Lecture 4[2hrs]

TROPICAL SPRUE

Tropical sprue is defined as chronic, progressive Malabsorption in a patient in the tropics associated with abnormalities of small intestinal structure and function.

Pathology

The changes resemble those of coeliac disease.

Etiology is not known because tropical sprue responds to antibiotics the tropical sprue may be caused by one or more infectious agents. Small bowel overgrowth with Klebsiella Enterobacter or E. coli is frequently seen.

Clinical features

*diarrhea, abdominal distension, anorexia, fatigue, and weight loss.
*The onset of diarrhea may be sudden and accompanied by fever.
*Megaloblastic anemia from folic acid Malabsorption, edema, glossitis, and stomatitis may occur.

Treatment

*Tetracycline 250mg 6-hourly for 28 days is the treatment of choice.
*Folic acid 5mg three times daily for 2 months.

Whipple's Disease

Whipple's disease is a chronic systemic infection caused by gram-positive bacteria Tropheryma whippelli. only humans are affected by the disease. the small intestine is the most affected organ. from the intestinal mucosa, bacteria are spread via lymphatic's into mesenteric and Mediastinal lymph nodes and into the systemic circulation affecting other organs like joints, cardiovascular system, and central nervous system.

Clinical features.

The onset is insidious, more common in middle age men, Presentation depends on the pattern of organ involvement.

Gastrointestinal

both small-intestinal mucosal injury and lymphatic obstruction causing
*Malabsorption
*Abdominal pain, weight loss, protein-losing Enteropathy, Ascites, hepato-splenomegaly skin pigmentation, finger clubbing, and fever

Central nervous system symptoms include

*Apathy, fits, myoclonus, Meningitis, Cranial nerve lesion, and Dementia.

Pulmonary

*Chronic cough, pleurisy, pulmonary infiltrate.

Hematological. *Anemia, lymphadenopathy**.**

Cardiac

*Pericarditis, myocarditis, endocarditis, and coronary arteritis.

Joint *Seronegative large-joint arthropathy,

Diagnosis

*Suggested by a multisystem disease associated with diarrhea and Steatorrhea.
*OGD and duodenal biopsies. The mucosa has whitish to yellow patches [reflect lipid deposits or lymphangectasia].

Histologic examination shows -blunted villi that are distended by a dense accumulation of PAS-positive macrophage.

Bacteria whippelli also can be isolated from pleural fluid, peripheral mononuclear cells by PCR

Treatment

*Penicillin [6-24million] +Streptomycin [1gr IM] or ceftriaxone [2grIV] for 10-14 days.
Followed by Trimethoprim/Sulfamethoxazole [160/800mg po bid] for 1 year

Lymphatic disorders

Intestinal Lymphangiectasia

Obstruction of intestinal lymphatic vessels causes dilatation of lymphatic's [lymphangectasia] and loss of protein and fat-rich lymph into the gastrointestinal lumen.
This condition maybe
*Primary resulting from congenital malunion of lymphatic's.
*Secondary to lymphatic obstruction due to [lymphoma, TB, Whipple's disease, filariasis, constrictive pericarditis, mesenteric TB, retroperitoneal fibrosis].

Pathogenesis

Obstruction of lymphatic drainage from the intestine causes dilatation of the lymphatics and loss of fat and protein in the stool.

Presentation

*Peripheral edema.*Pleural effusions or chylous Ascites*Steatorrhea.

Investigations

*Hypoalbuminemia, lymphocytopenia, and reduced serum immunoglobulin concentrations.
*Endoscopy of the small intestine – the mucosa of distal duodenum and jejunum mucosa has whitish to yellow patches [reflect lymphangectasia].
*biopsies show dilated lacteals.*Lymphangiography shows lymphatic obstruction.

Treatment

***Treatment of the cause**

*Low-fat diet. With fat-soluble vitamins.

Specific absorptive defects

Abetalipoproteinemia

Pathogenesis

The lack of beta-lipoproteins results in an accumulation of fat within the enterocyte and consequent fat malabsorption. Because lipoproteins are necessary for the formation of apoprotein that combines with triglycerides, cholesterol, and phospholipids within the intestinal absorptive cells to form chylomicrons.

Diagnosis

*Stool fat increased.
*D-xylose tolerance and small bowel D-Xylose are normal.
*Serum cholesterol and triglycerides are low and lipoprotein is absent.
*Biopsy shows small bowel villous epithelial cells are distended with fat.

Treatment

*Medium-chain triglycerides which do not require chylomicron formation for absorption but rather absorbed directly in the blood*fat soluble vitamins

Lactose intolerance

Disaccharide lactose is usually digested by brush border enzyme lactase prior to absorption to glucose and galactose. Undigested lactose enters the colon, where bacterial fermentation produces short-chain fatty acids, hydrogen, and carbon dioxide.
Lactose intolerance Maybe
*Primary lactase deficiency in which jejunal morphology is normal,
*Secondary' occurs as a consequence of disorders which damage the jejunal mucosa
Like [Coeliac disease, viral gastroenteritis, giardiasis, Crohn's disease].

Clinical features

Undigested lactose enters the colon, it becomes a substrate For colonic bacterial fermentation, causing osmotic Diarrhea, flatulence, abdominal pain, and borborygmi after eating milk product.

Diagnosis

*Suggested by clinical improvement on lactose withdrawal.
* lactose hydrogen breath test.

Treatment

*Dietary exclusion of lactose.
*Addition of commercial lactase preparations to milk may be effective.

Bacterial Overgrowth Syndrome

[Stagnant bowel syndrome or blind loop syndrome]

Small intestinal bacterial overgrowth (SIBO) occurs rarely in the healthy population. Bacterial contamination of the small intestine [proliferation of colon-type bacteria such as [E. coli or Bacteroides.] results in diarrhea or typical features of Malabsorption.

Pathogenesis

Bacterial overgrowth leads to

*Deconjugation of bile salts which results in Steatorrhea.

*Bacteria require cobalamin resulting in anemia,

*Metabolizing carbohydrate (resulting in calorie malnutrition and halitosis).

Clinical Conditions Associated with Bacterial Overgrowth of the Small intestine.

1-Gastric hypochlorhydria or achlorhydria

Causes include

*Pernicious anemia

*Partial gastrectomy

*Long term PPI therapy

2-Small intestinal stagnation

Causes include

Anatomical

*duodenal-jejunal diverticulosis

*Obstruction [stricture, adhesion, tumor]

*Surgical blind loop after Billroth ll operation

Motor

*Pseudo-obstruction

*Scleroderma

*Diabetic autonomic neuropathy

3-Abnormal communication between the distal And proximal gastrointestinal tract

Causes include

*ileocecal resection

*Fistulae

4-impaired immune function-Hypogammaglobulinemia

Diagnosis.

1-Combination of a low serum cobalamin level and an elevated serum folate level [as enteric bacteria frequently produce folate compounds that will be absorbed].

2-Jejunal aspiration is the gold standard.[increased levels of colonic-type bacteria in a jejunal aspirate]

3-Small bowel radiology to look for anatomical causes like [jejunal diverticulosis or strictures].

4-Duodenal biopsy to exclude coeliac disease.

5-Glucose hydrogen breath test. Bacterial overgrowths within the small bowel cause an early rise in breath hydrogen.

Management

*Surgical correction of an underlying anatomic problem contributing to bacterial overgrowth.

*Broad-spectrum antibiotics. for 1 week per month In the presence of frequent recurrences.

*Intramuscular Vit B12.

*Prokinetics for motility disorders.

Short bowel syndrome[SBS]

*SBS-Malabsorption due to congenital absence or resection of large portions of the small intestine.

*Intestinal failure- Insufficient intestinal surface due to SBS or others unable to absorb sufficient fluid, macronutrients, and micronutrients.

Many factors determine the severity of short bowel syndrome including

1-The length and health of the remaining bowel.2-The presence of the ileocecal valve.

3-The presence of the colon. 4-The degree of adaptation in the remaining intestine.

5-Age and comorbidity

Typically when there is<100 cm of small bowel remaining, malabsorption will occur(resulting in malnutrition and weight loss, when the colon is also missing, severe dehydration and malabsorption occur.

Causes of short bowel syndrome

In adults.

1-Mesenteric vascular disease including atherosclerosis, thrombosis, and vasculitis.

2-Primary mucosal and submucosal disease, e.g. Crohn's disease, refractory sprue, radiation enteritis

3-Operations without the preexisting small intestinal disease, such as trauma and jejuno-ileal bypass for, obesity

In children

1-Congenital anomalies [mid gut volvulus, atresia].

2-Necrotizing Entero-colitis.

Clinical Features include

*Diarrhea, *Malabsorption*Dehydration and signs of hypovolemia. *Weight loss* electrolyte imbalance

Loss of muscle bulk and malnutrition Chronic vitamin and trace element deficiency.

Factors contributing to diarrhea and Steatorrhea

1- Loss of surface area for digestion and absorption [the proximal small bowel normally absorbs around 8 of 9 L of fluid receives daily].
2-Removal of the ileum [site of bile acids and Vit B12 absorption] and leads to
* Exacerbation of diarrhea occurs When < 100 cm of ileum removed. because of increased bile acids entering the colon leading to stimulation of colonic fluid and electrolyte secretion.
* When extensive ileal resection > 100 cm. Steatorrhea occurs because bile acids loss exceeds hepatic synthesis this leads to bile acid deficiency.
*Vitamin B12 Malabsorption. This occurs when more than 60cm of ileum has been resected.
*Decrease in intestinal transit time and bacterial overgrowth from the colon.
3-increase in renal calcium oxalate.
4-increase in cholesterol gall stones.
5-Gastric hypersecretion of acid.
Reduced pH in the duodenum can inactivate pancreatic lipase and/or precipitate bile acids, thereby increasing Steatorrhea and an increase in gastric secretion can create a volume overload relative to the reduced small-intestinal absorptive capacity.

Complications

*Liver disease- include -Steatohepatitis and cholestasis [due to extensive parenteral caloric administration].
*Gall stone
*Bacterial overgrowth
*Nutrient deficiencies
*Hyperoxaluria inpatient with an intact colon [because free calcium is bound to fatty acids in the small intestine and to increased colonic oxalate absorption].
*Lactic acidosis-seen inpatient with an intact colon –delivery of unabsorbed carbohydrate to the colon leads to the production of lactate by gram-positive anaerobes.

Treatment

Depends on the severity of symptoms and whether the individual is able to maintain caloric and electrolyte balance with oral intake alone.
Initial treatment includes
*PPI to reduce gastric hypersecretion.
*Anti-diarrheal agents [Lopromide 2-4mg 6hr.]Or codeine phosphate [30mg 4-6 hr] to reduce stool output
*Cholestyramine - which binds bile salts in the intestinal lumen, Aluminum may be also used.
*Low fat diet to minimize diarrhea from fatty acid stimulation of colonic fluid secretion.
*Lactose restriction.
*Oxalate restriction.
* vitamins and calcium Supplementation.
*Enteral feeding
*Small bowel transplantation.

Protein –Losing Enteropathy

is defined as gut loss of protein sufficient to reduce serum albumin. Patients present with edema in the absence of proteinuria, signs of heart failure, or liver disease.
Causes can be classified into three primary groups.
1-Mucosal ulceration or erosions include*Ulcerative colitis, gastrointestinal carcinomas, lymphoma, radiation damage, Crohn's disease.
2-Intact Mucosa include*Celiac sprue, Menetriers disease, Tropical sprue, Eosinophilic gastroenteritis, SLE, Bacterial overgrowth.
3-Lymphatic obstruction include*Intestinal Lymphangiectasia, Constrictive pericarditis, lymphoma, Whipple's disease.
Diagnosis
*The diagnosis is suggested by the presence of peripheral edema, low serum albumin, and globulin levels in the absence of renal, cardiac and hepatic disease.
*Measurement fecal clearance of Alpha 1-Antitrypsin or Cr-labelled albumin after intravenous injection.
Treatment
*of an underlying disease process. *Nutritional support
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Chronic intestinal Pseudo-Obstruction

The clinical syndrome caused by ineffective intestinal propulsion and characterized by symptoms and signs of intestinal obstruction in the absence of an obstructing lesion of the intestinal lumen.
Common causes include
1-Primary or idiopathic
*Familial visceral-Myopathies
- Neuropathies
*Congenital aganglionosis
2-Secondary
*Drugs [opiates, tricyclic antidepressants, phenothiazine's].
*Smooth muscle disorders [Scleroderma, Amyloidosis and mitochondrial myopathy].
*Myenteric plexus disorders [Para neoplastic syndrome in small-cell lung cancer].
*CNS disorders [Parkinsonism, autonomic neuropathy].
*Endocrine and metabolic disorders [hypothyroidism, pheochromocytoma, acute intermittent porphyria].
Clinical features
*Recurrent episodes of nausea, vomiting, abdominal discomfort and distension after food.
*Alternating constipation and diarrhea.
*Weight loss results from Malabsorption (due to bacterial overgrowth).
*Dysmotility leads to dysphagia and bladder dysfunction.

Investigations
*Plain radiographs show distended loops of bowel and air-fluid levels.
*Barium studies to exclude mechanical obstruction.
*Laparoscopic full-thickness biopsies of the small intestine to confirm both the diagnosis and whether it is myopathic or neuropathic in origin.

Management
*****Underlying causes should be addressed.
*Surgery should be avoided if possible.
*Prokinetic agents may enhance motility.
*Antibiotics are given for bacterial overgrowth.
*Nutritional and psychological support.

Ulceration of the Small Intestine

Causes of small intestinal ulcers include
*Idiopathic
*Inflammatory bowel disease [Crohn's disease].
*Drugs [NSAIDs, enteric-coated potassium tablets].
*Ulcerative jejuno-ileitis
*Lymphoma and carcinoma.
*Infections [tuberculosis, typhoid, Yersinia].
*Radiation, vacuities.
Ulcers are more common in the ileum
The presentation includes bleeding, perforation, stricture formation, or obstruction.
Diagnosis. Barium studies and Enteroscopy.

Eosinophilic Gastroenteritis

This rare disorder of unknown etiology can affect any part of the gastrointestinal tract.
Characterized by
1-increase eosinophilic infiltrate that may be
*Mucosal form - leading to mucosal absorption defects.
*Muscularis form -leading to thickening of the bowel wall.
*Serosal form- leading to exudative ascites with high eosinophil count.
2-Peripheral blood eosinophilia.in the absence of parasitic infection and other causes of eosinophilia.

Clinical features include-
*****Vomiting, abdominal pain, diarrhea,wt loss, iron deficiency anemia, protein-losing Enteropathy, malabsorption
*Features of intestinal obstruction.
*Ascites with a high eosinophil.

Diagnosis
*Histologically by multiple Endoscopic biopsies or full-thickness biopsies.
*Excluding parasitic infection and other causes of eosinophilia.
*A raised serum IgE concentration.

Management
*Dietary manipulations are rarely effective although elimination diets, especially of milk, may benefit a few patients.
Systemic or topical corticosteroid if failure of diet therapy
*Prednisolone 20-40 mg daily for 2-6 w and/or disodium cromoglycate [which stabilizes mast cell membranes]. The prognosis is good.

Meckel's Diverticulum

This is the commonest congenital anomaly of the gastrointestinal tract and occurs in 0.3-3% of people. The diverticulum results from failure of closure of the vitelline duct. With the

persistence of a blind-ending sac arising from the antimesenteric border of the ileum, usually occurs within 100 cm of the ileocecal valve and is up to 5 cm long. Approximately 50% contain ectopic gastric mucosa rarely contain [colonic, pancreatic or endometrial tissue]. Most patients are asymptomatic.

Complications.

*Bleeding results from ulceration of ileal mucosa adjacent to the ectopic parietal cells and presents as recurrent melena or altered blood per rectum.

*Intestinal obstruction, diverticulitis, intussusception, bacterial overgrowth, and perforation.

Diagnosis can be made by scanning the abdomen using a gamma counter following intravenous injection of 99m-technetium pertechnetate, which is concentrated by ectopic parietal cells.

Treatment

Surgical resection when complications occur

Adverse Food Reactions

Adverse food reactions are common and are subdivided into food intolerance and food allergy.

1-Food intolerance discussed in malabsorption syndrome page[30-31]

2-Food allergy

Food allergies are immune-mediated disorders due to IgE- mediated type I hypersensitivity reactions, incidence 2%- 27% of children, and 2-5% of adults are affected. The foods most frequently implicated in food allergy are peanuts, milk, eggs, Soya, and shellfish.

Food allergy Occur when a food antigen crosses the gut epithelium and binds to an IgE molecule on the surface of a mast cell. mast cell degranulation causes the release of inflammatory and vascular mediators like [histamine, proteases, prostaglandins, PAF, serotonin].

These lead to

*Bronchoconstriction.

*Mucus hypersecretion.

*Increased vascular permeability.

*Recruitment of inflammatory cells.

Clinical Manifestations include

1-Oral allergy Syndrome

Contact with a certain fresh fruit juices results in urticaria and angioedema of the lips and oropharynx.

2-Allergic gastro Enteropathy

colicky abdominal pain, bloating, vomiting, and diarrhea.

3-Gastrointestinal anaphylaxis

Nausea, vomiting, diarrhea, and cardiorespiratory collapse.

Diagnosis

The diagnosis of food allergy is difficult.

*Skin prick tests and measurements of antigen-specific IgE antibodies in serum have limited predictive value.

*Double-blind placebo-controlled food challenges are the gold standard.

Treatment

*Specific food should be avoided.

*Antihistamines or disodium cromoglycate.

*Anaphylaxis should be treated as a medical emergency with resuscitation, airway support, and intravenous adrenaline.

Abdominal tuberculosis

Gastrointestinal infection with TB usually results from human Mycobacterium tuberculosis. intestinal infection may be caused by*ingestion of infected milk,* blood-borne spread from the lung, * direct spread from adjacent organs.

TB can affect any part of the gastrointestinal tract the area most commonly affected is the ileo-caecal region.

Clinical features depend on the infected area

1- ileo-caecal involvement causing- *Abdominal pain can be acute or chronic,
* diarrhea *wt. loss *RIF mass*Low- grade fever.
2-TB adenitis- mimic appendicitis
3-TB peritonitis -exudative Ascites, abdominal pain, and fever.
4-Granulomatous hepatitis may occur.

Differential diagnosis

Crohn's disease, Yersinia infection, lymphoma, caecal tumor

Diagnosis

Many patients have no pulmonary symptoms and normal chest radiography.
-Elevated erythrocyte sedimentation rate (ESR).
-A raised serum alkaline phosphatase suggests hepatic involvement.
-Histological confirmation.
-Culture may be helpful.
-PCR
-CT, Colonoscopy
-Ascitic fluid aspiration [exudative with increased lymphocytes]
-Culture, peritoneal biopsy

Management

Triple therapy [rifampicin,isonised and pyrazinamide for 2 m followed by dual therapy[rifampicin,isonised]for 4 m
Ethambutol may be needed if resistance is suspected
Surgery is indicated for obstruction, perforation, hemorrhage

Tumors of the small intestine

Benign tumors

The most common benign tumors are adenomas, Leiomyoma's, lipomas, and hamartomats[Peutz-Jeghers syndrome,cornkite-Canada syndrome, juvenile polyposis, Cowden disease].
*****Adenomas mostly found in the periampullary region. Transformation to Adenocarcinoma may occur but it is rare. Multiple adenomas are common in the duodenum of patients with familial adenomatous polyposis [FAP].

Malignant tumors

These are rare and include- adenocarcinoma, Carcinoid tumors, Leiomyosarcomas, and lymphoma.
The majority occur in middle age or later.

Adenocarcinomas.

Conditions associated with an increased risk of primary small intestinal neoplasia
*Familial adenomatous polyposis.
*Coeliac disease.
*Peutz-Jeghers syndrome.
* Crohn's disease.

Clinical presentation includes.

*bleeding.
*intestinal Obstruction partial or complete manifested by abdominal pain, vomiting.
*perforation
*biliary stasis if a duodenal tumor located near the ampulla of Vater.
*weight loss

Investigation

*Blood test may shows
Anemia, Hypoalbuminemia, high alkaline phosphatase, and bilirubin level may indicate liver secondary's

*****Upright Plain abdominal X-ray may show air-fluid levels in patients with small bowel obstruction.
*US and computed tomography may show dilatation, obstructing lesions, Bowell wall abnormalities
*Barium follow-through may show narrowing or polypoidal lesion.
*Enteroscopy and biopsy
*Mesenteric angiography may be helpful to the surgeon in planning surgery.

Treatment

*Surgery
*Endoscopic therapy
*Radiation therapy and chemotherapy

Carcinoid Tumors of GIT.

Carcinoid tumors are well-differentiated neuroendocrine tumors. These tumors are derived from enterochromaffin cells and are most commonly found in the ileum, duodenum, jejunum, rectum, appendix, and stomach. The risk of metastasis to the liver and Localized spread is increased when tumor size > 2 cm in diameter. These tumors are less aggressive than carcinomas and their growth is usually slow. secretory products produced by the carcinoid tumor include [5-hydroxytryptamine, serotonin, bradykinin] are usually metabolized in the liver and do not reach the systemic circulation**.**

Carcinoid syndrome

Systemic manifestations produced when hormonal products[5-HT, serotonin, bradykinin] are released by hepatic metastases direct in the systemic circulation.

Clinical features of the Carcinoid syndrome.

1-Small-bowel obstruction.constipations,bleeding per rectum
2-Intestinal ischemia [due to mesenteric infiltration or vasospasm].
3-Hepatic metastases causing [pain, hepatomegaly, and jaundice].
4-Flushing and wheezing
5-Diarrhoea
6-Cardiac involvement [tricuspid regurgitation, pulmonary, stenosis, right ventricular endocardial plaques] leading to heart failure
7-Facial telangiectasia

Diagnosis

*****24 h urinary for 5-hydroxy indole acetic acid [5-HIAA].
*Chest X-ray, abdominal US, CT, small bowel radiology, and echocardiography.
*Radiolabelled Octreotide scans can be used for localization of lesions.

Management

*Surgical resection of the primary tumor is curative if the tumor is < 2 cm and has not metastasized to the liver
*Hepatic artery embolization retards growth of hepatic metastasis.
*Palliative treatment for the disseminated disease by *Octreotide [a synthetic somatostatin analog] 200 microgram 8- hourly SC.
*Radioactive Octreotide.