Lecture (9)

Stomach (Gastritis, Ulcer, Carcinoma)

Disorders of the stomach are a frequent cause of clinical disease, with inflammatory and neoplastic lesions being particularly common.

The stomach is divided into four major anatomic regions: the cardia, fundus, body, and antrum. The cardia is lined mainly by mucin-secreting *foveolar cells* that form shallow glands. The antral glands are similar but also contain endocrine cells, such as *G cells,* that release gastrin to stimulate luminal acid secretion by *parietal cells* within the gastric fundus and body. The well-developed glands of the body and fundus also contain *chief cells* that produce and secrete digestive enzymes such as pepsin.

GASTROPATHY AND ACUTE GASTRITIS

Gastritis results from mucosal injury. When neutrophils are present, the lesion is referred to as ***acute gastritis***. When cell injury and regeneration are present but inflammatory cells are rare or absent, the term ***gastropathy*** is applied.

Agents that cause gastropathy include nonsteroidal anti-inflammatory drugs, alcohol, bile, and stress-induced injury. Acute

mucosal erosion or hemorrhage, such as Curling ulcers or lesions following disruption of gastric blood flow, for example, in portal hypertension, can also cause gastropathy that typically progresses to gastritis. The term *hypertrophic gastropathy* is applied to a specific group of diseases exemplified by Ménétrier disease and Zollinger Ellison syndrome.

Both gastropathy and acute gastritis may be asymptomatic or cause variable degrees of epigastric pain, nausea, and vomiting. In more severe cases, there may be mucosal erosion, ulceration, hemorrhage, hematemesis, melena, or, rarely, massive blood loss.

Pathogenesis

The gastric lumen is strongly acidic, with a pH close to 1—more than 1 million times more acidic than the blood. This harsh environment contributes to digestion but also has the potential to damage the mucosa. Multiple mechanisms have evolved to protect the gastric mucosa (Fig.1)

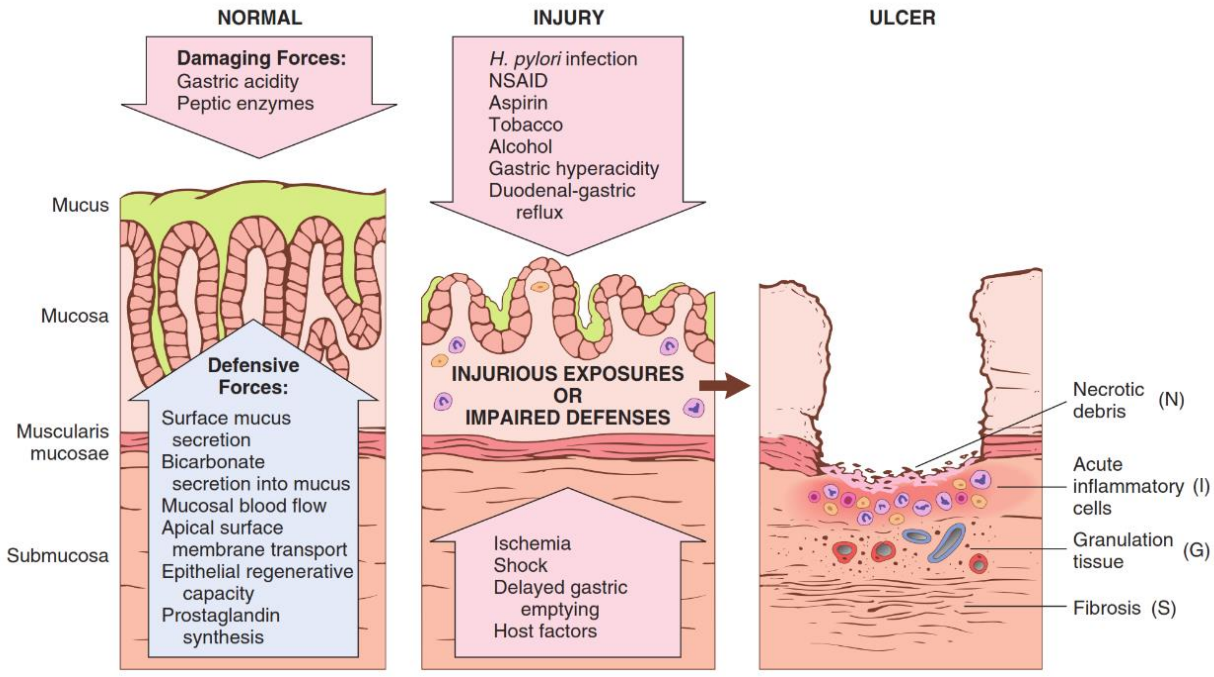

Fig. (1) Mechanisms of gastric injury and protection.

This diagram illustrates the progression from mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrotic debris (N), inflammation (I), and granulation tissue (G); scarring (S), which develops over time, is present only in chronic lesions.

Mucin secreted by surface foveolar cells forms a thin layer of mucus that prevents large food particles from directly touching the epithelium. The mucus layer also promotes formation of an "unstirred" layer of fluid over the epithelium that protects the mucosa; it has a neutral pH as a result of secretion of bicarbonate ions by surface epithelial cells. Finally, the rich blood supply of the gastric mucosa efficiently buffers and removes protons that back diffuse into the lamina propria.

Gastropathy, acute gastritis, and chronic gastritis can occur after disruption of any of these protective mechanisms.

The main causes include:

1. Nonsteroidal anti-inflammatory drugs (NSAIDs)
2. The gastric injury that occurs in uremic patients and those infected with urease-secreting *H. pylori* may be due to inhibition of gastric bicarbonate transporters by ammonium ions.
3. Reduced mucin and bicarbonate secretion.
4. Hypoxemia and decreased oxygen delivery.
5. Ingestion of harsh chemicals, particularly acids or bases.
6. Direct cellular damage also contributes to gastritis induced by excessive alcohol consumption.

7. Radiation therapy. Agents that inhibit DNA synthesis or the mitotic apparatus, including those used in cancer chemotherapy, may cause generalized mucosal damage due to insufficient epithelial renewal

CHRONIC GASTRITIS

The most common cause of chronic gastritis is **infection with the bacillus *Helicobacter pylori*. *Autoimmune gastritis,*** typically associated with gastric atrophy, represents less than 10% of cases of chronic gastritis but is the most common cause in patients without *H. pylori* infection. **Chronic NSAID** use is a third important cause of gastritis in some populations. Less common causes include **radiation injury and chronic bile reflux.**

The ***signs and symptoms*** associated with chronic gastritis typically are less severe but more persistent than those of acute gastritis. Nausea and upper-abdominal discomfort may occur, sometimes with vomiting, but hematemesis is uncommon.

COMPLICATIONS OF CHRONIC GASTRITIS

Here are three important complications of chronic gastritis:

1. Peptic ulcer disease,

2. Mucosal atrophy and intestinal metaplasia, and
3. Dysplasia.

Each of these is discussed shortly.

Peptic Ulcer Disease

Peptic ulcer disease (PUD) most often is associated with *H. pylori* infection or NSAID use. The imbalances of mucosal defenses and damaging forces that cause chronic gastritis are also responsible for PUD. (Fig. 1)

PUD may occur in any portion of the gastro intestinal tract exposed to acidic gastric juices but is most common in the gastric antrum and first portion of the duodenum. Peptic (acid-induced) injury may occur in the esophagus as a result of acid reflux (GERD) or acid secretion by ectopic gastric mucosa. Peptic injury in the small intestine may also be associated with gastric heterotopia, including that within a Meckel diverticulum.

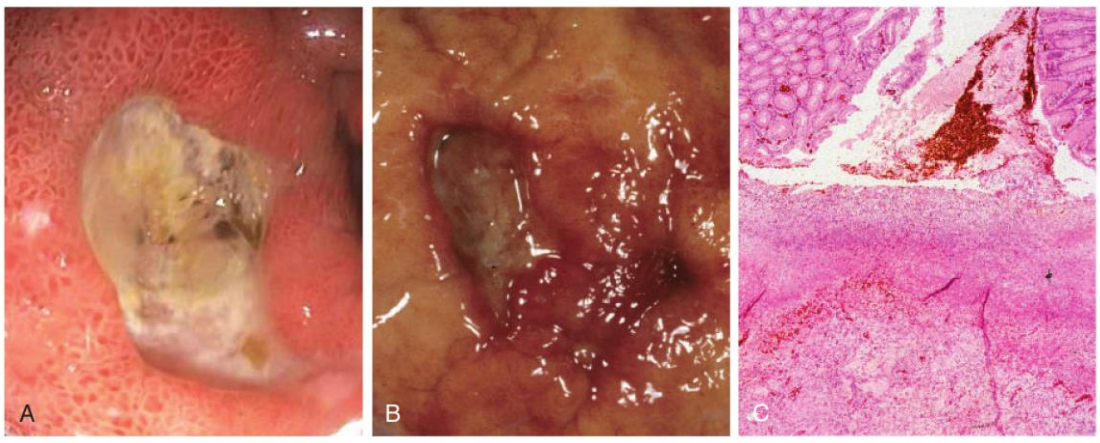

Fig. 1 Peptic ulcer disease.

(A) Endoscopic view of typical antral ulcer associated with NSAID use. (B) Gross view of a similar ulcer that was resected due to gastric perforation, presenting as free air under the diaphragm. Note the clean edges. (C) The necrotic ulcer base is composed of granulation tissue overlaid by degraded blood.

GASTRIC POLYPS AND TUMORS

Polyps are nodules or masses that project above the level of the surrounding mucosa. They are identified in up to 5% of upper gastrointestinal tract endoscopies. Polyps may develop as a result of epithelial or stromal cell hyperplasia, inflammation, ectopia, or neoplasia. Although many different types of polyps can occur in the stomach, the most common are:

- *Inflammatory and Hyperplastic Polyps*
- *Fundic Gland Polyps*
- *Gastric Adenoma*

Gastric Adenocarcinoma

Adenocarcinoma is the most common malignancy of the stomach, comprising more than 90% of all gastric cancers.

Early symptoms resemble those of chronic gastritis, including:

1. Dyspepsia,
2. Dysphagia, and
3. Nausea.

As a result, the cancer is often diagnosed at advanced stages when clinical manifestations such as **weight loss**, **anorexia**, **altered bowel habits**, **anemia**, and **hemorrhage** trigger diagnostic evaluation.

Pathogenesis

1) *Mutations.* While the majority of gastric cancers are not hereditary, mutations identified in familial gastric cancer have provided important insights into the mechanisms of carcinogenesis in sporadic cases.
2) *H. pylori.* Chronic gastritis, most commonly due to *H. pylori* infection, promotes the development and progression of cancers that may be induced by diverse genetic alterations.
3) *Epstein-Barr virus (EBV).* While *H. pylori* is most commonly associated with gastric cancer, approximately 10% of gastric adenocarcinomas are associated with Epstein-Barr virus (EBV) infection.

Lymphoma

Although extranodal lymphomas can arise in virtually any tissue, they do so most commonly in the gastrointestinal tract, particularly the stomach. Nearly 5% of all gastric malignancies are primary lymphomas

Neuroendocrine (Carcinoid) Tumor

Neuroendocrine tumors, also referred to as *carcinoid tumors,* arise from neuroendocrine organs (e.g., the endocrine pancreas) and neuroendocrine-differentiated gastrointestinal epithelia (e.g., G cells). A majority of these tumors are found in the gastrointestinal tract, and more than 40% occur in the small intestine.

Gastrointestinal Stromal Tumor

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the abdomen, and more than half of these tumors occur in the stomach. A wide variety of other mesenchymal neoplasms may arise in the stomach. Many are named according to the cell type they most resemble; for example, smooth muscle tumors are called *leiomyomas* or *leiomyosarcomas,* nerve sheath tumors are termed *schwannomas,* and those resembling glomus bodies in the nail beds and at other sites are termed *glomus tumors.* These tumors are all rare.