GIT Pathology

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The intestine

It is composed of the small and large intestine.
Histologically:

1- The small intestinal mucosa usually has a mucosal villi and crypts, lined by columnar cells with goblet cells.
2- The large intestine has a flat mucosa with numerous vertically oriented crypts.

CONGENITAL ANOMALIES

Anomalies of the intestine are rarely encountered; these include ***duplication*** of the small intestine or colon; ***malrotation*** of the entire bowel; ***omphalocele*** (birth of an infant with herniation of abdominal contents into a ventral membranous sac related to umbilicus); ***heterotopia*** of pancreatic tissue or gastric mucosa; ***atresia and stenosis; imperforate anus*** **(**due to failure of the cloacal diaphragm to rupture).

Meckel diverticulum

- Occur in **2%** of normal population
- It lies **2 feet** (85cm) from the ileocecal valve
- It measures about **2 inches**
- It results from **failure of obliteration** of the vitelline duct (which connects the lumen of the gut to the yolk sac), this will leave a solitary tubular diverticulum
- It is considered as a true diverticulum since it contains the three layers of normal bowel mucosa.
- Sometimes there is **heterotopic** gastric mucosa that functions as the stomach, so peptic ulcer might develop in the adjacent intestinal mucosa which may cause complications.
- **Complications:**

1- Diverticulitis
2- Intestinal obstruction
3- Complication of peptic ulcer (bleeding, perforation, peritonitis)

Congenital aganglionic megacolon (Hirschsprung disease)

This disorder characterized by:

- Absence of ganglionic cells in a segment of large bowel that become constricted leading to functional obstruction and progressive colonic dilation proximal to the affected segment.

Morphologically:

1- **Absence** of ganglion cells in the muscle wall (Auerbach plexus) and from the submucosa (Meissner plexus) in the affected segment.
2- Progressive dilation and hypertrophy of the colon proximal to that segment.

Clinical features:

1- It is noticed in the immediate neonatal period by failure to initially pass meconium.
2- Constipation

3- Abdominal distension

Complications:

* Enterocolitis with water and electrolyte imbalance
* Perforation of the colon with superadded peritonitis

INTESTINAL OBSTRUCTION

The small intestine is most often involved due to its narrow lumen. Tumors and infarction, although the most serious, account for only up to 20% of small bowel obstructions. The remaining 80% are due to:

1. Hernias
2. Intestinal adhesion
3. Intussusception
4. Volvulus

The clinical manifestations include abdominal pain and distention, vomiting, constipation, and in complete obstruction failure to pass flatus.

Hernias

- Any weakness or defect in the wall of the peritoneal cavity may permit protrusion of a serosa -lined pouch of peritoneum (hernial sac). The usual sites of such weakness are at the:

1. Inguinal canal 2. Femoral canal 3. Umbilicus 4. In surgical scars

- Pressure at the neck of the pouch may impair venous drainage of the entrapped viscus , in severe cases both arterial & venous blood supply lead to strangulation &infarction

Adhesions

Surgical procedures, infection, or other causes of peritoneal inflammation, such as endometriosis, may result in development of adhesion, these fibrous bridges can create closed loops through which other viscera may slide and become entrapped

Volvulus

Complete twisting of a loop of bowel about its mesenteric base of attachment, occurs most often in large redundant loops of sigmoid colon, followed in frequency by the cecum and small intestine.

Intussusception

This occurs when a segment of the intestine, constricted by a wave of peristalsis, telescopes into the immediately distal segment.

In infant & young children there is usually no underlying anatomic lesion or defect in the bowl, but some cases of intussusception are associated with rotavirus infection, suggesting that localized intestinal inflammation may serve as a traction point for the intussusception.

However, intussusception in adults signifies an intraluminal mass or tumor as a point of traction.

Malabsorption

- Is characterized by decrease absorption of fat, fat soluble and other vitamins, proteins, carbohydrates, electrolyte and minerals and water.
- Malabsorption results from disturbance in at least one of the four phases of nutrient absorption:

1- **Intraluminal digestion**: assisted by enzymes present in saliva, gastric juice, bile acids (salts) and pancreatic enzymes.
2- **Terminal digestion**: by the presence of special enzymes on the small intestinal brush boarder.
3- **Transepithelial transport** (absorption): where the nutrients cross the epithelium of the small intestine to reach the vascular element of the small intestine.
4- **Lymphatic transport** of absorbed lipids

Clinical features:

There is a wide range of presentations

1- Hallmark of malabsorption is steatorrhea, characterized by excessive fecal fat and bulky, frothy, greasy, yellow or clay-colored stools.
2- Anorexia (loss of appetite)
3- Anemia (iron deficiency or megaloblastic)
4- Edema and ascites
5- Signs of vit. deficiency e.g hypocalcemia (def. of vit D)

Classification:

1. Defective intraluminal digestion

- Pancreatic insufficiency Primarily from chronic pancreatitis or cystic fibrosis, is a major cause of defective intraluminal digestion that leads to diarrhea and steatorrhea.

2. Defective terminal digestion

- **Disaccharidase deficiency (lactose intolerance)**

In which there is a deficiency of the enzyme **lactase** which is normally present on the apical cells of the villous epithelium. This deficiency is usually acquired.
This will lead to inability to break down the lactose into simple monosaccharides (glucose and galactose).
This will lead to osmotic diarrhea and malabsorption.

3. Defective transepithelial transport

- **Abetalipoproteinemia**

  It is a rare A.R inborn error of metabolism characterized by absence of apoprotein B. This will lead to accumulation of triglyceride in the epithelial cell, since this lipoprotein is essential for mobilization of T.G from the epithelium to the circulation.
  And the fat will appear as vacuoles inside the epithelial cells

- **Gluten-sensitive enteropathy (celiac disease)**

- Is an autoimmune enteropathy
- Triggered by the ingestion of gluten-containing foods, such as wheat, rye, or barley, in genetically predisposed individuals.
- Characterized by mucosal lesion of the small intestine with impaired absorption that usually improves on withdrawal of gliadin which is a component of gluten.

Pathogenesis:

- Gluten that contain Gliadin (in wheat, barley and rye) act as a foreign substance in those individuals which lead to accumulation of CD8+ (cytotoxic T cells) on the

surface of the small intestinal mucosa, this will cause an inflammatory reaction that damages the intestinal epithelium leading to villous atrophy…malabsorption.

- The patients have antigliadin Ab (antibodies against tissue transglutaminase and endomysium) which is diagnostic.
- There is strong genetic association exists between celiac disease and HLA haplotypes DQ2 and DQ8.

Microscopically:

1-Partial or complete villous atrophy.

2-Increase intraepithelial lymphocytes and lymphocyte and plasma cell infiltration of the lamina propria.

3- Crypt hyperplasia

Clinical features*:*

At childhood, the patient presented with:

- diarrhea
- weight loss
- growth retardation
- anemia

Complication:

Malignant transformation in 10-15%, the most common is lymphoma, adenocarcinoma

Tropical sprue (Environmental Enteropathy)

- Is a celiac like disease, it is malabsorption due to intestinal infection but no causative agent identified. It has a certain world distribution (Caribbean), South Africa….etc.

***Microscopically*:**

- Partial villous atrophy

Clinical features:

- The patient presented with acute diarrhea following a visit to those areas

Treatment:

- Broad spectrum antibiotic supporting the infectious nature

4. Defective lymphatic transport of absorbed lipids; Lymphatic Obstruction

- Lymphoma
- Tuberculosis and tuberculous lymphadenitis
- ***Whipple disease***
- A rare systemic disease, may involve any organ in the body

Causative agent: Gram +ve actinomycete (rod shape bacilli) ***(Tropheryma whippelii)***

Clinical features:

Diarrhea with other organ involvement like CNS and joints.

Microscopically:

The villi of the small intestine are filled with macrophages containing PAS +ve granules and rod shape bacilli under electron mic.

Iatrogenic causes of malabsorption:

- Subtotal or total gastrectomy
- Short-gut syndrome, following extensive surgical resection
- Distal ileal resection

INFECTIOUS ENTEROCOLITIS

Enterocolitis can present with a broad range of symptoms including diarrhea, abdominal pain, urgency, perianal discomfort, incontinence, and hemorrhage. This global problem is responsible for over 1 million deaths each year. Half of the mortality occurs in children

under the age of 5, in whom diarrheal disease is the fourth most common cause of death worldwide.

Viral enterocolitis

The lesions caused by enteric viruses in the intestinal tract are similar. The small intestinal mucosa shows partial villous atrophy (shortening of the villi) with infiltration of the lamina propria by lymphocytes. However, in infants, **rotavirus and adenoviruses** can produce total villous atrophy (flat mucosa), thus resembling celiac disease.

Bacterial enterocolitis

- Salmonellosis and Typhoid Fever
- Campylobacter Enterocolitis
- Cholera
- Antibiotic-Associated Colitis (Pseudomembranous Colitis)
- Tuberculous enteritis

Parasitic enterocolitis:

- Ascaris lumbricoides
- Strongyloides
- Hookworm (*Necator duodenale* and *Ancylostoma duodenale*) infection
- Enterobius vermicularis (pinworms)
- Amebiasis
- Giardiasis

Amebiasis:

Cause: Entamoeba histolytica.

Site: 1- The colon which manifest as amoebic dysentery.

2-Extraintestinal which manifest itself as liver and lung abscesses.

Morphologically:

The characteristic lesion in the colon is the **flask shape ulcer** caused by the trophozoite.

Mic.: Mucosal necrosis, invasion of the submucosa &spread laterally.

Giardiasis

Caused by Giardia Lamblia.

Route of infection: Contaminated food and water by giardia cyst.

Site: Duodenum & small intestine.

The cyst will hatch into a trophozoite that adheres to the mucosal surface without penetrating it.

Mic.:

- Villous atrophy
- Chronic inflammatory cells infiltrating the area (lymphocytes and plasma cells)
- Trophozoite can be detected near the mucosal surface.

Clinically: most patients are Asymptomatic, 10% develop chronic diarrhea.

Diagnosis: GSE to detect the cyst.

Intestinal biopsy to detect the trophozoite.

Idiopathic Inflammatory Bowel Diseases

Two inflammatory disorders of unknown cause affect the GIT, namely, **Crohn** disease and **ulcerative colitis.** They share many common features and are collectively known as **inflammatory bowel disease.**
And since the actual, real cause remains unexplained thus they are termed idiopathic.

Pathogenesis:
These two diseases share partly or totally the same pathogenesis. many theories shared in this explanation.

1- Genetic predisposition:

- High incidence in first degree relatives (3-20 times).
- Associated with HLA –class II gene located on chromosome (6).
- Other gene association e.g mutated NOD2 which is important in host response to bacteria

2- Infectious cause:

Specially unidentified m.o e.g viruses, Chlamydia, atypical bacteria

3- Abnormal host immunoreactivity:

Inappropriate exposure to luminal antigens →the mucosal immunity is stimulated and then→ fail to down-regulate. Also the presence of plasma cells indicates the immune mediated mechanism.

The fact that immunosuppressive drugs, e.g corticosteroids improve the symptoms supports the immune mediated nature.

4- Inflammation:

Activation of inflammatory cells which cause non-specific tissue injury.

Crohns disease

Is a chronic relapsing inflammatory disease, it is common in the western countries, can occur at any age (peak in the 20s) &affect the whites more than black and females more than males. Smoking was found to be a strong risk factor. It is characterized by the followings:

1. It can involve **any part of the GIT** (mouth, esophagus, duodenum,……anus). But most commonly it affects the small intestine 40% specially the terminal ileum hence the term (terminal ileitis), colon 30%.
2. 25% of patients have **extra intestinal manifestations.**
3. It affects the whole wall thickness of the affected part (**transmural involvement**) with its surrounding mesentery and s.t lymph nodes. Thus, the wall will get thick and rubbery.
4. The mucosa first shows an aphthous like superficial ulcer, when it unites it will form a serpentine linear ulcer, and if it extends deep it will form **fissures** which are a longitudinal ulcer, that if extend through the wall it will lead to fistula formation.
5. It is characterized by **skip lesions** which mean there is a sharp demarcation between the normal unaffected areas and those with diseased mucosa.
6. **Cobblestone** appearance is the result of fissures surrounding an edematous mucosa.
7. Mic:

   * There is transmural infiltration by lymphocyte, plasma cells.

   * **Non caseating granuloma** presents in 50% of cases at any site from the mucosa to the surrounding structure and even lymph nodes.

Clinical features:

1. Abdominal pain.
2. Recurrent diarrhea.
3. Generalized malabsorption
4. Extraintestinal manifestations e.g clubbing of the fingers, sacroiliitis, ankylosing spondylitis
5. Complications which are:
    - Intestinal obstruction
    - Perforation of deep fissures
    - Fistula with the bladder, colon, abdominal wall
    - Carcinoma but less frequent than ulcerative colitis.

Ulcerative colitis

* Is a chronic disease with remission and relapse presented with bloody diarrhea with abdominal cramps s.t fever and weight loss
* More in whites than blacks.
* No sex predilection.
* The onset of the disease is usually at 2^{nd} -3^{rd} decades.
* The pathogenesis is still unknown as with Crohn's dis. but it results from many **environmental** factors that lead to **loss of tolerance** of the mucosa for normal flora in genetically susceptible individuals.

It is characterized by:

1- It involves **only the colon** hence the name "colitis"
2- The involvement is **continuous** (not skip) starting from the rectum and ascend upwards in a continuous way till it reaches the ileum (s.t. it involves the distal ileum where it is called backwash ileitis)
3- It involves the **mucosa and submucosa** only (not trasmural)
4- The ulcer is **superficial** and never forms (fissures)
5- There is no cobblestone appearance instead there is inflamed hyperemic mucosa with islands of regenerating mucosal cells forming the **pseudopolyps**

Mic:

* congested mucosa.
* Acute and chronic inflammatory cell infiltration of the lamina propria
* Crypt abscess (collection of neutrophils in the glandular lumen)
* There is goblet cell depletion
*** No granuloma**

Complications:

1- massive hemorrhage (bleeding per rectum)
2- perianal and ischiorectal abcesses
3- colorectal carcinoma cause by continuous regeneration → dysplasia→carcinoma