



Gastric heterotopic pancreas in children: A prospective endoscopic study

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ABSTRACT

Purpose: To document the prevalence and variable appearance of gastric heterotopic pancreas (HP) in children undergoing upper gastrointestinal (GI) endoscopy.

Methods: A prospective 4-year study of children undergoing flexible upper GI endoscopy in a single institution. **Results:** A total of 607 upper GI endoscopies were performed in 478 pediatric patients during the 4-year period. Eleven children (6 girls, 5 boys) aged 2.9 to 16.9 years had endoscopic features typical of gastric HP. All but one lesion was located in the gastric antrum and most appeared as an umbilicated submucosal nodule measuring 1–2 cm in diameter. Five of 13 children with repaired esophageal atresia (EA) and two of nine children with trisomy 21 had gastric HP. The prevalence of endoscopically visualized gastric HP in children without a history of EA or trisomy 21 was 1.1%.

Conclusions: Gastric HP is present in about 1% of pediatric upper GI endoscopies. It is significantly more common in patients with EA and may also be associated with trisomy 21. Gastric HP typically appears as a single 1–2 cm antral submucosal nodule, usually with a central pit. Recognition of this lesion is important to avoid misdiagnosis and inappropriate treatment.

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Heterotopic pancreatic (HP) tissue (also known as a 'pancreatic rest', ectopic pancreas, aberrant pancreas and accessory pancreas) lacks anatomic continuity with the normal pancreas and usually presents as an isolated intramural nodule of tissue in the gut. It is most commonly found in the stomach or a Meckel diverticulum but may also be present in the esophagus, small bowel, appendix, or other intra-abdominal viscera [1]. HP is frequently asymptomatic but may cause intussusception or complications from inflammation [1]. HP may be seen in the stomach during upper gastrointestinal (GI) endoscopy when it can be confused with other pathologies. Gastric HP typically appears as a single well-circumscribed broad based submucosal nodule in the gastric antrum, more often on the greater curve, and frequently surmounted by a dimple or pit representing the drainage orifice of the ectopic pancreatic tissue [2]. The aims of this prospective endoscopic study were to document the prevalence and variable appearance of gastric HP in children undergoing upper GI endoscopy in order to promote increased awareness and discourage inappropriate intervention.

1. Patients and methods

Wellington hospital provides a regional gastrointestinal endoscopy service for children in the southern region of the North Island of New Zealand. Almost all procedures are performed directly or under the supervision of a single experienced pediatric GI endoscopist (MDS). All children undergoing flexible upper GI endoscopy between October 2015 and September 2019 were included in this prospective audit. Gastric HP was recognized by its typical endoscopic features of a non-inflamed, usually umbilicated, submucosal nodule. Clinical and endoscopic details of all affected children were recorded prospectively.

2. Results

A total of 607 flexible upper GI endoscopies were performed in 478 pediatric patients during the 4-year period; 75 children underwent two or more endoscopies, some of whom had also had an upper GI endoscopy before 2015. The primary indications for upper GI endoscopy are shown in Table 1 and are consistent with international guidelines [3]. Eleven children aged 2.9 to 16.9 years had endoscopic features of a typical gastric HP lesion (Table 2), giving an overall prevalence of 2.3% in this consecutive series of pediatric endoscopies. All but one lesion was located in the gastric antrum and most appeared as an umbilicated submucosal nodule measuring 1–2 cm in diameter (Fig. 1). By comparison, during the study period, a single small duodenal HP lesion was identified in a 15-year old boy.

Abbreviations: HP, heterotopic pancreas; EA, esophageal atresia; TEF, tracheoesophageal fistula; GI, gastrointestinal.

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Table 1

Indications for upper gastrointestinal endoscopy.

Indication	No. of endoscopies	No. of patients
Post EA ± TEF repair – esophageal symptoms or surveillance	14	13
Celiac disease – suspected	186	180
Inflammatory Bowel Disease – suspected or confirmed	69	64
Eosinophilic esophagitis – diagnosis or follow up	79	41
Balloon dilatation of esophageal stricture (caustic, post button battery ingestion, epidermolysis bullosa, post EA repair, peptic, eosinophilic, achalasia)	45	9
Percutaneous endoscopic gastrostomy (and subsequent endoscopy to change PEG to gastrostomy button)	71	36
Gastroesophageal reflux disease – investigation	71	66
Chronic or recurrent upper abdominal pain	21	21
Gastrointestinal bleeding/unexplained iron deficiency anemia/esophageal varices	11	10
Other esophageal symptoms e.g. dysphagia, unexplained recurrent vomiting, regurgitation, unexplained failure to thrive	23	22
Surveillance e.g. polyposis syndromes, Barrett esophagus	4	3
Removal of ingested foreign body	4	4
Miscellaneous e.g. unexplained chronic diarrhea, suspected Candida esophagitis, intestinal pseudo-obstruction	9	9
Total	607	478

EA, esophageal atresia; TEF, tracheoesophageal fistula.

Among the 478 children undergoing upper GI endoscopy there were 13 with a history of esophageal atresia (EA) and nine with trisomy 21. Five children with gastric HP had a history of repaired EA and one of these also had extensive patches of heterotopic gastric mucosa in her esophagus, which was the subject of a previous report [4]. Two children with gastric HP had trisomy 21. The prevalence of endoscopically visualized gastric HP in children *without* a history of esophageal atresia or trisomy 21 was therefore 1.1% (5/456).

3. Discussion

In this prospective endoscopic study the prevalence of gastric HP in children was just over 1% but in those with a history of EA or trisomy 21 the prevalence was much greater. None of the patients with gastric HP had symptoms or complications from the lesion. In four children who underwent repeat upper GI endoscopy during periods of up to 6 years the lesion remained unchanged. We do not have histologic proof but the typical appearances of the lesions on endoscopy (their position, submucosal appearance, size, umbilication, constancy etc.) indicate that they were all gastric HP nodules. This study highlights the variable appearance of these lesions.

Table 2

Characteristics of pediatric patients with endoscopically diagnosed pancreatic rests.

Age (y)	Sex	Other conditions	Pancreatic rest	Comments
2.9	M	Repaired long gap isolated EA (Gross type A), Nissen fundoplication, eosinophilic esophagitis with stricture	Lesser curve <1 cm umbilicated nodule	Static appearance on 3 occasions over 3.3y
3.7	M	Repaired EA/TEF (Gross type C). Mild reflux esophagitis	Prepyloric 1–2 cm umbilicated nodule	Biopsy showed normal gastric mucosa
13.6	F	Repaired EA/TEF (Gross type C), low anorectal malformation, horseshoe kidney, 13 pairs ribs (VACTERL), eosinophilic esophagitis	Prepyloric ~1 cm umbilicated nodule	Static appearance on 3 occasions over 6.5y
16.9	F	Repaired EA/TEF (Gross type C), Trisomy 21, heterotopic gastric mucosa in esophagus	Prepyloric 1 cm umbilicated nodule	Static appearance on two occasions over 2.2y
15.2	F	Trisomy 21, hypothyroidism	Prepyloric 1 cm umbilicated nodule	
8	M	Celiac disease	Prepyloric 1 cm umbilicated nodule	
12.8	M	Asperger syndrome, reflux esophagitis	Prepyloric <1 cm nodule	
14	F	Chronic abdominal pain of unknown cause	Prepyloric 1–2 cm nodule	
13.3	M	Type 1 diabetes mellitus, autism	Prepyloric 2 cm umbilicated nodule	Static appearance on 2 occasions over 1y
14.6	F	Crohn's colitis, reflux esophagitis	Prepyloric 1–2 cm umbilicated nodule	
8.6	F	Repaired EA/TEF (Gross type B). Mild reflux esophagitis	Prepyloric 1 cm umbilicated nodule	Biopsy showed normal gastric mucosa

EA, esophageal atresia; TEF, tracheoesophageal fistula, VACTERL association (3 or more of the following anomalies: vertebral, anorectal, cardiac, tracheoesophageal, renal, and limb).

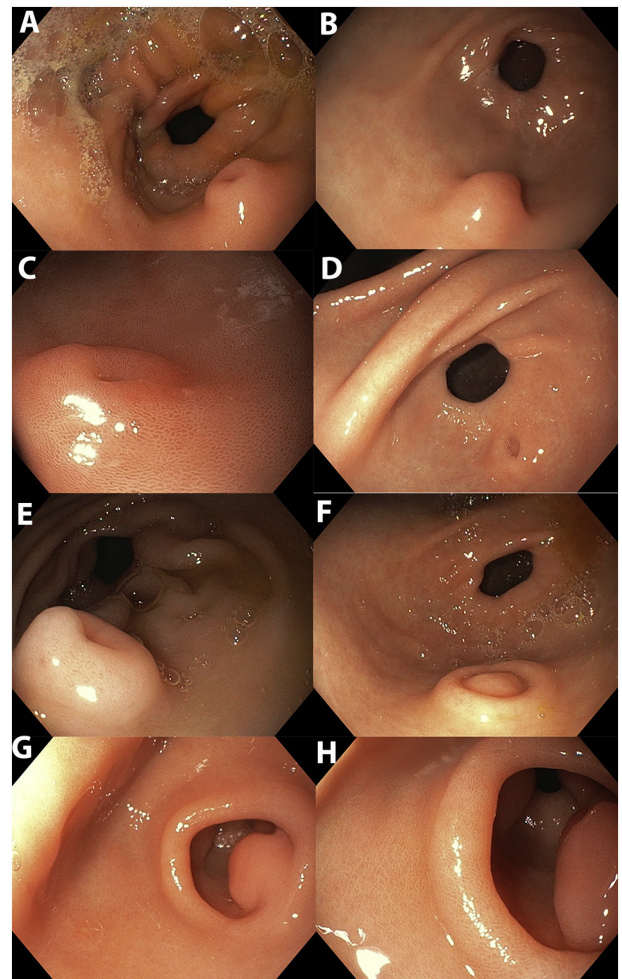


Fig. 1. Endoscopic appearances of gastric heterotopic pancreas in children. A, typical appearance of an umbilicated prepyloric submucosal nodule; B nodular variety with no obvious dimple; C and D shallow nodules with central craters; E and F larger cratered prepyloric nodules; G and H polypoid variant – in this patient the central pit was only visible on close inspection.

An association between gastric HP and trisomy 21 has not been reported before although a link between gastric HP and EA has been documented. Ormarsson et al. reported a 9-year-old boy with a previous EA/TEF repair who had a 5 mm prepyloric nodule that was considered to be causing pyloric obstruction; the lesion was excised and confirmed as HP [5]. Park reported a neonate with gastric HP at the site of a gastric perforation after an isolated EA repair [6]. Pouessel et al. described two children

who had an upper GI endoscopy for swallowing difficulties after EA/TEF repair but attributed the finding of gastric HP to a chance association [7]. The best evidence for a link between EA and gastric HP comes from a retrospective Canadian endoscopic study, which reported a 19% prevalence of gastric HP among 91 children with repaired EA as compared to 0.5% in controls [8]. Our greater prevalence of 1.1% in patients without EA or trisomy 21 may be related to the prospective nature of our study, especially since HP lesions may be overlooked at endoscopy [9–11]. Our figure is also consistent with the 0.9–1.5% prevalence reported in adult autopsies [12,13]. Our findings confirm an association between EA and gastric HP, which was present in five of 13 children (38%) who had previously undergone EA \pm TEF repair. This expands the potential upper GI

endoscopic findings in children following EA repair, which include strictures (anastomotic, peptic, bronchial remnants), reflux esophagitis, Barrett esophagus [14], heterotopic gastric and/or pancreatic mucosa in the esophagus [4,15,16], gastric metaplasia [17] and eosinophilic esophagitis [18].

3.1. Heterotopic pancreas in children

Heterotopic pancreatic tissue has been reported at numerous sites in children, most commonly in the stomach or a Meckel diverticulum but also in the duodenum, jejunum, ileum, esophagus, biliary tree, gut mesentery, liver, spleen, appendix, omentum, and umbilicus [1,19–23].

Table 3
Reports of symptomatic gastric heterotopic pancreas in children.

First author, year, country	Sex	Age	Presenting symptoms	Principal investigation (s)	Treatment	Follow up	Comment
Collett 1946 USA [19]	M	6y	Abdo pain, vomiting	UGI – 1.5 cm prepyloric nodule	Excision	Not stated	Pyloric obstruction speculative
Eklöf 1973 UK [30]	F M	8 y 4 wk	Abdo pain Vomiting	UGI – small prepyloric nodule UGI – IHPS + probable HP	Excision Pyloromyotomy	Well postop Died postop	Prepyloric HP probably an incidental finding in both cases
Matsumoto 1974 Japan [31]	F	5 d	Vomiting, melena	UGI – partial pyloric obstruction	Gastrojejunostomy and biopsy; antrectomy 6 m	Well postop	
Lucaya 1976 Spain [32]	F	3 m	Vomiting	UGI – prepyloric HP but no obstruction	Excision & pyloroplasty	Well postop	HP likely incidental
Mollitt 1984 USA [33]	4 M 2F	6 m-13 y	Vomiting & FTT or chronic abdo pain	UGI (5), EGD (2)	Excn & pyloroplasty (4), enucleation (2)	4 well 2 not cured	None with definite obstruction 2 with persistent vomiting postop
Visentin 1991 France [34]	M	18 d	Vomiting	US – ? IHPS	Pyloric “abscess” Gastrojejunostomy	GJ reversed 2y; HP left	HP with probable acute pancreatitis
De’Angelis 1992 Italy [20]	M	7 wk	Vomiting, hematemesis	EGD – 15 mm prepyloric nodule + esophagitis	Excision	Well 1y	HP likely incidental
Allison 1995 USA [35]	M	17 m	Intermittent abdo pain, vomiting	UGI – antroduodenal prolapsing lesion	Excision	Well postop	
Hackett 1997 USA [36]	F	15 y	Abdo pain	UGI, EGD – nodule gastric body greater curve	Excision	Well postop	HP nodule likely incidental; no inflammation or obstruction
Hayes-Jordan 1998 USA [21]	M	2 d	Vomiting	UGI – small prepyloric nodule EGD – 5 mm nodule	Excision	Well 2 m	Prepyloric nodule only 4–5 mm
Wolters 2001 Netherlands [37]	M	5 y	Abdo pain, vomiting, FTT	EGD – prepyloric diverticulum & pyloric stenosis	Antrectomy	Well 1 y	HP diverticulum causing pyloric obstruction
Le Luyet 2002 France [38]	M F	14 y 9y	Vomiting & FTT in both	EGD Delayed gastric emptying in 1	Excision	Well postop	
Özcan 2002 Turkey [39]	F	1 m	Vomiting & FTT	US, UGI-? IHPS	Excision	Well 2 y	Prepyloric nodule only 4–5 mm
Ormarsson 2003 Norway [5]	M	9 y	Vomiting	EGD, CT	Excision	Well 3 m	Prepyloric nodule maximum 5 mm on CT
Chandan 2004 USA [40]	M	17 y	Abdo pain	EGD – 1 cm prepyloric nodule	Excision	Not stated	HP likely incidental
Sharma 2004 India [41]	M	1 m	Vomiting & FTT	UGI – ? IHPS	Excision – pylorus normal	Well 8 m	Prepyloric nodule only 5–6 mm
Hsu 2005 China [42]	F	15 y	Abdo pain, melena	EGD – 1.5 cm nodule gastric body with adjacent gastric ulcer	Excision	Well postop	HP likely incidental; adjacent gastric ulcer probably resected
Ertem 2006 Turkey [43]	F	11 y	Vomiting & weight loss	UGI, EGD – antral nodularity and stenosis, <i>H. pylori</i> gastritis	Excision	Well 4 m	
Stefanescu 2008 France [28]	M	15 y	Abdo pain & weight loss	EGD – antral stenosis CT – 5 cm cystic mass	Antrectomy	Well 8 m	HP with cystic inflammatory changes
Park 2010 South Korea [6]	F	11 d	Gastric distention	Laparotomy – gastric body perforation	Partial gastric resection	Well 18 m	HP at site of gastric perforation
Goto 2011 Japan [29]	F	2 y	Abdo pain	CT – 4 cm antral mass with pyloric stenosis	Antrectomy	Well 10 m	
Lhewa 2011 USA [44]	F	14 y	Abdo pain	UGI, EGD – 2 cm antral diverticulum + eosinophilic gastritis	Excision	Recurrent pain	Antral diverticulum containing HP may have been incidental
Carbonero-Celis 2013 Spain [45]	-	22 m	Minor hematemesis	EGD – esophagitis + prepyloric 1 cm diverticulum	Excision	Well 1 y	HP likely incidental
Karakus 2015 Turkey [10]	M	3 m	Melena	EGD – prepyloric nodule	Excision	Continued GI bleeding	Later found to have colonic juvenile polyp
Rodriguez 2015 USA [46]	F	16 y	Abdo pain, vomiting, hematemesis	EGD – antral nodularity and stenosis, <i>H. pylori</i> gastritis	Excision + Gastrojejunostomy	Ongoing symptoms	
Henderson 2018 UK [11]	M F	9 m 14 y	Hematemesis, FTT Melena	EGD, CT – 5 mm antral nodule EGD, CT	Excision Excision	Well 4 y Well 3 y	Uncertain link between gastric HP and GI bleeding but resolved after surgery in both

UGI, upper gastrointestinal contrast study; EGD, esophagogastroduodenoscopy; US, ultrasound scan; HP, heterotopic pancreas; FTT, failure to thrive; IHPS, infantile hypertrophic pyloric stenosis.

More distant locations such as the mediastinum, lungs and Fallopian tubes have been described in adults [9,24,25]. Heterotopic pancreas usually appears as a single, firm, somewhat lobulated nodule, which is yellowish or white on cross-section [1,13,22]. The nodule is usually submucosal rather than subserosal and extends into the muscularis propria to a variable degree [1,13,22,26]. This explains why endoscopic biopsies frequently sample the overlying mucosa only and do not show pancreatic tissue [5,7,9]. HP may be discovered incidentally at laparotomy or autopsy [1,19]. Symptomatic lesions usually present with intussusception [1] or less commonly with inflammation [24] or as part of duplication cyst pathology [9,27]. Histology varies from pancreatic lobules with ducts and acini with or without islet cells to ducts with connective tissue only. The origin of HP is unknown but two main theories have been proposed: (i) attachment of pancreatic tissue from the lateral buds of the developing dorsal or ventral pancreas to an adjacent organ and its subsequent separation or (ii) pancreatic metaplasia or abnormal differentiation of local endodermal tissue [9,12,13,26].

3.2. Gastric heterotopic pancreas in children

In most cases involving the stomach the lesion is localized to the pyloric antrum and canal and typically appears as a single 0.5–2 cm diameter submucosal nodule, often with a central pit or crater [5,20]. Larger lesions are rare [28,29]. Gastric HP is usually asymptomatic although there are numerous case reports of apparent complications (Table 3) [5,6,10,11,19–21,28–46]. Whilst some of these describe a convincing causal relationship between gastric HP and symptoms [6,11,28,29,34] many do not [30,33,36,40]. In some of these cases, gastric HP may well have been an incidental finding with symptoms more readily explained by concomitant reflux esophagitis [20,38,45], *H. pylori* gastritis [9,43,46], or another upper GI pathology [32,44,47]. In some publications, the infant underwent surgery for a presumptive diagnosis of infantile hypertrophic pyloric stenosis but at laparotomy was found to have a small gastric HP nodule that was then removed [31,39,41]. In other cases, unfamiliarity with gastric HP led to diagnostic confusion with other gastric tumors such as a leiomyoma, which may have prompted unnecessary treatment [9,36,42]. Yet other lesions have been assumed to cause pyloric obstruction from antral mucosal prolapse even though the prepyloric nodule was only 4–5 mm [5,21]. Symptoms have not been invariably relieved by excision [33,46], a finding also reported in adults [26].

Despite these comments, gastric HP in children may on occasions cause recurrent epigastric pain, vomiting from gastric outlet obstruction [28,29,34,35,37] and GI bleeding [10,11]. Rare complications include gastric perforation [6], cystic degeneration [28,29] and acute pancreatitis [34]. Similar complications have been reported in adults in whom neoplastic change (islet cell adenoma and adenocarcinoma) has also been described [13,22,26,48]. As with children, most adults with gastric HP are asymptomatic [9,13,24,26] and the lesion is commonly found as an incidental finding at endoscopy [9,22].

For children with an incidentally discovered asymptomatic lesion with typical endoscopic appearances, we do not recommend excision as advocated by some authors [39,41]. In one study of EA associated gastric HP in children, no complications were recorded during a short follow up period of up to 3 years [8]. We do not support the use of deep biopsies using larger forceps, fine-needle aspiration or regular surveillance endoscopies [7,9]. If there is doubt about the nature of the lesion then endoscopic ultrasound may be helpful in differential diagnosis [49]. Indications for treatment are complications such as bleeding or pyloric obstruction. Endoscopic submucosal resection has been reported in adults [50,51].

In conclusion, gastric HP is not rare and is present in about 1% of pediatric upper GI endoscopies. It is significantly more common in patients with EA and may also be associated with trisomy 21. Gastric HP typically appears as a single 1–2 cm diameter antral submucosal nodule, often with a central pit or crater. Recognition of this lesion is important to

avoid misdiagnosis and inappropriate treatment. Incidentally detected asymptomatic lesions do not require treatment or surveillance but if there is robust evidence of symptoms related to the lesion, then excision is appropriate.

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Competing interests

None.

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