic tissue. In this paper we present heterotopy characteristics in particular locations. Gastric or pancreatic heterotopy, although rare, should be taken into consideration in differential diagnosis of unexplainable abdominal pain, bleeding from the GI tract or weight loss. Once heterotopy has been detected, appropriate treatment can be implemented which will reduce the risk of complications.

**Key words:** heterotopic pancreas • heterotopic gastric mucosa • gastrointestinal tract

**Full-text PDF:** <http://www.phmd.pl/fulltxt.php?ICID=1119720>

**Word count:** 3013

**Tables:** –

**Figures:** –

**References:** 76

**Author's address:** Agnieszka Mądro PhMD, Department of Gastroenterology with Endoscopic Unit, Medical University, 8 Jaczewski Street, 20-950, Lublin, Poland, e-mail: agnieszka.madro@wp.pl

**List of abbreviations:** **CDHP** – cystic dystrophy in heterotopic pancreas, **CT** – computed tomography, **ERCP** – endoscopic retrograde cholangiopancreatography, **EUS** – endoscopic ultrasound, **GERD** – gastroesophageal reflux disease, **GI tract** – gastrointestinal tract, **HGM** – heterotopic gastric mucosa, **HGMPE** – heterotopic gastric mucosa of the proximal esophagus, **HP** – heterotopic pancreas, **LES** – low esophageal sphincter, **MRI** – magnetic resonance, **NSAID** – non-steroidal anti-inflammatory drug.

## INTRODUCTION

Heterotopic or ectopic tissue is a congenital anomaly, defined as the presence of the tissue outside its normal location, without neural, vascular or anatomic connection with the main body of an organ in which it normally exists. This tissue is usually discovered incidentally and may be asymptomatic or may present with non-specific gastrointestinal symptoms [17,57].

Two types of heterotopic tissues, i.e. pancreatic and gastric, predominantly occur in the gastrointestinal (GI) tract [6,27].

## HETEROTOPIC PANCREAS (HP)

Heterotopic pancreas was first described by Jean Schultz in 1727. In 1909, Heinrich et al. classified heterotopic pancreas into three types [69]:

- Type I – with ducts, acini and endocrine islets similar to those seen in normal pancreatic tissues.
- Type II – with a large number of acini, a few ducts and no islets.
- Type III – with numerous ducts, a few acini, and no islets.

The frequency of ectopic pancreas found in autopsy studies is approximately 0.5%-13.7%. Heterotopic pancreatic tissue can be located anywhere along the GI tract; the most common sites are the stomach (27.5%), duodenum (25.5%), colon (15.9%), esophagus, and Meckel's diverticulum [69,75]. It has been found in approximately one per 500 surgical procedures involving the upper GI tract [58]. It can also occur in the gallbladder, biliary tract, spleen, liver, omentum, mesentery, thorax (e.g. lung), and pelvis [69].

## HETEROTOPIC GASTRIC MUCOSA (HGM)

Ewell and Jackson were the first to report HGM in the English literature in 1939 [22]. This congenital abnormality can be imitated by acquired changes (for instance, pyloric epithelial lining) in some organs such as the lower esophagus, duodenal bulb and gallbladder [52]. HGM can occur anywhere along the GI tract, similarly to HP; however, its most common locations are different. The number of cases of heterotopic gastric mucosa localized in the lower gastrointestinal tract available in the literature is very low [11,46,49,56].

HGM or HP can appear in various segments of the GI tract. Below we present heterotopy characteristics in particular locations.

## ESOPHAGUS

In the esophagus nearly entirely HGM is observed. An "inlet patch" or "cervical inlet patch" is a designation of heterotopic gastric mucosa of the proximal esophagus (HGMPE). It is a common congenital abnormality, which

can be seen in up to 10% [63] of the general population (1-18%) [14]. Autopsy studies have reported higher incidence – up to 70% [70]. A flat, salmon-colored patch located in the proximal third of the esophagus, distal to the upper esophageal sphincter, is usually incidentally discovered during withdrawal of the gastroscope while evaluating other gastrointestinal complaints [14,15].

Clinicopathologic classification distinguishes 5 types of HGMPE [14], based on clinical, histological and endoscopic characteristics:

- HGM I – asymptomatic, the most common;
- HGM II – symptomatic, without further morphologic findings;
- HGM III – symptomatic due to morphologic changes;
- HGM IV (intraepithelial neoplasia) – malignant transformation via dysplasia (however, in contrast to Barrett's esophagus, HGM should not be regarded as a precancerous lesion);
- HGM V – cervical esophageal adenocarcinoma.

The clinical manifestations can be divided into non-neoplastic (II-III) reported in younger patients and neoplastic (IV-V) observed mainly in the elderly population [14,70].

Acid-related type II and III manifestations include the most common laryngopharyngeal reflux symptoms (prevalence 20-73%), such as heartburn, regurgitation, dysphagia, hoarseness, globus sensation, throat irritation, sore throat and chronic cough. Non-neoplastic groups can also occur as ulceration, bleeding, perforation, stricture, esophago-tracheal fistula, polyps and cysts. Moreover, chronic ear or sinus complications have been reported [6,12,13,14,15,20,48,63,73]. HGMPE can manifest as acute or chronic esophagitis in response to acid suppression therapy [74]. Coexistence with gastritis may be related to infection with *Helicobacter pylori*, which is identified on the inlet patch and in the stomach simultaneously. *H. pylori* is not found in all cases but 73% prevalence of this finding intimates that another event, e.g. reflux, may be required for *H. pylori* to colonize HGM. Density of bacteria is comparable in both locations. Active inflammation correlates with active infection in the inlets and the presence of antral type mucosa [33]. Study findings have revealed that *H. pylori* was identified in 23.5% of all patients with an inlet patch and that those patients had globus sensation [2]. The reported data of eradication therapy resulting in clinical improvement and amelioration of histopathological changes in the HGM suggest that the treatment may affect not only gastric but also extragastric manifestations of *H. pylori* infection [74].

A manometric investigation demonstrated abnormal esophageal motility: non-specific motor disorder, hypomotility and hypotensive LES (low esophageal sphincter) in patients with HGMPE. The 24-h pH monitoring in the same study showed pathological acid reflux (<4) in 30% and "acid independent episodes" in only 13.3% of patients. These abnormalities may determine some of the symptoms of HGMPE patients [41].

Although clinical symptoms and the histological mucin staining pattern of HGMPE and Barrett's esophagus are similar, which intimates their congenial pathogenesis, their different origin and secretion of gastrin, bombesin and somatostatin in HGM negate the identicalness of the two anomalies [14]. Studies concerning the association between these disorders provided conflicting results. Four of them have reported higher risk of Barrett's esophagus compared to patients without HGMPE, whereas the other five found no correlation [15]. Pediatric population symptoms differing from those reported in adults include higher incidence of respiratory symptoms, laryngospasm, and pulmonary aspiration [21,45]. An autopsy study revealed a positive correlation between the presence of HGMPE and unexplained death, probably associated with respiratory disorders. The symptom of the highest prevalence is still dysphagia associated in the pediatric population with esophageal atresia, stricture, or gastroesophageal reflux disease (GERD). However, very rare manifestations were also observed such as ear, nose and throat symptoms or recurrent cervical abscess connected with the fistula [14,20].

Neoplastic transformation in HGMPE is extremely rare. Non-malignant changes such as chronic inflammation, intestinal metaplasia (also reported in the pediatric population) and dysplasia similar to those in the stomach have been noted. To date, there have been only 43 cases of adenocarcinoma reported since first described in 1950. Based on earlier studies, the frequency of adenocarcinoma and low-grade dysplasia in patients with HGMPE is likely to be overestimated at 0-1.56%. According to the reported data, malignancies mostly affect men at the average age of 60.4 years diagnosed in the advanced state of neoplasm. Smoking appears to be a risk factor. The most common complaint is dysphagia. Lesions observed include ulceration, protrusion and polyploid changes [1,14,70]. The first reported case of laryngeal carcinoma associated with the inlet patch developed in a patient with long-standing asthma, gastroesophageal reflux and symptoms commonly accompanying HGMPE [14].

## STOMACH

The most common localization of the ectopic pancreas is the stomach, with more than 95% of the lesions being discovered in the antrum and close to the greater curvature; next in frequency is the duodenum. Like in other localizations, ectopic pancreas is usually asymptomatic; however, there are many reports describing the development of clinical symptoms, including the most common one, outlet obstruction [27,66]. Inflammation or chemical irritation of the gastric mucosa induced by the secretion of hormones and enzymes by HP may cause pain; in fact epigastralgia is the most frequent complaint, especially when the lesion's diameter is larger than 1.5 cm [27]. Pain is chronic or recurrent, rarely postprandial; it can be associated with nausea and vomiting [17,27,29,55,66]. Moreover, anorexia and weight loss can be observed. Ectopic pancreas also manifests as postprandial dyspepsia

and gastroesophageal reflux (commonly if HP is situated in the gastroesophageal junction) and in consequence may suggest peptic ulcer [25,51]. Ulceration and secondary perforation of HP in the stomach or gastric tissue may also appear and manifest as upper gastrointestinal bleeding, e.g. hematemesis [3,27,32].

Malignant transformation is mostly found to be adenocarcinoma followed by acinar cell carcinoma or carcinoid tumor [27,30,50,53,54,67].

## DUODENUM

Cystic dystrophy in heterotopic pancreas (CDHP) is an uncommon but serious complication of dilatation of ectopic pancreatic ducts of heterotopic pancreatic tissue [64]. Clinically, it can manifest as abdominal pain, nausea, vomiting, jaundice and weight loss [18,64,76]. Imaging studies reveal nonspecific inflammatory changes, detected mostly in the second part of the duodenum, causing stenosis. Histologically, these changes are seen as multiple cysts, fibrosis of normal glands and adenocarcinoma in HP [64]. Laboratory examinations may show elevated pancreatic enzymes and suggest inflammation [76]. Interestingly, patients with CDHP are usually male alcoholics (smokers in some cases) in the age range of 37-63 years [64].

Symptomatic inflammation of HP in the duodenal wall without atypia may also induce complications such as ulceration, bleeding, and perforation [31, 62]. Prevalence of bleeding in patients with HP in the duodenum is low (3%) however, cases in which the presence of ectopic pancreatic tissue caused massive hematochezia have also been reported [72].

There is only one report describing intractable diarrhea accompanying abdominal pain, regressing with defecation as a manifestation of ectopic pancreatic tissue in the duodenum [68].

The neoplasm arising from HP in the duodenal wall is usually adenocarcinoma, seen as increased wall thickness [40,60,65]. It may give symptoms evidencing duodenal or gastric disorders, e.g. vomiting or distension, if it causes gastric outlet obstruction due to its localization [7,65]. An islet cell tumor is extremely rare; in recent reports HP was only composed of endocrine islet carcinoid tumor, at least focally. Serum hormone levels may not be increased but immunostaining reveals cell positivity for chromogranin, synaptophysin, neuron-specific enolase, insulin, less frequently for gastrin, calcitonin, somatostatin, glucagon, and pancreatic polypeptide. Clinically, it can present with GI bleeding, or epigastralgia due to a mass in the stomach, sometimes with ulceration [65].

HGM is a rare discovery in the duodenum except the bulb. According to study findings, in patients with duodenitis it is correlated with gastric pathology. In addition, a strong association between HGM and concurrent fundic gland polyps has been found [26].

## VATER'S AMPULLA AND BILIARY TREE

The common bile duct and ampulla of Vater are considered as one topographical site, since manifestations of heterotopic pancreas in both locations are the same and result from common bile duct obstruction. Less than 30 cases have been reported, with over twofold higher frequency in Vater's ampulla; the male-to-female ratio is 3:1 with a peak incidence at the age of 30-70. The most common symptoms include epigastric pain and progressive, obstructive jaundice [8,16,71]. Back pain, gas indigestion, postprandial abdominal fullness, weight loss, tea-colored urine, and general malaise have also been observed, albeit with lower prevalence [13,35].

The mechanism of biliary tract obstruction by heterotopic pancreas may be determined by:

1. Secondary irritation as a result of a foreign body effect and excessive irritative secretion inducing spasm and hyperirritability of the local duodenal and biliary segment.
2. Production of some degree of intermittent obstruction to biliary flow due to pressure, tissue edema leading to acute or chronic cholangitis [8].

Imaging examinations, including endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT) with contrast and abdominal sonography show distal bile duct stricture and biliary dilatation, hydrops of the gallbladder and dilation of the intrahepatic bile ducts, common bile duct, and Wirsung duct, and ampullary protruding mass, sometimes with mucosa ulceration. Characteristic central umbilication is usually absent on endoscopy, which arouses the suspicion of cholangiocarcinoma. Laboratory data can be abnormal [8].

Although rare, HP should be considered in the differential diagnosis of papillary tumors, particularly as the diagnosis in the biliary tree is very difficult [19]. According to some studies, the relationship between the presence of pancreatic tissue and pancreatic carcinoma should be examined [8]. The preoperative diagnosis based on magnetic resonance (MRI) or endoscopic ultrasound (EUS) cannot be established. The biopsy seldom reveals chronic inflammation. Although EUS indicates benign pathology, presenting HP as hypoechoic and heterogeneous changes with indistinct margins, it can be misdiagnosed as a leiomyoma [8].

Heterotopic gastric mucosa can also be detected in the bile duct and masquerade as cholangiocarcinoma. An example can be found in the report of a female with mild liver dysfunction symptoms, who had HGM forming a polypoid lesion in the hilar bile duct, which caused stenosis at the junction of the left hepatic bile duct [24].

A case of upper gastrointestinal tract bleeding as the result of ectopic pancreas located in the minor duodenal papilla has been reported [62].

## GALLBLADDER

The gallbladder is an extremely rare location of the heterotopic pancreas (34 cases have been reported) and can be associated with cholecystitis or cholelithiasis. Patients may be asymptomatic or complain of pain in the right upper abdomen, attacks of right hypochondriac pain and vomiting [4,23].

Tenderness to palpation of the right upper abdomen with a positive Murphy's sign is likely to be observed on physical examination [44]. Abnormalities in laboratory results may be noticed; the first case of HP in the gallbladder causing elevations in bile amylase and lipase was reported in 2012. [59]. Ultrasonographic examinations show a polyp or the thickened gallbladder wall, occasionally with a calcified lesion, usually located in or near to the neck. The yellowish intramural nodule is lymph node or gallbladder cancer [44]. Histological examinations reveal HP or tissue without islet cells corresponding to incomplete heterotopia in symptomatic patients with cholecystitis [44].

Cholecystitis symptoms may be also induced by heterotopic gastric tissue in the gallbladder, found as a mass causing obstruction of the biliary ducts. Diarrhea and fever are also observed. Histopathologically, the resected specimen shows a polypoid lesion composed of gastric fundic glands. Moreover, cases of duplication cyst lined by HGM coexisting with secondary ulceration and fibrosis have been reported [24,34,39,43].

Ectopic tissue should be differentiated from gallbladder cancer but ectopic tissue also can promote carcinogenesis; in both cases surgery is necessary, because of the lack of specific clinical and imaging signs [43].

## LARGE BOWEL

Although heterotopic gastric mucosa is a very rare discovery in the large bowel location, it is the most common ectopic tissue in this orientation. Studies suggest that abnormal epithelial differentiation might be determined by gene deregulation, for instance induced by local inflammation. Heterotopic-like lesions can result from fetal displacement as well as an inflammatory reaction [61].

The most common manifestation of HGM in this location is painless rectal bleeding (with accompanying ulceration, but in more than 50% of cases connected with colonic duplication of about 33% prevalence) [36,37,42,61]. Other symptoms in decreasing order of frequency are perineal ulceration, anal pain, abdominal (chronic or colicky) pain and melena [37,42,56,61]. According to a review of the literature, ectopic gastric tissue is found as a result of investigation of symptoms such as abnormal bowel habits suggesting irritable bowel syndrome [52]. HGM is usually connected with polyps, followed by diverticula, ulcer and in reddish appearing mucosal plaque, folds, or flaps [56,61]. On microscopy, HGM is found as a fundic type, followed by a mixed type, and body type, not specified or definable [56]. Only a single case

was composed of pyloric-type mucosa and was associated with adenocarcinoma. *H. pylori* was identified in the rectal HGM [37,56,61].

In the anorectal location as well as in others, HGM may develop into neoplasms, benign (adenoma) or malignant (adenocarcinoma) [61].

HGM should be excluded in the differential diagnosis of rectal bleeding also in association with abdominal pain and proctitis in the pediatric population, though rare cases have been reported [11,49]. In children stricture formation and obstruction are likely to occur [11].

Compared to the upper GI tract, the frequency of HP in colorectal location is lower. Its presence can also be complicated by inflammation and stricture. Ductal adenocarcinoma arising from rectal HP has been described [28].

### MECKEL'S DIVERTICULUM (MD)

Meckel's diverticulum is the most common congenital malformation of the gastrointestinal tract, which is quite frequently complicated by the presence of ectopic tissue [9]. The most frequent ectopic tissue is gastric mucosa, whose common complication is bleeding induced by inflammation, which can also be accompanied by ulceration [9,47]. Gastritis may be the result of *Helicobacter*-like bacteria found in HGM [47]. Clinically, non-steroidal anti-inflammatory drug (NSAID) administration is a significant cause of acute bleeding from HGM; furthermore it can be associated with Meckel's diverticulum perforation, yet there are no studies confirming that HGM can also be perforated due to the NSAID effect [9,38,47].

Neoplasm is a rare complication of MD; the most common are neuroendocrine tumors. Adenocarcinoma arising in MD can intimate the presence of HGM, from which it usually develops in this localization. HP is an uncommon discovery in MD, although well described in the literature [10].

Dystrophic calcification may appear in both gastric and pancreatic ectopic tissue in MD [47]. Acute abdominal pain, tenderness, vomiting, diarrhea and other nonspecific symp-

toms from the GI tract are likely to be reported by patients with ectopic tissue in the MD but they are not pathognomonic for this pathology [47].

### CONCLUSIONS

Ectopic tissue, both gastric and pancreatic, is usually asymptomatic; if complicated, it gives non-specific symptoms from the GI tract such as abdominal pain, nausea, vomiting, abdominal dilatation and indigestion.

The mass effect of HP in the GI tract can present as reflux symptoms, dilatation and pain induced by compression.

Secretion of enzymes by the ectopic tissue affects the surrounding tissue, causing its irritation, or damage as well as other consequences such as inflammation and pathologies secondary to this process. Successful alleviation of symptoms such as bleeding with H<sub>2</sub> inhibitors or proton pump inhibitors suggests that the mechanism of secretion in HGM is the same as in the gastric tissue in the normal location. Increased secretion of hydrochloric acid in HGM can result in the same complications as those observed in the stomach, i.e. inflammation, ulceration, bleeding, and perforation.

NSAID and other risk factors inducing ulceration in the stomach may also be associated with this disorder in HGM. HP in the duodenum and stomach can cause life-threatening conditions; it should be excluded in the differential diagnosis of acute abdomen, which may be the result of perforation secondary to pancreatitis or gastritis, especially in the duodenum and stomach. Symptomatic or asymptomatic HP, found incidentally during imaging examinations performed due to other disorders, should be considered in the neoplasm differential diagnosis.

Gastric or pancreatic heterotopy, although rare, should be taken into consideration in the differential diagnosis of unexplainable abdominal pain, bleeding from the gastrointestinal tract or weight loss. The detection of heterotopy enables one to implement appropriate treatment and reduce the risk of complications. Once heterotopy has been detected, appropriate treatment can be implemented, which will reduce the risk of complications.

### REFERENCES

- [1] Akanuma N., Hoshino I., Akutsu Y., Shuto K., Shiratori T., Kono T., Uesato M., Sato A., Isozaki Y., Maruyama T., Takeshita N., Matsubara H.: Primary esophageal adenocarcinoma arising from heterotopic gastric mucosa: report of a case. *Surg. Today*, 2013; 43: 446-451
- [2] Alagozlu H., Simsek Z., Unal S., Cindoruk M., Dumlu S., Dursun A.: Is there an association between *Helicobacter pylori* in the inlet patch and globus sensation? *World J. Gastroenterol.*, 2010; 7: 42-47
- [3] Almashat S., Sepehr A.: Obstructive and inflammatory gastric heterotopic pancreatic tissue. *Arch. Iran Med.*, 2011; 14: 357-358
- [4] Al-Shraim M., Rabie M.E., Elhakeem H., Kandeel A., Shah M.T., Jamil S.: Pancreatic heterotopia in the gallbladder associated with chronic cholecystitis: a rare combination. *J. Pancreas*, 2010; 11: 464-466
- [5] Basseri B., Conklin J.L., Mertens R.B., Lo S.K., Bellack G.S., Shaye O.A.: Heterotopic gastric mucosa (inlet patch) in a patient with laryngopharyngeal reflux (LPR) and laryngeal carcinoma: a case report and review of literature. *Dis. Esophagus.*, 2009; 22: E1-E5
- [6] Baudet J.S., Alarcón-Fernández O., Sánchez Del Río A., Aguirre-Jaime A., León-Gómez N.: Heterotopic gastric mucosa: a significant clinical entity. *Scand. J. Gastroenterol.*, 2006; 41: 1398-1404
- [7] Bini R., Voghera P., Tapparo A., Nunziata R., Demarchi A., Capocefalo M., Leli R.: Malignant transformation of ectopic pancreatic cells in the duodenal wall. *World J. Gastroenterol.*, 2010; 14: 1293-1295



- [8] Biswas A., Husain E.A., Feakins R.M., Abraham A.T.: Heterotopic pancreas mimicking cholangiocarcinoma. Case report and literature review. *J. Pancreas*, 2007; 9: 28-34
- [9] Brar A.S., Gill R.S., Gill S.S., Wang H.: NSAID-associated perforation of a Meckels diverticulum: a case report. *J. Clin. Med. Res.*, 2011; 4: 96-98
- [10] Cates J.M., Williams T.L., Suriawinata A.A.: Intraductal papillary mucinous adenoma that arises from pancreatic heterotopia within a meckel diverticulum. *Arch. Pathol. Lab. Med.*, 2005; 129: e67-e69
- [11] Cheli M., Alberti D., Vavassori D., Sonzogni A., Pedretti E., Locatelli G.: Heterotopic rectal gastric mucosa: a rare cause of lower gastrointestinal bleeding in children. Case report and review of pediatric literature. *Eur. J. Pediatr. Surg.*, 2007; 17: 50-54
- [12] Chen C.H., Yang C.C., Yeh Y.H., Yang J.C., Chou D.A.: Pancreatic tuberculosis with obstructive jaundice - a case report. *Am. J. Gastroenterol.*, 1999; 94: 2534-2536
- [13] Chen Y.R., Wu M.M., Nan Q., Duan L.P., Miao Y.L., Li X.Y.: Heterotopic gastric mucosa in the upper and middle esophagus: 126 cases of gastroscopy and clinical characteristics. *Hepatogastroenterology*, 2012; 59: 1123-1125
- [14] Chong V.H.: Clinical significance of heterotopic gastric mucosal patch of the proximal esophagus. *World J. Gastroenterol.*, 2013; 21: 331-338
- [15] Chong V.H., Jalihal A.: Heterotopic gastric mucosal patch of the esophagus is associated with higher prevalence of laryngopharyngeal reflux symptoms. *Eur. Arch. Otorhinolaryngol.*, 2010; 267: 1793-1799
- [16] Chou S.J., Chou Y.W., Jan H.C., Chen V.T., Chen T.H.: Ectopic pancreas in the ampulla of Vater with obstructive jaundice. A case report and review of literature. *Dig. Surg.*, 2006; 23: 262-264
- [17] Christodoulidis G., Zacharoulis D., Barbanis S., Katsogridakis E., Hatzitheofilou K.: Heterotopic pancreas in the stomach: a case report and literature review. *World J. Gastroenterol.*, 2007; 13: 6098-6100
- [18] Chung J.P., Lee S.I., Kim K.W., Chi H.S., Jeong H.J., Moon Y.M., Kang J.K., Park I.S.: Duodenal ectopic pancreas complicated by chronic pancreatitis and pseudocyst formation - a case report. *J. Korean Med. Sci.*, 1994; 9: 351-356
- [19] Contini S., Zinicola R., Bonati L., Caruana P.: Heterotopic pancreas in the ampulla of Vater. *Minerva Chir.*, 2003; 58: 405-408
- [20] Daher P., Francis E., Raffoul L., Riachy E.: Ectopic gastric mucosa in the cervical esophagus presenting as a recurrent neck abscess: a case report. *J. Pediatr. Surg.*, 2010; 45: e15-e17
- [21] di Palma E., Cazzato S., Tursini S., Salfi N.C., Mazzotta A., Di Silverio Carulli C., Lima M., Bergamaschi R., Bernardi F., Cicognani A.: A rare association of inlet patch with laryngospasm: a report of two children and literature review. *Pediatr. Pulmonol.*, 2011; 46: 934-938
- [22] Ewell G.H., Jackson R.H.: Aberrant gastric mucosa in the rectum with ulceration and hemorrhage. *Wis. Med. J.*, 1939; 38: 641-643
- [23] Foucault A., Veilleux H., Martel G., Lapointe R., Vandembroucke-Menu F.: Heterotopic pancreas presenting as suspicious mass in the gallbladder. *J. Pancreas*, 2012; 10: 700-701
- [24] Fukuda S., Mukai S., Shimizu S., Kouchi M., Fujisaki S., Takahashi M., Sakimoto H., Eto T., Takahashi M., Nishida T.: Heterotopic gastric mucosa in the hilar bile duct mimicking hilar cholangiocarcinoma: report of a case. *Surg. Today*, 2013; 43: 91-95
- [25] Garn T., Hallenscheidt T., Schumacher B., Krämling H.J.: Tumor of the esophagocardiac junction. *Chirurg*, 2011; 82: 447-449
- [26] Genta R.M., Kinsey R.S., Singhal A., Suterwala S.: Gastric foveolar metaplasia and gastric heterotopia in the duodenum: no evidence of an etiologic role for *Helicobacter pylori*. *Hum. Pathol.*, 2010; 41: 1593-1600
- [27] Gokhale U.A., Nanda A., Pillai R., Al-Layla D.: Heterotopic pancreas in the stomach: a case report and a brief review of the literature. *JOP*, 2010; 11: 255-257
- [28] Goodarzi M., Rashid A., Maru D.: Invasive ductal adenocarcinoma arising from pancreatic heterotopia in rectum: case report and review of literature. *Hum. Pathol.*, 2010; 41: 1809-1813
- [29] Green P.H., Barratt P.J., Percy J.P., Cumberland V.H., Middleton W.R.: Acute pancreatitis occurring in gastric aberrant pancreatic tissue. *Am. J. Dig. Dis.*, 1977; 22: 734-740
- [30] Guillou L., Nordback P., Gerber C., Schneider R.P.: Ductal adenocarcinoma arising in a heterotopic pancreas situated in a hiatal hernia. *Arch. Pathol. Lab. Med.*, 1994; 118: 568-571
- [31] Gunjaca I., Mlinac-Lucijanić M., Pavlović A., Gunjaca M.: Inflammation of ectopic pancreatic tissue as unusual cause of duodenal perforation - a case report. *Coll. Antropol.*, 2010; 34: 1119-1122
- [32] Gurocak B., Gokturk H.S., Kayacetin S., Bakdik S.: A rare case of heterotopic pancreas in the stomach which caused closed perforation. *Neth. J. Med.*, 2009; 67: 285-287
- [33] Gutierrez O., Akamatsu T., Cardona H., Graham D.Y., El-Zimaity H.M.: *Helicobacter pylori* and heterotopic gastric mucosa in the upper esophagus (the inlet patch). *Am. J. Gastroenterol.*, 2003; 98: 1266-1270
- [34] Hayama S., Suzuki Y., Takahashi M., Hazama K., Fujita M., Kondo S., Katoh H.: Heterotopic gastric mucosa in the gallbladder: report of two cases. *Surg. Today*, 2010; 40: 783-787
- [35] Hsu S.D., Chan D.C., Hsieh H.F., Chen T.W., Yu J.C., Chou S.J.: Ectopic pancreas presenting as ampulla of Vater tumor. *Am. J. Surg.*, 2008; 195: 498-500
- [36] Janneck C.: Anal hemorrhage caused by tubular rectal duplication with ectopic gastric mucosa. *Z. Kinderchir.*, 1988; 43: 353-354
- [37] Kestemberg A., Mariño G., de Lima E., Garcia F.T., Carrascal E., Arredondo J.L.: Gastric heterotopic mucosa in the rectum with *Helicobacter pylori*-like organisms: a rare cause of rectal bleeding. *Int. J. Colorectal. Dis.*, 1993; 8: 9-12
- [38] Khosa J.K., Kimble R.M.: Bleeding postoperatively from a Meckel diverticulum, secondary to NSAIDs: a cautionary note. *Pediatr. Surg. Int.*, 2007; 23: 203-204
- [39] Kim J., Jarboe M.D., Arnold M.A., DiPietro M.A., Bloom D.A., Teitelbaum D.H.: Biliary duplication cyst with heterotopic gastric mucosa resulting in obstruction of the biliary system: a case report. *J. Pediatr. Surg.*, 2012; 47: e5-e8
- [40] Kinoshita H., Yamaguchi S., Shimizu A., Sakata Y., Arai K., Mori K., Nasu T.: Adenocarcinoma arising from heterotopic pancreas in the duodenum. *Int. Surg.*, 2012; 97: 351-355
- [41] Korkut E., Bektaş M., Alkan M., Ustün Y., Meco C., Ozden A., Soykan I.: Esophageal motility and 24-h pH profiles of patients with heterotopic gastric mucosa in the cervical esophagus. *Eur. J. Intern. Med.*, 2010; 21: 21-24
- [42] Kumar R., Shun A., Arbuckle S., Gaskin K.: Diverticular rectal duplication with heterotopic gastric mucosa in a child: a rare cause of rectal bleeding. *J. Paediatr. Child. Health*, 2000; 36: 191-192
- [43] Liang Y.L., Liang X., Wang Y.F., Cai X.J.: Heterotopic gastric mucosa with mild dysplasia in the gallbladder. *Chin. Med. J.*, 2013; 126: 978-979
- [44] Limaïem F., Jedidi S., Hassan F., Korbi S., Aloui S., Lahmar A., Bouraoui S., Mzabi S.: Pancreatic heterotopia in the gallbladder neck associated with chronic cholecystitis. *Pathologica*, 2012; 104: 446-448
- [45] Macha S., Reddy S., Rabah R., Thomas R., Tolia V.: Inlet patch: heterotopic gastric mucosa - another contributor to supraesophageal symptoms? *J. Pediatr.*, 2005; 147: 379-382
- [46] Madro A., Celinski K., Prozorow-Krol B., Lozowski C.T., Buk L., Swatek J., Pilat J., Slomka M.: Colonic duplication with heterotopy of gastric mucosa. *Endoscopy*, 2013; 45, Suppl. 2: E153-E154

- [47] Maieron R., Stimac D., Avellini C., Zoratti L., Rizzi C., Scott C., Rubinić M., Beltrami C.A., Da Broi G.L.: Acute gastrointestinal bleeding due to Meckel's diverticulum heterotopic gastric mucosa. *Ital. J. Gastroenterol.*, 1996; 28: 225-228
- [48] Meining A., Bajbouj M.: MD Erupted cysts in the cervical esophagus result in gastric inlet patches. *Gastrointest. Endosc.*, 2010; 72: 603-605
- [49] Menchaca Marines M.C., Posselt H.G., Waag K.L.: Ectopic gastric mucosa in rectum: a rare cause of rectal bleeding in children. *J. Pediatr. Gastroenterol. Nutr.*, 1988; 7: 293-297
- [50] Mizuno Y., Sumi Y., Nachi S., Ito Y., Marui T., Saji S., Matsutomo H.: Acinar cell carcinoma arising from an ectopic pancreas. *Surg. Today*, 2007; 37: 704-707
- [51] Mulholland K.C., Wallace W.D., Epanomeritakis E., Hall S.R.: Pseudocyst formation in gastric ectopic pancreas. *JOP*, 2004; 10: 498-501
- [52] Ok C.Y., Akalina A.: Gastric heterotopia in the rectum. *Elmer Case Report J. Med. Cases*, 2012; 3: 113-115
- [53] Okamoto H., Kawaoi A., Ogawara T., Fujii H.: Invasive ductal carcinoma arising from an ectopic pancreas in the gastric wall: a long-term survival case. *Case. Rep. Oncol.*, 2012; 5: 69-73
- [54] Patel N., Berzin T.: Intraductal papillary mucinous neoplasm arising in a heterotopic pancreas: a case report. *Am. J. Gastroenterol.*, 2010; 105: 2513-2514
- [55] Reggoug S., Errabih I., Ouazzani L., Benzoubeir N., Krami H., Raiss M., Hrorra A., Ahallat M., Ouazzani H.: Heterotopic pancreas: an unusual cause of epigastric pain. *Gastroenterol. Clin. Biol.*, 2010; 34: 726-727
- [56] Rifat Mannan A.A., Kahvic M., Bharadwaj S., Grover V.K.: Gastric heterotopia of the anus: report of two rare cases and review of the literature. *Indian J. Pathol. Microbiol.*, 2008; 51: 240-241
- [57] Rubin E., Farber J.L.: Ectopia or heterotopia is an anomaly in which an organ is outside its normal anatomic site. *J.B. Lippincott Company, Pathology*, 1994
- [58] Ryu D.Y., Kim G.H., Park do Y., Lee B.E., Cheong J.H., Kim D.U., Woo H.Y., Heo J., Song G.A.: Endoscopic removal of gastric ectopic pancreas: An initial experience with endoscopic submucosal dissection. *World J. Gastroenterol.*, 2010; 28: 4589-4593
- [59] Sato A., Hashimoto M., Sasaki K., Matsuda M., Watanabe G.: Elevation of pancreatic enzymes in gallbladder bile associated with heterotopic pancreas. A case report and review of the literature. *J. Pancreas*, 2012; 10: 235-238
- [60] Sharma D.K., Agarwal S., Saran R.K., Agarwal A.K.: Pseudocyst of ectopic pancreas of the duodenal wall masquerading as malignant cystic tumor of pancreas. *Saudi J. Gastroenterol.*, 2009; 15: 271-273
- [61] Steele S.R., Mullenix P.S., Martin M.J., Ormseth E., Weppler E., Graham J., Place R.J.: Heterotopic gastric mucosa of the anus: a case report and review of the literature. *Am. Surg.*, 2004; 70: 715-719
- [62] Tanemura A., Yano T., Tamaki H., Sanda T., Ohashi N., Ishihara A., Fukutome K., Shiraki K.: Ectopic pancreas in the minor duodenal papilla presenting as upper-GI bleeding. *Gastrointest. Endosc.*, 2005; 62: 324-326
- [63] Tanpowpong P., Katz A.J.: Heterotopic gastric mucosa causing significant esophageal stricture in a 14-year-old child. *Dis. Esophagus.*, 2011; 24: E32-E34
- [64] Tison C., Regenet N., Meurette G., Mirallié E., Cassagnau E., Frampas E., Le Borgne J.: Cystic dystrophy of the duodenal wall developing in heterotopic pancreas: report of 9 cases. *Pancreas*, 2007; 34: 152-156
- [65] Tolentino L.F., Lee H., Maung T., Stabile B.E., Li K., French S.W.: Islet cell tumor arising from a heterotopic pancreas in the duodenal wall with ulceration. *Exp. Mol. Pathol.*, 2004; 76: 51-56
- [66] Trifan A., Târcoveanu E., Danciu M., Huțanașu C., Cojocariu C., Stanciu C.: Gastric heterotopic pancreas: an unusual case and review of the literature. *J. Gastrointest. Liver Dis.*, 2012; 21: 209-212
- [67] Tsapralis D., Charalabopoulos A., Karamitopoulou E., Schizas D., Charalabopoulos K., Liakakos T., Macheras A.: Pancreatic intraductal papillary mucinous neoplasm with concomitant heterotopic pancreatic cystic neoplasia of the stomach: a case report and review of the literature. *Diagn. Pathol.*, 2010; 5: 4
- [68] Uğur Kantar F., Akarsu M., Atilla K., Sağol O., Soytürk M., Akpınar H.: Ectopic pancreas presenting with intractable diarrhea: case report. *Turk. J. Gastroenterol.*, 2011; 22: 426-429
- [69] von Heinrich H.: Ein Beitrag zur histologie des sogen: akzessotischen pancreas. *Virchows Arch. Pathol. Anat. Histopathol.*, 1909; 198: 392-401
- [70] von Rahden B.H., Stein H.J., Becker K., Liebermann-Meffert D., Siewert J.R.: Heterotopic gastric mucosa of the esophagus: literature-review and proposal of a clinicopathologic classification. *Am. J. Gastroenterol.*, 2004; 99: 543-551
- [71] Wagle P.K., Shetty G.S., Sampat M., Patel K.: Ectopic pancreatic tissue mimicking ampullary tumor. *Indian J. Gastroenterol.*, 2005; 24: 265-266
- [72] Wall I., Shah T., Tangorra M., Li J.J., Tenner S.: Giant heterotopic pancreas presenting with massive upper gastrointestinal bleeding. *Dig. Dis. Sci.*, 2007; 52: 956-959
- [73] Weickert U., Wolf A., Schröder C., Autschbach F., Vollmer H.: Frequency, histopathological findings, and clinical significance of cervical heterotopic gastric mucosa (gastric inlet patch): a prospective study in 300 patients. *Dis. Esophagus*, 2011; 24: 63-68
- [74] Wüppenhorst N., Viebahn B., Theile A., Radü H.J., Kist M.: Culture and successful eradication of *Helicobacter pylori* from heterotopic gastric mucosa. *Z. Gastroenterol.* 2012; 50: 677-679
- [75] Yan M.L., Wang Y.D., Tian Y.F., and Lin Y.: Adenocarcinoma arising from intrahepatic heterotopic pancreas: a case report and literature review. *World J. Gastroenterol.*, 2012; 14; 18: 2881-2884
- [76] Yoshida N., Nakayama H., Hemmi A., Suzuki T., Takayama T.: Duodenal stenosis caused by cystic dystrophy in heterotopic pancreas: report of a case. *Surg. Today*, 2009; 39: 803-806

The authors have no potential conflicts of interest to declare.