Zollinger-Ellison Syndrome

ZES, an acid hypersecretory state caused by gastrin-secreting tumors, accounts for 0.1% of patients who have PUD and should be considered in patients with ulcers in unusual sites (e.g., distal duodenum, jejunum); multiple, recurrent, or complicated duodenal ulcers; or ulcers associated with chronic diarrhea. This disorder is discussed in detail below.

Clinical Presentation

Peptic ulcer disease can be clinically silent or can exhibit a variety of manifestations ranging from iron deficiency anemia to abdominal pain, obstruction, perforation, and hemorrhage. Symptoms may mimic those of other diseases, including cholecystitis, pancreatitis, gastric cancer, and gastroesophageal reflux. Myocardial ischemia or infarction, especially of the inferior wall, can cause abdominal pain that resembles peptic ulcer. Abdominal pain in PUD is generally epigastric and is usually described as a dull ache but may be sharp or burning. Less than 20% of patients report the hunger-like pain traditionally associated with both gastric and duodenal ulcers. Similarly, the character of the symptoms and their relation with meals, specifically pain relief after food intake for duodenal ulcer and pain worsening for gastric ulcer, do not always correlate with endoscopic diagnosis and are less useful in predicting ulcer location. Nocturnal pain and pain relief with milk or antacids are common with duodenal ulcers but can also occur with gastric ulcers. NSAID-associated ulcers typically produce painless bleeding. Nausea and vomiting are commonly associated with peptic ulcers, being slightly more common with gastric ulcers. Gastric outlet obstruction may be caused by antropyloric or duodenal ulcers but should be differentiated from malignant obstruction resulting from gastric or pancreatic cancer. Weight loss, while suggestive of malignancy, is reported frequently by patients with peptic ulcer disease.

Diagnosis

Because the clinical features of gastroduodenal ulcers may overlap with other disorders, and the physical examination is often not helpful in the diagnosis, imaging studies of the GI tract are required to confirm the presence of peptic ulcers. Although contrast radiology (barium upper GI series) can be used, endoscopy is preferred because, in addition to characterizing the ulcer, it allows tissue sampling to exclude malignancy, assessment of *H. pylori* infection, and, in cases of acute ulcer hemorrhage, delivery of endoscopic therapy for the control of hemorrhage.

Diagnostic Tests for *Helicobacter pylori*

Eradication of *H. pylori* infection is associated with a significant reduction in ulcer recurrence. *H. pylori* testing is thus essential in all patients with PUD, and the diagnostic options and the indications for their use are summarized in Figure 36-6. Immunoglobulin G serologic testing is the noninvasive test of choice for diagnosing *H. pylori* infection in the untreated patient. However, because the antibodies may persist for several years, serologic analysis is not useful as a means to document cure of the infection since positive results may reflect past exposure but not necessarily current infection with *H. pylori*. Another noninvasive approach to detecting *H. pylori* is the ^{13}C- or ^{14}C-labeled urea breath test. When present, *H. pylori* urease splits the urea, which may be detected as labeled carbon dioxide in the breath of a patient. The urea breath test is more accurate than serologic tests, and although more expensive and less widely available, it is the noninvasive test of choice to document successful *H. pylori* eradication after antibiotic therapy. Patients should not receive PPIs for at least 14 days before administration of breath tests to avoid false-negative results. Stool antigen testing is also available and useful in the initial diagnosis of *H. pylori* infection. If endoscopic examination is performed, the diagnosis is made by the rapid urease test or histologic testing. In the rapid urease test, mucosal biopsies are placed in a urea-containing medium with a pH-sensitive indicator that changes color when ammonia is produced from urea by the urease of the organism. The rapid urease test has high sensitivity and specificity, equivalent to histologic analysis, and is inexpensive. Recent treatment with antibiotics or PPIs, however, may decrease the yield of the test. Histologic analysis is frequently the standard for detecting *H. pylori* infection and can establish the degree, type, and location of inflammation. Gastric biopsy specimens should be taken from both the antrum and the corpus because the bacteria are not uniformly distributed throughout the stomach. The presence of chronic active gastritis is strongly suggestive of *H. pylori* infection, even if bacteria are difficult to identify.

Treatment

Treatment of Peptic Ulcer Disease

Healing Ulcers by Suppressing Acid Secretion

Regardless of the cause, inhibition of gastric acid secretion continues to be the cornerstone of therapy for PUD. Antacids are effective agents for healing ulcers and may provide some symptom relief. However, because of the need to take these drugs multiple times each day, and the associated adverse effects, antacids are now rarely used as initial therapy.

H_2 receptor antagonists reduce acid secretion by competitively and selectively inhibiting histamine receptors on the parietal cell. H_2 receptor antagonists increase intragastric pH and inhibit pepsin activity. In general, H_2 receptor antagonists are safe and well tolerated, although the occurrence of adverse effects is slightly increased with cimetidine because of binding to cytochrome P-450 and hence increased risk for drug interactions. H_2 receptor antagonists heal 90% to 95% of duodenal ulcers and 88% of gastric ulcers after 8 weeks. Given as a single full dose at bedtime, cimetidine (800 mg), ranitidine and nizatidine (300 mg), and famotidine (40 mg) have comparable efficacies for ulcer healing. The recommended duration of treatment is 4 weeks for duodenal ulcers and 8 weeks for gastric ulcers.

Proton pump inhibitors, or PPIs, are the most potent inhibitors of gastric acid secretion available and heal gastroduodenal ulcers more rapidly than H_2 receptor antagonists. However, because they are most effective when the parietal cell is stimulated to secrete acid in response to a meal, PPIs should only be taken before a meal and should not be used in conjunction with H_2 receptor antagonists or other antisecretory agents. Moreover, because acid secretion must be stimulated for maximal efficacy, PPIs are administered before the first meal of the day. These agents are safe and well tolerated; adverse effects are unusual and include headache, diarrhea, and nausea. Single daily doses