Lecture (8)

Esophagus

The esophagus develops from the cranial portion of the foregut. It is a hollow, highly distensible muscular tube that extends from the epiglottis to the gastroesophageal junction, located just above the diaphragm. Acquired diseases of the esophagus run the gamut from lethal cancers to the persistent "heartburn" of gastroesophageal reflux that may be chronic and incapacitating or merely an occasional annoyance.

OBSTRUCTIVE AND VASCULAR DISEASES

Mechanical Obstruction

Atresia, fistulas, and duplications may occur in any part of the gastrointestinal tract. When they involve the esophagus, they are discovered shortly after birth, usually because of regurgitation during feeding. Prompt surgical repair is required. Absence, or agenesis, of the esophagus is extremely rare. Atresia, in which a thin, noncanalized cord replaces a segment of esophagus, is more common.

It occurs most frequently at or near the tracheal bifurcation and usually is associated with a fistula connecting the upper or lower esophageal pouches to a bronchus or the trachea. This abnormal connection

can result in aspiration, suffocation, pneumonia, or severe fluid and electrolyte imbalances.

Esophageal stenosis may be congenital or more com monly acquired. When acquired the narrowing generally is caused by fibrous thickening of the submucosa and atrophy of the muscularis propria. Stenosis due to inflammation and scarring may be caused by chronic gastroesophageal reflux, irradiation, ingestion of caustic agents, or other forms of severe injury. Stenosis-associated dysphagia usually is progressive; difficulty eating solids typically occurs long before problems with liquids.

Functional Obstruction

Efficient delivery of food and fluids to the stomach requires coordinated waves of peristaltic contractions. *Esophageal dysmotility* interferes with this process and can take several forms, all of which are characterized by discoordinated contraction or spasm of the muscularis. Because it increases esophageal wall stress, spasm also can cause small diverticula to form. Esophageal dysmotility can be separated into several forms depending on the character of the contractile abnormalities.

Achalasia is characterized by the triad of incomplete lower esophageal sphincter (LES) relaxation, increased LES tone, and esophageal aperistalsis.

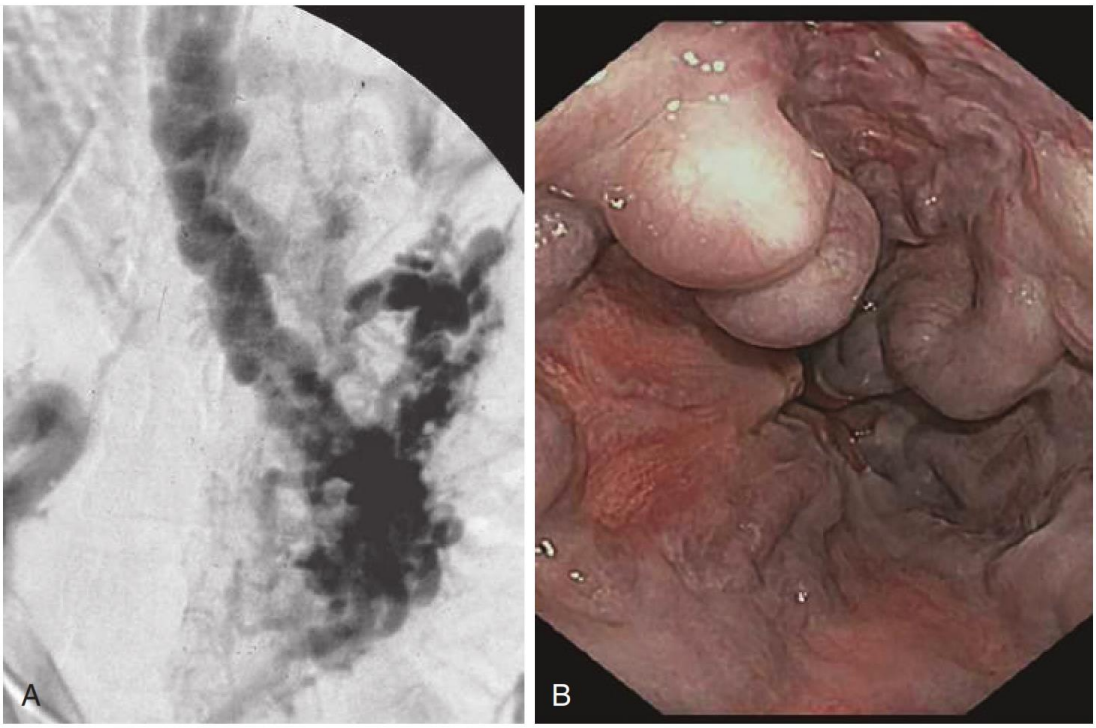
Ectopia

Ectopic tissues (developmental rests) are common in the gastrointestinal tract. The most frequent site of ectopic gastric mucosa is the upper third of the esophagus, where it is referred to as an *inlet patch.*

Esophageal Varices

Instead of returning directly to the heart, venous blood from the gastrointestinal tract is delivered to the liver via the portal vein before reaching the inferior vena cava. This circulatory pattern is responsible for the first-pass effect, in which drugs and other materials absorbed in the intestines are processed by the liver before entering the systemic circulation. Diseases that impede portal blood flow cause portal hypertension, which can lead to the development of esophageal varices, an important cause of massive and frequently life-threatening bleeding.

Varices can be detected by angiography, but are most commonly detected during endoscopy (Fig.1, A &B), and appear as tortuous dilated veins within the submucosa of the distal esophagus and proximal stomach (Fig.1, C &D). The overlying mucosa can be intact or ulcerated and necrotic, particularly if rupture has occurred.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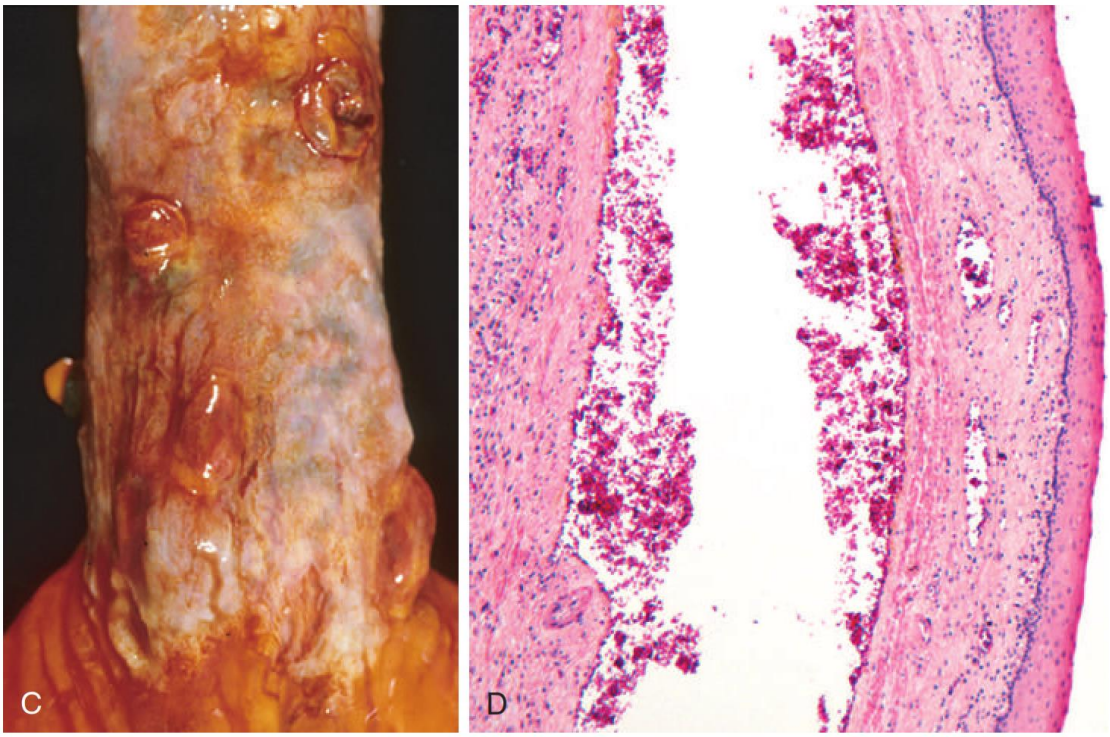
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Fig. 1 Esophageal varices. (A) Angiogram showing several tortuous esophageal varices. (B) Although the angiogram is striking, endoscopy is more commonly used to identify varices. (C) Collapsed varices are present in this postmortem specimen corresponding to the angiogram in (A). The polypoid areas are sites of variceal hemorrhage that were ligated with bands. (D) Dilated varices beneath intact squamous mucosa.

Esophageal Lacerations

The most common esophageal lacerations are **Mallory Weiss tears**, which are often induced by severe retching or vomiting. Normally, a reflex relaxation of the gastroesophageal musculature precedes the anti-peristaltic contractile wave associated with vomiting. This relaxation may fail during prolonged vomiting, with the result that refluxing gastric contents cause the esophageal wall to stretch and tear. Patients usually present with hematemesis.

The roughly linear lacerations of Mallory-Weiss syndrome are longitudinally oriented and usually cross the gastroesophageal junction (Fig. 2A). These superficial tears generally heal quickly without surgical intervention. By contrast, severe, transmural esophageal tears (Boerhaave

syndrome) result in mediastinitis, are catastrophic, and require prompt surgical intervention.

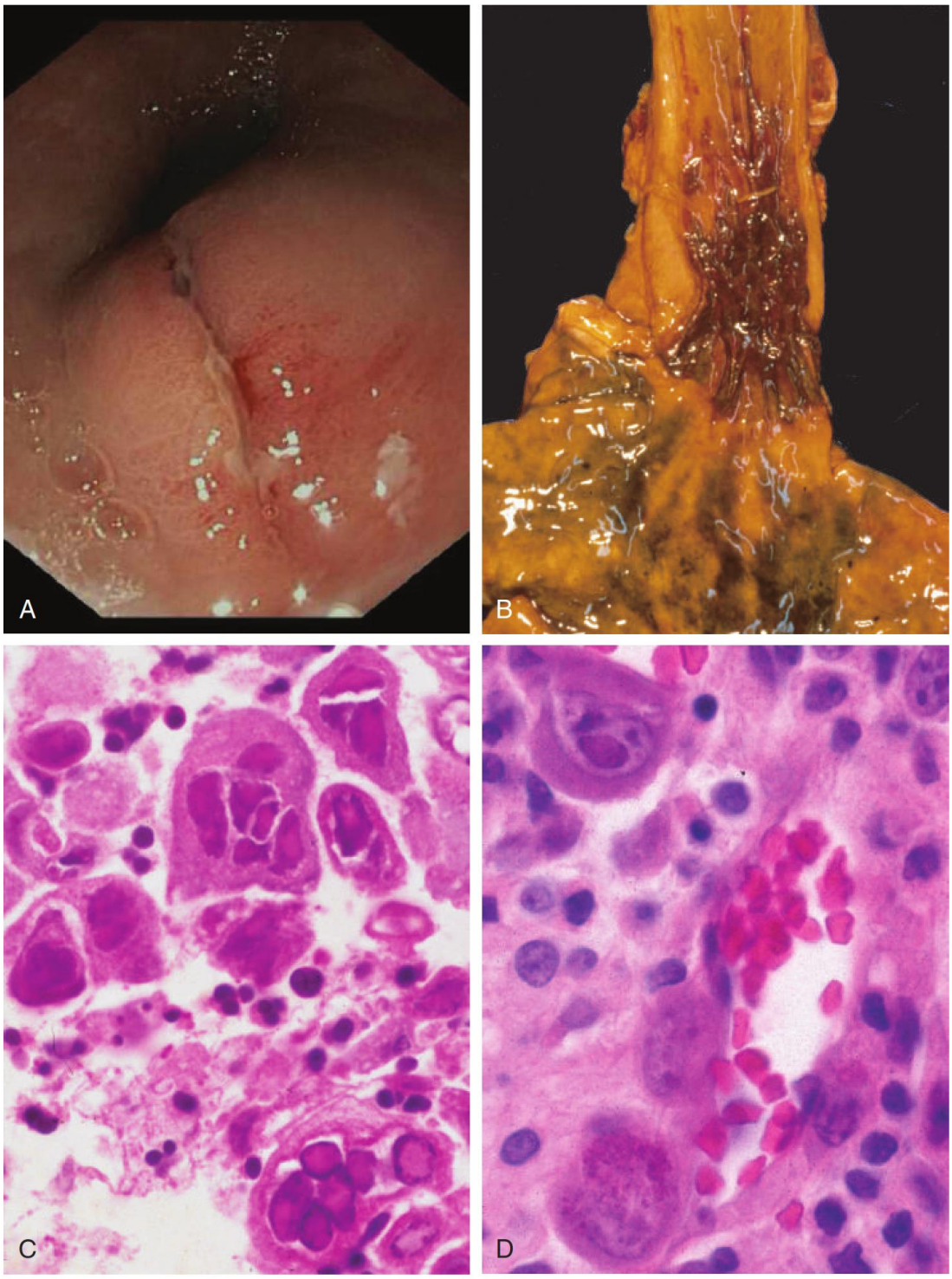

Fig. 2 Traumatic and viral esophagitis. (A) Endoscopic view of a longitudinally-oriented Mallory-Weiss tear. These superficial lacerations can range from millimeters to several centimeters in length. (B) Postmortem specimen with multiple herpetic ulcers in the distal esophagus. (C) Multinucleate squamous cells containing herpesvirus nuclear inclusions. (D) Cytomegalovirus-infected endothelial cells with nuclear and cytoplasmic inclusions.

ESOPHAGEAL TUMORS

Two morphologic variants account for a majority of esophageal cancers: adenocarcinoma and squamous cell carcinoma.

Worldwide, squamous cell carcinoma is more common, but adenocarcinoma is on the rise. Other rare tumors are not discussed here.

Adenocarcinoma

Esophageal adenocarcinoma typically arises in a background of Barrett esophagus and long-standing GERD. Risk for development of adenocarcinoma is greater in patients with documented dysplasia and in those who use tobacco, are obese, or who have had previous radiation therapy.

Morphology

Esophageal adenocarcinoma usually occurs in the distal third of the esophagus and may invade the adjacent gastric cardia (Fig. 3A). While early lesions may appear as flat or raised patches in otherwise intact mucosa, later tumors may form large exophytic masses, infiltrate diffusely, or ulcerate and invade deeply.

On microscopic examination, Barrett esophagus frequently is present adjacent to the tumor. Tumors typically produce mucin and form glands (Fig. 3B).

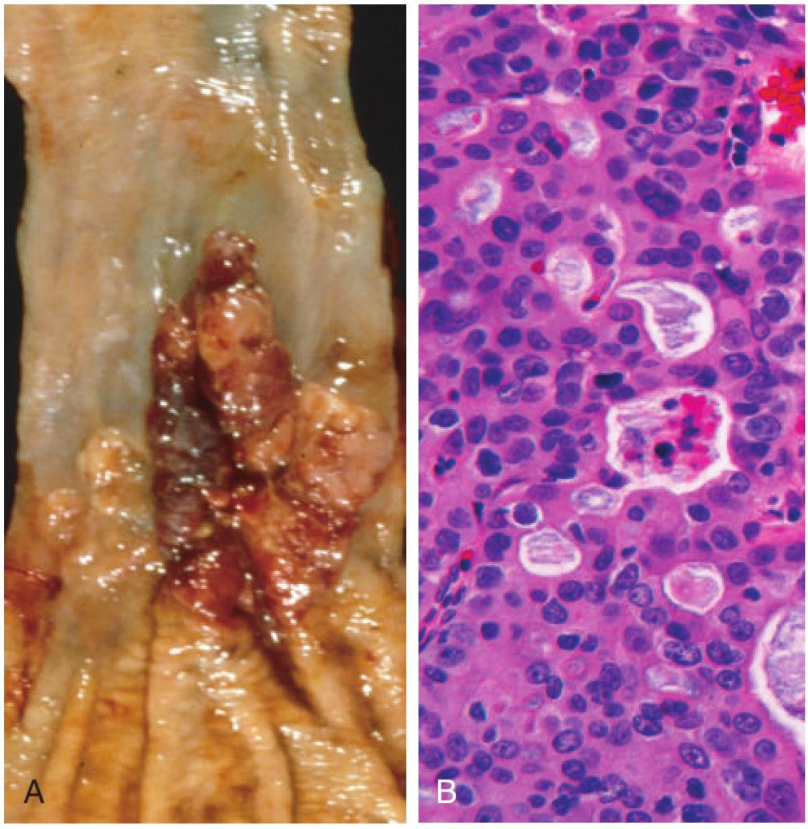

Fig.(3) Esophageal adenocarcinoma. (A) Adenocarcinoma usually occurs distally and, as in this case, often involves the gastric cardia.

(B) Esophageal adenocarcinoma growing as back-to-back glands.

Clinical Features

Patients most commonly present with pain or difficulty in swallowing, progressive weight loss, chest pain, or vomiting. By the time signs and symptoms appear, the tumor usually has invaded submucosal lymphatic vessels.

Squamous Cell Carcinoma

Risk factors include alcohol and tobacco use, poverty, caustic esophageal injury, achalasia, Plummer-Vinson syndrome, frequent

consumption of very hot beverages, and previous radiation therapy to the mediastinum.

Pathogenesis

A majority of esophageal squamous cell carcinomas are at least partially related to the use of alcohol and tobacco, the effects of which synergize to increase risk. Nutritional deficiencies, as well as exposure to polycyclic hydrocarbons, nitrosamines, and other mutagenic compounds, such as those found in fungus-contaminated foods, are suspected to be the risk factors. HPV infection also has been implicated in esophageal squamous cell carcinoma in high-risk but not in low-risk regions. The molecular pathogenesis of esophageal squamous cell carcinoma remains incompletely defined.

MORPHOLOGY

In contrast to the distal location of most adenocarcinomas, half of squamous cell carcinomas occur in the middle third of the esophagus (fig.4 **A**).

Squamous cell carcinoma begins as an in situ lesion in the form of squamous dysplasia. Early lesions appear as small, gray-white plaque like thickenings. Over months to years, they grow into tumor masses that may be polypoid and protrude into and obstruct the lumen. Other tumors are

either ulcerated or diffusely infiltrative lesions that spread within the esophageal wall, where they can cause thickening, rigidity and luminal narrowing.

These cancers may invade surrounding structures including the respiratory tree, causing catastrophic exsanguination; or the mediastinum and pericardium.

Most squamous cell carcinomas are moderately to well differentiate (**fig.4 B**).

Clinical Features

Clinical manifestations of squamous cell carcinoma of the esophagus begin insidiously and include dysphagia, odynophagia (pain on swallowing), and obstruction. As with other forms of esophageal obstruction, patients may unwittingly adjust to the progressively increasing obstruction by altering their diet from solid to liquid foods. Extreme weight loss and debilitation may occur as consequences of both impaired nutrition and tumor-associated cachexia. As with adenocarcinoma, hemorrhage and sepsis may accompany tumor ulceration. Occasionally, squamous cell carcinomas of the upper and mid esophagus present with symptoms caused by aspiration of food via a tracheoesophageal fistula.

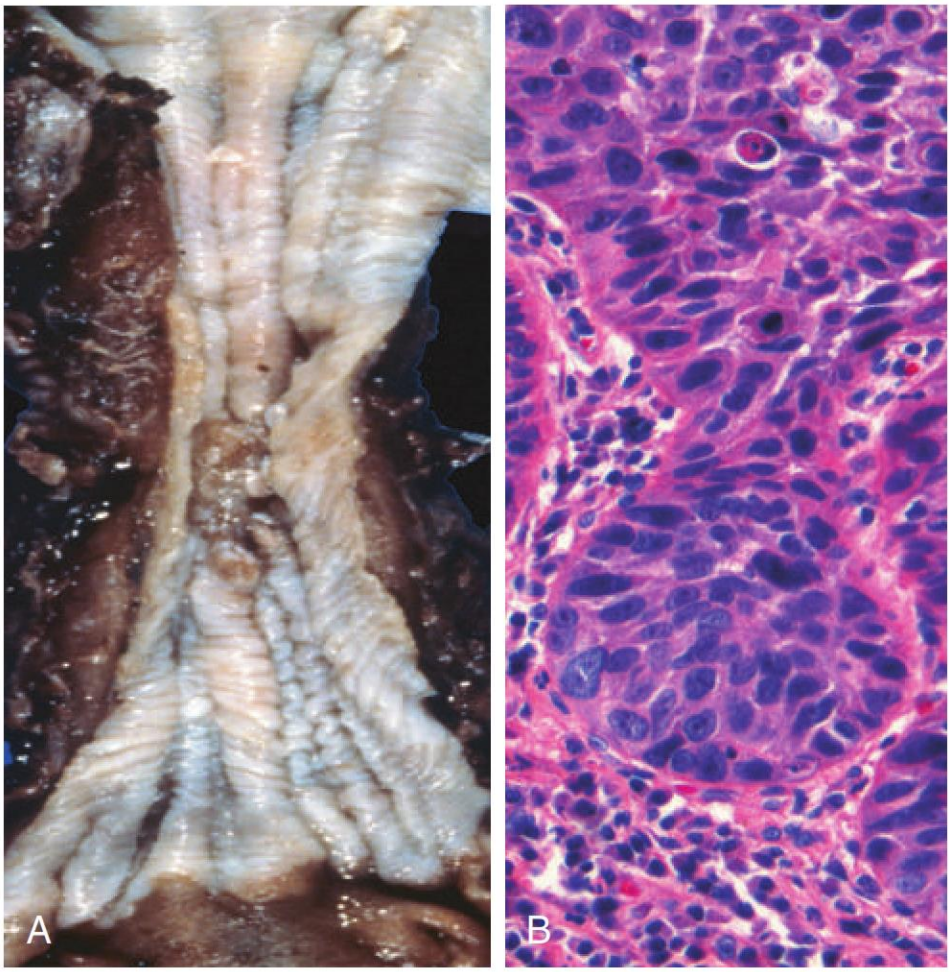
A
B

Fig. 4 Esophageal squamous cell carcinoma. (A) Squamous cell carcinoma most frequently is found in the mid-esophagus, where it commonly causes strictures. (B) Squamous cell carcinoma composed of nests of malignant cells that partially recapitulate the stratified organization of squamous epithelium.