Peptic ulcer disease

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Abstract

Peptic ulcer disease (PUD) is an uncommon disease of childhood. Peptic ulceration of the stomach or duodenum is usually associated with abnormalities of the gastric mucosa such as gastritis and/or gastropathy. Gastritis and ulcers of the stomach and duodenum can be classified into either primary or secondary depending on their aetiologies. The majority of primary or unexplained peptic ulcers are the result of chronic inflammation caused by *Helicobacter pylori* infection. However, an increasing number of children with PUD without evidence of *H. pylori* infection are now being seen. Rarely PUD is caused by hypersecretory states. Secondary ulceration occurs in response to acute stress from severe systemic illnesses such as sepsis, head injury, burns, and as sequelae to use of certain drugs. The prognosis for recovery from peptic ulcers is good as most patients will respond to treatment.

Keywords children; duodenum; gastritis; gastropathy; *Helicobacter pylori*; stomach; ulcer

Introduction

Peptic ulcer disease is uncommon in childhood and peptic disorders such as oesophagitis, gastritis, gastropathy and duodenitis are far less common in children than in adults. Peptic ulcer disease in childhood is estimated to account for one in 2,500 hospital admissions. Peptic ulcers are deep mucosal lesions extending beyond the muscularis mucosa coat of the gastrointestinal tract that are exposed to hydrochloric acid and pepsin. Gastritis describes any inflammation of the gastric mucosa. The imbalance between mucosal defence and aggressive factors results in varying degrees of gastritis and/or frank ulceration. Peptic ulcer disease is classified according to the underlying aetiology (Table 1). The commonest cause of primary peptic ulcers is *Helicobacter pylori* infection. Improved socio-economic conditions, effective medical treatments and pervasive use of antibiotics for unrelated conditions have led to a steady decline in the rates of *H. pylori* infections, particularly in the developed world, and an increasing proportion of cases are *H. pylori* negative. Primary peptic ulcers tend to be chronic, are often duodenal and are rare in children aged younger than 10 years.

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Classification of gastritis and peptic ulcers in children

Primary peptic ulcers	Secondary peptic ulcers
• *Helicobacter pylori*-associated	• Infectious
• Helicobacter-negative	• Bacterial
• Hypersecretory states:	• Viral
○ Zollinger—Ellison syndrome	• Parasitic
○ G-Cell hyperplasia	• Fungal
○ Systemic mastocytosis	• Phlegmonous and emphysematous gastritis
○ Cystic fibrosis	• Chemical or reactive gastropathy
○ Hyperparathyroidism	○ Drug induced gastropathy
○ Short bowel syndrome	○ Stress gastritis/ulceration
	○ Corrosive gastropathy
	○ Bile gastropathy
	○ Radiation gastropathy
	• Lymphocytic gastritis
	• Autoimmune atrophic gastritis
	• Allergic (Eosinophilic) gastritis
	• Vascular gastropathy
	○ GAVE
	○ Portal hypertensive gastropathy
	• Collagenous gastritis

Table 1

Secondary peptic ulcers are usually acute, can occur at any age and are associated with a higher mortality in young children. In this article, the term gastritis and ulcer have an overlap, as many conditions described will cause gastritis rather than ulcers, and some may cause both.

Primary peptic ulcer disease

H. pylori

Epidemiology: *H. pylori* infection is usually acquired in early childhood. Prevalence rates are higher in developing countries. Although the prevalence is decreasing globally and is low in Western Europe and North America, prevalence remains relatively high in most Asian, South American, African and Aboriginal populations. Interfamilial spread by direct person-to-person contact is an important aspect of transmission.

Clinical manifestations

H. pylori infection in children is usually asymptomatic. In the absence of ulcer disease, there is inadequate evidence supporting a causal relationship between *H. pylori* gastritis and recurrent abdominal pain.

In comparison to adults, peptic ulcer disease is found less often in infected children undergoing upper gastrointestinal endoscopy. In a European multicentre study including 1233 symptomatic children with *H. pylori* infection, peptic ulcer disease was diagnosed in less than 5% of children under the age of 12 years and in about 10% of teenagers.

There is an established causal relationship between *H. pylori* infection and duodenal ulcer disease in children. A strong relationship between gastrointestinal bleeding due to duodenal ulcer

disease and *H. pylori* infection in childhood has also been reported.

Diagnosis of *H. pylori* infection

Invasive tests

Histopathology: an upper GI endoscopy is performed in children and young people suspected to have peptic ulceration. A variety of stains including haematoxylin and eosin, special stains and immunohistochemistry have been used to detect *H. pylori* (Figure 3). The sensitivity ranges from 66 to 100% and specificity 94–100% in published case series from children. The highest bacterial count is usually in the antrum but in patients on acid suppressing agents, the bacteria may be found in the corpus (Figures 1 and 2).

Rapid urease test

Rapid urease test can be performed in gastric biopsy specimens using a wide variety of commercially available reagents. This test is based on the activity of *H. pylori* urease enzyme, which splits the urea reagent to form ammonia. Ammonia increases the pH, which is detected by the indicator phenol red. False negative urease tests can be obtained in patients on proton pump inhibitors and adult studies recommend acid suppressants are discontinued for at least 2 weeks prior to endoscopy. The sensitivity of the rapid urease test varies from 75 to 100% and specificity 84–100% in published studies in children.

Fluorescent in-situ hybridisation (FISH) or polymerase chain reaction (PCR)

An advantage of FISH and PCR is the ability to determine clarithromycin resistance in frozen or formalin fixed paraffin embedded tissues which does not depend on bacterial growth. The use is currently limited to research only due to high costs and technically challenging methods.

Culture

H. pylori can be cultured from gastric biopsies. The colonies are gram negative, urease positive, oxidase positive and catalase positive. This test has 100% specificity and is a reference standard but sensitivity can vary.

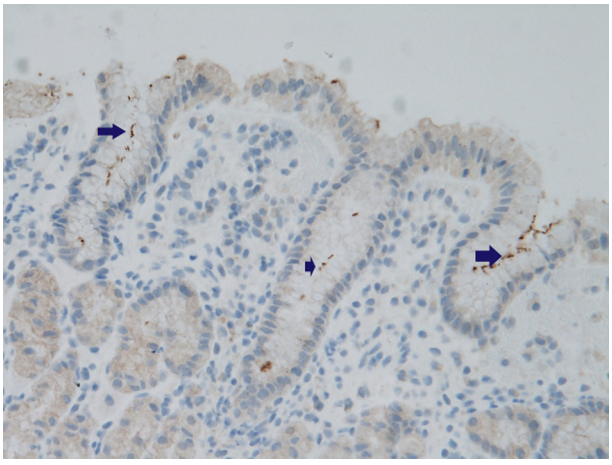

Figure 1 *H. pylori* organisms (arrow) on the surface of the gastric mucosa (H&E × 40).

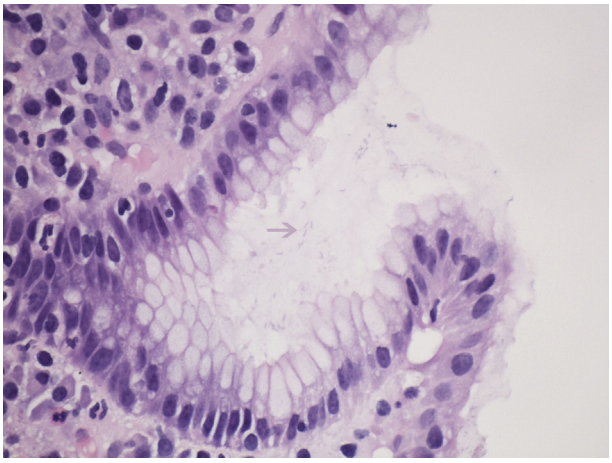

Figure 2 Fundic gastric mucosa with chronic gastritis. Note the inflammatory cells invading the gland necks (arrow) (H&E × 20).

Non-invasive tests

Antibodies to *H. pylori* in blood, urine and saliva: due to wide variability in the sensitivity and specificity for detection of antibodies (IgG and IgA) to *H. pylori* in serum, whole blood, urine and saliva in children, these assays cannot be used solely for either diagnosis of *H. pylori* infection or to monitor the success of therapy. A positive IgG serology test can occur several months or years after infection and cannot be used reliably for diagnosis or to confirm eradication.

^{13}C-urea breath test: *H. pylori* produces urease, an enzyme that splits urea into ammonia and carbon dioxide. The urea

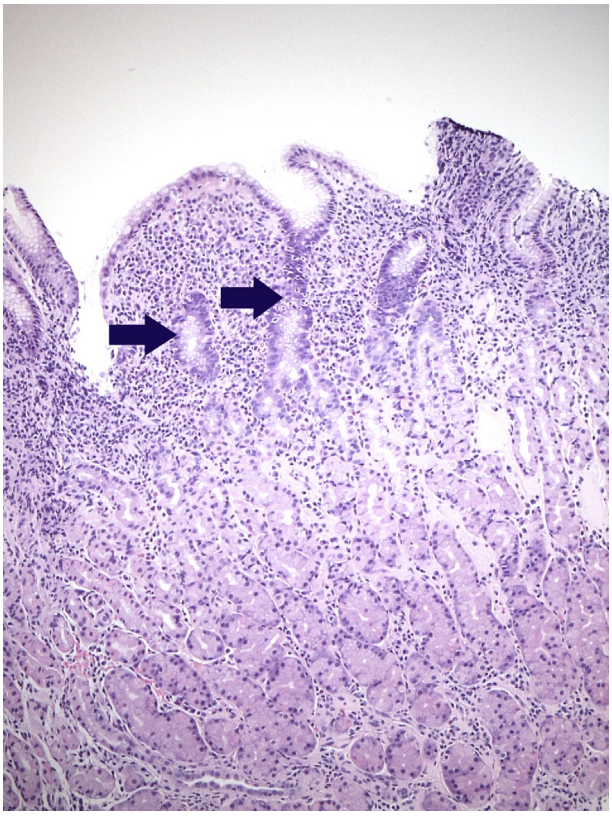

Figure 3 *H. pylori* stain positive with anti-H pylori immunostain (arrows) (× 20).