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***PEPTIC ULCER DISEASE***

An ulcer is defined as "a breach in the mucosa of the alimentary tract that extends into the submucosa or deeper." Although they may occur anywhere in the alimentary tract, they are most common in the duodenum and stomach. Ulcers have to be distinguished from erosions. The latter is limited to the mucosa and does not extend into the submucosa.

Peptic Ulcers are chronic, most often solitary lesions and usually small. They occur in any portion of the GIT exposed to the aggressive action of acid-peptic juices.

The male-to-female ratio for duodenal ulcers is 3:1, and for gastric ulcers 2:1.

Women are most often affected at or after menopause.

Pathogenesis of peptic ulcers

-Peptic ulcers are produced by an imbalance between gastro-duodenal mucosal defenses and the damaging forces, particularly of gastric acid and pepsin.

- Hyperacidity is not necessary; only a minority of patients with duodenal ulcers has hyperacidity, and it is even less common in those with gastric ulcers.

-H. pylori infection is a major factor in the pathogenesis of peptic ulcer. It is present in virtually all patients with duodenal ulcers and in about 70% of those with gastric ulcers; that is why peptic ulcer disease is now considered infectious in nature. Antibiotic treatment of the infection promotes healing of ulcers and prevents their recurrence. The possible mechanisms by which this tiny organism impairs mucosal defenses include:

1. H. pylori induce intense inflammatory and immune responses. As a result there is increased production of pro-inflammatory cytokines, most notably, IL-8, by the mucosal epithelial cells. This recruits and activates neutrophils with their damaging properties.

2. Several bacterial products cause epithelial cell injury.

3. H. pylori enhance gastric acid secretion and impair duodenal bicarbonate production, thus reducing luminal pH in the duodenum with its damaging effects on the duodenal mucosa.

4. Thrombotic occlusion of surface capillaries is provoked by a bacterial platelet-activating factor. Thus, an additional ischemic element may contribute to the mucosal damage.

Most persons (80-90%) infected with H. pylori do not develop peptic ulcers. Perhaps there are unknown interactions between H. pylori and the mucosa that occur only in some individuals.

Other factors may act alone or in concert with H. pylori to encourage peptic ulceration:

1. Gastric hyperacidity: this when present, may be strongly ulcerogenic. The classic example is Zollinger-Ellison syndrome, in which there are multiple peptic ulcerations in the stomach, duodenum, and even jejunum. This is due to excess gastrin secretion by a gastrinoma and, hence, excess gastric acid production.

2. Chronic use of NSAIDs: this suppresses mucosal prostaglandin synthesis; aspirin also is a direct irritant.

3. Cigarette smoking: this impairs mucosal blood flow and healing of the ulcer.

4. Corticosteroids: these in high doses and with repeated use encourage ulcer formation.

5. Rapid gastric emptying: this is present in some patients with duodenal ulcers; this phenomenon exposes the duodenal mucosa to an excessive acid load & hence ulcerations

6. Patients with the following diseases are more prone to develop duodenal ulcer exposes

a. alcoholic cirrhosis

b. chronic obstructive pulmonary disease

c. chronic renal failure

d. hyperparathyroidism.

7. Personality and psychological stress seems to be important contributing factors.

Gross features

The classic peptic ulcer is a round to oval with sharply demarcated crater. The margins are usually level with the surrounding mucosa or only slightly elevated,2 to 4cm in diameter.

Microscopic features

In active ulcers four zones are recognized

1. The base and walls have a superficial thin layer of necrotic fibrinoid necrosis. 2. Beneath this layer is a zone of predominantly neutrophilic inflammatory infiltrate.

3. Deeper still, there is granulation tissue infiltrated with inflammatory cells.

This rests on

4. Fibrous or collagenous scar.

The complications of peptic ulcer disease are:

1-Bleeding is the most frequent complication (20%). It may be life-threatening; fatal in 25% of the affected patients. It may be the first warning of an ulcer.

2-Perforation is much less frequent (5% of patients) but much more serious being fatal in 60% of patients.

3-Obstruction (from edema or scarring) occurs in 2%, most often due to pyloric channel ulcers but may occur with duodenal ulcers. Total obstruction with intractable vomiting is rare.

4-Malignant transformation does not occur with duodenal ulcers and is extremely rare with gastric ulcers.

TUMORS OF THE STOMACH

These can be classified as benign and malignant lesions.

BENIGN TUMORS

-Gastric polyps

In the alimentary tract, the term polyp is applied to any nodule or mass that projects above the level of the surrounding mucosa. They are uncommon and classified as non-neoplastic or neoplastic.

-Hyperplastic polyps (the most frequent; 90%) are small, sessile and multiple in about 25% of cases. There is hyperplasia of the surface epithelium and cystically dilated glandular tissue.

-Adenomatous polyp (adenoma) (10% of polypoid lesions) They contain proliferative dysplastic epithelium and hence have malignant potential. They are usually single, and may grow up to 4 cm in size before detection. Up to 40% of gastric adenomas contain a focus of carcinoma; there may also be an adjacent

carcinoma that is why histologic examination of all gastric polyps is obligate

CANCERS OF THE STOMACH

Carcinoma is the most important and the most common (90%) of malignant tumors of the stomach. Next in order of frequency are lymphomas (5%); the rest of the tumors are even rarer e.g. carcinoids, and gastrointestinal stromal tumors (GISTs), leiomyosarcoma, and schwannoma.

IDIOPATHIC INFLAMMATORY BOWEL DISEASE (IBD)

The two disorders known as inflammatory bowel disease (IBD) are Crohn's disease (CD) and ulcerative colitis (UC). These diseases have distinctly different clinical and pathological features. Both CD and UC are chronic, relapsing inflammatory disorders of obscure origin. CD is an autoimmune disease that may affect any portion of the gastrointestinal tract from mouth to anus, but most often involves the distal small intestine and colon. UC is a chronic inflammatory disease limited to the rectum and colon. Both exhibit extra-intestinal inflammatory manifestations.

Etiology and Pathogenesis

In the normal GIT, the mucosal immune system is always ready to respond against ingested pathogens but is unresponsive to normal intestinal microflora.

The exact cause (s) leading to the above is still not established, hence the designation idiopathic. It is postulated that IBD result from exaggerated local immune responses to microflora in the gut, in genetically susceptible individuals.

Thus, the pathogenesis of IBD involves

1. Failure of immune regulation

2. Genetic susceptibility

3. Environmental triggers specifically microbial flora.

Crohn Disease

Pathological features

When fully developed, Crohn disease is characterized pathologically by

1. Sharply segmental and typically transmural involvement of the bowel by an inflammatory process with mucosal damage

2. The presence of

- Small noncaseating granulomas

- Deep fissures that may eventuate in the formation of fistulae

Clinical Features

The disease usually begins with intermittent attacks of diarrhea, fever, and abdominal pain, spaced by asymptomatic periods lasting for weeks to many months. In those with colonic involvement, occult or overt fecal blood loss may lead to anemia.

Extraintestinal manifestations of this disease include

1. Arthritis & finger clubbing

2. Red nodules of the skin

3. Primary sclerosing cholangitis.

4. Renal disorders

5. Systemic amyloidosis

6. An increased incidence of cancer of GIT in patients with long standing progressive CD.

ULCERATIVE COLITIS

In contradistinction to CD, ulcerative colitis is a chronic ulcero-inflammatory disease limited to the colon and affecting only the mucosa and submucosa; it extends in a continuous fashion proximally from the rectum. Well-formed granulomas are absent. However, like CD, UC is a systemic disorder associated in some patients with arthritis, uveitis, hepatic involvement (primary sclerosing cholangitis), and skin lesions. The onset of disease peaks between ages 20 and 25 years.

Microscopic features

- The basic mucosal alterations in UC are similar to those of colonic CD, with inflammation, chronic mucosal damage, and ulceration.

- There is diffuse, predominantly chronic inflammatory infiltrate in the lamina propria.

- Neutrophilic infiltration of the epithelial layer may produce crypt abscesses. The latter are not specific for UC and may be observed in CD or any active inflammatory colitis.

- Unlike CD, there are no granulomas.

-Destruction of the mucosa leads to broad-based ulcerations that are superficial

i.e. extending at most into the submucosa.

- Isolated islands of regenerating mucosa bulge upward to create pseudopolyps. - Features of chronic but healed (inactive) disease include submucosal fibrosis; mucosal architectural distortion and atrophy

Tumors of the Colon and Rectum

Non-neoplastic and benign neoplastic lesions of the colo-rectum are collectively known as polyps, which are common in the older adult population. Epithelial polyps that arise as the result of proliferation and dysplasia are termed adenomatous polyps (adenomas). They are precursors of carcinoma.

Hyperplastic Polyps

These are the most common polyps of the colon and rectum. They are small (usually <5 mm in diameter) and appear as smooth protrusions of the mucosa. They are often multiple and consists of well-formed glands and crypts lined by non-neoplastic epithelial cells.

Adenomas (Adenomatous polyps)

Adenomas are intraepithelial neoplasms that range from small, often pedunculated lesions to large neoplasms that are usually sessile. The prevalence of colonic adenomas increases progressively with age. Males and females are affected equally. .

All adenomas by definition arise as the result of dysplastic epithelial proliferation. The dysplasia ranges from low-grade to high-grade. There is strong evidence that adenomas are precursors for invasive colorectal adenocarcinomas.

COLORECTAL CARCINOMA

Most carcinomas arise from preexisting adenomas. A great majority (98%) of all cancers in the large intestine are adenocarcinomas. The peak incidence for colorectal cancer is 60 to 70 years of age; fewer than 20% of cases occur before the age of 50 years. .Both genetic and environmental influences contribute to the development of colorectal cancers. When colorectal cancer is found in a young person, preexisting ulcerative colitis or one of the polyposis syndromes must be suspected.

Tumors in the proximal colon tend to grow as polypoid, exophytic masses that extend along one wall of the capacious cecum and ascending colon .

Obstruction is uncommon .

All colon carcinomas are microscopically similar. Almost all are adenocarcinomas that range from well-differentiated to undifferentiated, frankly anaplastic masses. Many tumors produce mucin, which is secreted into the gland lumina or into the interstitium of the gut wall. Because these secretions dissect through the gut wall, they facilitate extension of the cancer and worsen the prognosis. Cancers of the anal zone are predominantly squamous cell in origin.