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Intestinal pathology

General

- The wall of the small intestine is thinner than the large intestine
- The lumen of the small intestine is narrower than of the large intestine

Diseases of the intestines

1 ▶️ Intestinal obstruction
2▶️ Vascular disorders (hemorrhoids)
3▶️ Malabsorptive diseases (small intestine is the main site for nutrients absorption)
4▶️ Inflammatory bowel disease.
5▶️ Polyps and neoplastic diseases

1 Intestinal obstruction

In older patients
- ▶️ Tumors.
- ▶️ Diverticulitis
- ▶️ Infarction

80% of Mechanical obstruction:

- ▶️ Intussusception ((Usually seen in children))
- ▶️ Hernias.((complicated by infarction of these bowel segments / it's a complication of a previous inflammatory condition or after surgical procedures))
- ▶️ Adhesions((.between bowel segments
- ▶️ Volvulus (torsion)

We will talk about Intussusception

▶️ Segment of the intestine constricted by a wave of peristalsis, telescopes into the immediately distal segment.
▶️ Once trapped, invaginated segment is propelled by peristalsis, and pulls mesentery with it.
▶️ Most common cause of intestinal obstruction in children younger than 2years of age
▶️ Untreated progresses to infarction.

Causes of intussusception▶️ < 2years : Idiopathic in most cases
▶️ Peyer patches hyperplasia (rotavirus vaccine (rotavirus is responsible for the most cases of viral gastroenteritis in childhood) , viral infections)
▶️ Meckles diverticulum (ileum) (congenital)
▶️ Old children & adults: Intraluminal mass or tumors (intussusception is not common at that age group)

Clinical features:
■child (especially <2)
▶️ Abdominal swelling and distention
▶️ Vomiting
▶️ Passing stools mixed with blood and mucus (currant jelly stool)
▶️ Pain((in children 》crying and grunting))

Management
Depends on the degree or the stage of the disease
▶️ if it is early➡️ Contrast enemas
▶️ Surgery if complicated (infarction)or if masses are the leading point.

▶️ Non-mechanical obstruction (functional)

- ▶️ Hurschsprung disease
- ▶️ Neurological disorders.
- ▶️ Drugs….etc

We will talk about Hirschsprung Disease

▶️ Congenital defect in colonic innervations (intrinsic nervous system)
▶️ Congenital aganglionic megacolon (no ganglion cells+enlarged and dilated colon)
▶️ More common in males ▶️ More severe in females ▶️ Risk increase in siblings.

▶️ Typical presentation:
*Neonatal failure to pass meconium+*Obstructive constipation.(number of bowel motions per day is decreased or consistency of stool is different
Note:If we exclude organic causes of obstruction, we think about functional obstruction like hirschsprung disease

Pathogenesis
▶️ During embryogenesis
▶️ Disrupted migration of neural crest cells from cecum to rectum
[The disease affects the rectum almost all the cases however the length of the affected segment is different between patients]
▶️ Lack of Meissner submucosal plexus and the Auerbach myenteric plexus.
▶️ Failure of coordinated peristaltic contractions.(results in constipation)
▶️ Mutations in RET: in familial cases and 15% of sporadic
▶️ Other genes and environmental factors play role.

Morphology
▶️ Rectum always involved. ▶️ Extent is variable. ▶️ Most cases in rectosigmoid.
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*Macroscopic
▶️ Aganglionic region normal or contracted (lacks innervation)
▶️ Proximal normal segment progressively dilated.(normal innervated)
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* Diagnostic workup:
▶️barium enema(will help us in the typical characteristic feature of contracted aganglionic segment and a dilated normally innervated segment)
▶️BIOPSY (gold standard/ rectal full thickness biopsy is used examine multiple deeper levels from the rectal biopsy to be sure that there are no ganglion cells/not easy
▶️microscopic.
Note : ganglion cells have abundant cytoplasm with eccentrically located nucleus with prominent nucleolus

Complications
▶️ Enterocolitis (because we have stasis of stool in the bowel)
▶️ Fluid and electrolyte disturbances (dehydration)
▶️ Perforation ▶️ Peritonitis
Treatment:
▶️ Surgical resection of aganglionic segment and anastomosis
Of normal segments(.patients need time to adjust the new situation)

Clinical picture of intestinal obstruction.

((common site for intestinal obstruction is usually the small bowel))
▶️ Abdominal pain ▶️ Distention (due to gaseous distention)
▶️ Vomiting ▶️ Constipation.
▶️ Acute (intussusception or volvulus or infarction)
▶️chronic(hurschsprung disease or tumors)

2 VASCULAR DISORDERS OF BOWEL

- Ischemic Bowel Disease (usually it's seen in elderly)
- Hemorrhoids

▶️ Dilated anal and perianal collateral vessels that connect the portal and caval venous systems.

Predisposing factors:
▶️ Constipation and straining (will increase the intraluminal pressure within the rectum)
▶️ Venous stasis of pregnancy,▶️ Portal hypertension(like liver cirrhosis)
▶️ External and internal hemorrhoids (according to the location, if it below the anorectal line it's called external and if above in the rectal mucosa it's internal)
▶️Thin -walled, dilated, submucosal vessels beneath anal or rectal mucosa.
(Place the vessels under the risk of rupture and bleeding)

Symptoms:
▶️ Bleeding (usually the blood is fresh colored) pain, thrombosis andinflammation

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DIARRHEAL DISEASE
- Diarrhea: increase in stool mass, frequency or fluidity
- Dysentery: painful , bloody, small volume diarrhea

General

A ● Malabsorptive Diarrhea due :
- Pancreatic insuffciency. (Due to lack in pancreatic enzymes)
- Celiac disease (inflammatory bowel diseases /affects the small bowel and the terminal ilium [the site for absorption of many nutrients especially b12 , proteins and albumin and bile salts])
- Cystic Fibrosis (genetic mutation) ▶ Lactase (Disaccharidase) Deficiency
- Abetalipoproteinemia

B ●Infectious Enterocolitis (or infectious diarrhea)
C ●Inflammatory bowel diseases

A● Malabsorptive Diarrhea

- Chronic.
- Defective absorption of fats, fat- and water-soluble vitamins, proteins, carbohydrates, electrolytes, minerals and water
- Hallmark is : steatorrhea. (is the greasy fatty bulky yellow or clay colored stool

Defect in one of the following:
- Intraluminal digestion.(of the large substances like fats/ main enzymes deficiencies like pancreatic deficiency)
- Terminal digestion.(the digestion of the end products of the carbohydrates and proteins/ deficiency of some disaccharidases and peptidases which are usually seen at the brush border
- Transepithelial transport.(transport of nutrients through the epithelial cells to the other (vascular) side)
- Lymphatic transport.(of the absorbed lipids)

Manifestations:
- Weight loss (due to lack of absorption of proteins,carbohydrates and fats), anorexia,
- Flatus, abdominal distention (lack of absorption of disaccharides or carbohydrates cause their fermentation)
- Borborygmi (sounds of the stomach and the intestines due to the presence of gas+ Muscle wasting
- Anemia and mucositis (iron, pyridoxine (VB6), folate, or vitamin B12 deficiency) (mucositis is the inflammation of the mucous membrane at the angle of the mouth)
- Bleeding (vitamin K deficiency) (vitamin K is fat soluble) (because vitamin K is needed for thrombotic cascade)
- Osteopenia (and osteoporosis a t e a r l y a g e) and tetany (calcium, magnesium, or vitamin D deficiency)
- Neuropathy (vitamin A or B12 deficiency)
- Skin and endocrine disorders(malabsorption of iodine can result in thyroid hormone deficiency)

1 Cystic Fibrosis

- Mutations in cystic fibrosis transmembrane conductance regulator (CFTR)
- Defects in ion transport across intestinal and pancreatic epithelium.
- thick viscous secretions. Due to defect in ion transport defect in transport of sodium ions across these membranes , water will not follow sodium and secretion from pancreas will be highly viscous and thick which will cause mucus plugs)
- Mucus plugs in pancreatic ducts >>> pancreatic insufficiency (80% of patients).(causing blockage of the ducts and the pancreatic enzymes will not reach the intestine)
- Defect in intraluminal digestion. (The end result will be malabsorptive diarrhea)

2Celiac Disease

- Gluten sensitive enteropathy
- Immune mediated enteropathy ▶ Wheat, rye or barley.
- Genetically predisposition, HLA-DQ2 or HLA-DQ8.
- Treatment: gluten free diet.(it's difficult to follow up)
- Association with: type 1 diabetes, thyroiditis, and Sjogren syndrome

Pathogenesis
- Gluten >>> gliadin >>> react with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells >>> CD4+ T cells activation >>> cytokines >>> tissue damage.

- Serology: (it's still unknown if they are the result or the cause of the disease but they are elevated in these patients):
Anti- tissue transglutaminase antibodies+
Anti-gliadin antibodies.+ Anti -endomysial antibodies

Explain for first point
*Normally gluten is digested into gliadin in the bowel, this gliadin is deaminated by an enzyme called tissue trans glutaminase TTG , and the deaminated gliadin will enter into the lamina propria of the small intestine, if the patient is inheriting HLA-DQ2 and HLADQ8 and presented on the antigen presenting cells in the lamina propria of the intestine there will be activation of antigen presenting cells with activation of T helper cells which will activate an inflammatory reaction and production of cytokines and inflammatory mediators which leads to tissue damage (the tissue damage mainly is the loss of villus architecture which is important for increasing the surface area for absorption of nutrients and conversion into flat mucosa)

MORPHOLOGY
- Second portion of the duodenum or proximal jejunum (we take a biopsy from the second part of the duodenum)
- Triad: intraepithelial lymphocytosis (CD8+ T cells) , crypt hyperplasia (as a result of damage so there is increase in the turn over of the epithelium),and villous atrophy (most important feature which can be total in severe cases or subtotal or partial or villus shortening
- Lamina propria: lymphocytes(mainly t helper cells), plasma cells, eosinophils…….
- IEL & villous atrophy are not pathognomonic, seen in viral enteritis.
- Diagnosis: Clinical, histologic and endoscopic and serologic correlation

Clinical Features
- Children 6-24 months : classical or non classical symptoms (as well as adults)

A) Classical: Irritability, abdominal distention, anorexia, diarrhea, failure to thrive, weight loss, or muscle wasting
B) Non-classical: abdominal pain, nausea, vomiting, bloating, or constipation.
- Blistering skin lesion,(blisters , skin rash that is itchy , looks like herpes simplex virus) dermatitis herpetiformis, in 10% of Pnts.
- Adults (30-60 years)
- Anemia: iron deficiency (because duodenum and proximal jejunum are the main sites for iron absorption
- B12 and folate deficiency: less common.
- abdominal distention, weight loss , muscle wasting , Diarrhea , bloating, and fatigue.(fatigue is duo to iron deficiency)
- Missed diagnosis:

A)Silent celiac [we have a histological diagnosis and serological diagnosis However the patient is asymptomatic]
B)latent celiac.(the patient has positive serology but histology is normal and symptoms are absent)
- Increased risk of enteropathy associated T cell lymphoma & Small intestinal adenocarcinoma

Diagnosis:
■Non invasive serologic tests:
- Most sensitive:

-Anti tissue transglutaminase antibody, IgA in the blood
-Anti deamidated gliadin antibodies, IgA & IgG
- Most specific, but less sensitive :Antiendomysial antibody. (not in all cases) So the best thing is to do all of these antibodies tests or starting from the most sensitive then the most specific , if thy are positive then we do endoscopy and take biopsy and preferably multiple biopsies because disease can be sometimes focal , and we can follow up the response for the gluten free diet

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■Invasive tests: small bowel biopsy.

Note:the patient comes to you complaining of an unexplained iron deficiency anemia in adults or a baby not gaining weight so you start with the diagnostic modalities

3 Lactase (Disaccharidase) Deficiency

- Osmotic diarrhea
- Lactose remains in the gut lumen
- Lactase found at apical brush border membrane
- Normal biopsy findings. (brush border enzymes deficiency))

- Two types:
- Congenital : AR(autosomal recessive), genetic mutation, rare, explosive diarrhea, watery, frothy stools & abdominal distention, after milk ingestion
- Acquired : follow viral or bacterial enteritis /downregulation of gene (due to decrease ingestion of milk) , after childhood.(more common)

4 Abetalipoproteinemia

- No beta lipoproteins in the body which is synthesized by the reaction between the lipids and proteins
- Autosomal recessive, rare.
- Infants w/ failure to thrive, diarrhea, and steatorrhea
- Lack of absorption of fat and fat soluble vitamins
- Inability to synthesize triglyceride-rich lipoproteins.
- Transepithelial transport defect of TG and FAs.
- Monoglycerides and triglycerides accumulate in epithelial cells(can't enter the blood).

microscopic findings
-taking a biopsy from the small bowel
-The cells have clear cytoplasm(whitish) and this indicates the accumulation of fat and lipids

سوف تتحدث عن ما يرتبط بها من امراض