Lec7

Celiac disease

Autoimmune disease Trigger by exposure to a protein called gluten
In small bowle the glaring partly digested into short peptide called gliadin which induce secretion of IL-15 from epithelial cells which activate CD8+ lymphocytes

These lymphocytes express NKG2D, a receptor for MIC-A.
Enterocytes that have been induced to express surface MIC-A in response to stressful condition

The resulting epithelial damage may enhance passage of other gliadin peptides into the lamina propria where they are deamidated by tissue transglutaminase.

These gliadin peptides interact with HLA-DQ2 or HLA-DQ8 on antigen-presenting cells and in turn stimulate CD4+ T cells to produce cytokines (mainly interferon gamma) that exacerbate tissue damage

Gluten is found in (wheat , rye and barley)

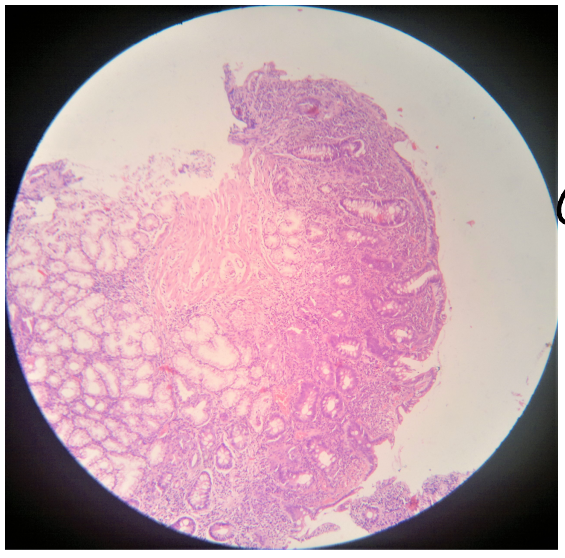
This patients with gluten sensitivity have a genetic factor (with HLA genes) for their sensitivity .. these patients have more HLA-DQ2 and HlADQ-8 expression than normal people

almost all people with celiac disease carry the class II HLA-DQ2 or HLA-DQ8 allele. However, the HLA locus accounts for less than half of the genetic component of celiac disease. Remaining genetic factors may include polymorphisms of genes

Serology is the detection of Ab

1% incidence

In adults, celiac disease presents most commonly between the ages of 30 and 60.
Delayed diagnosis patients they will have
1-malnutrition (reduction of absorption of Various food stuff) so they will have Wight loss + vitamin deficiency
2-malabsorptive diarrhea



b4 microscope
it contain
① Flat surface (No villi) in Small intestine
So there's a Villous atrophy
② there's nuclear Stratification
③ Large number of lymphocytes in endothelial cells.
④ Crypt hyperplasia (to replace damaged entrocytes)

Celiac disease associated with increase risk of adenocarcinoma and lymphoma (mainly T cell lymphoma)

Villous atrophy And inflammatory process not specific for celiac this may seen in other disease as infectious disease or other

So to determine if the microscopic biopsy is celiac it should associated with clinical symptoms and serology (Specific Antibodies)

Lactase deficiency or lactose intolerance

Lactase is a disaccharidase (involved in terminal digestion)
Found as glycocalx around microvillus (integral protein of plasma membrane)

It's a serious condition in children (who depend on milk)

Lead to osmotic diarrhea

irritable bowel syndrome

Diagnosis of exclusion
Colon is normal (mask the cancer) + is partial obstruction may later become complete obstruction ... risk factors : diet and psychology
Syptoms: crampy abdominal pain , irregular bowel habits (diarrhea or constipation),

Inflammatory bowel disease

Include ulcerative colitis and crohn disease

Is a disease under immune system influence

Previously it called Idiopathic bowel diseases but studies show that bowel normal flora may trigger exaggerated immune response against some antigens

UC :
only in colon and rectum (should be an involvement of rectum)
from most distal part of the rectum extended (المسافة بتختلف من مريض لاخر)
Involve only the mucosa and may a part of submucosa

CD:
from mouth to anus and most frequently the distal of small intestine
skip lesions (healthy mucosa between ulcerated ones)
Involve all bowel layers (as fissuring extend deeply and may lead to perforation or fistulation between the organ and skin)

IBD occur in young age in 20s

Smoking protect from UC

The hygiene hypothesis suggests that this increasing incidence is related to improved food storage conditions, decreased food contamination, and changes in gut microbiome composition that result in inadequate development of regulatory processes that limit mucosal immune responses

Other potential explanations for increased IBD prevalence include the idea that preserva- tives and other materials added to processed foods induce low-grade mucosal damage that predisposes to IBD.

In uc : if rectum involved celled ulcerative rectocolitis , if rectum and sigmoid ulcerative rectosigmoiditis

If all colon called ulcerative pancolitis

Pathogenesis:

IBD results from a combination of abnormalities in immune regulation, host-microbe interactions, and epithelial barrier functions in genetically susceptible individuals.

Morphology :

CD :

most commonly iliocecal area

40% limited to small intestine

30% both the colon and small intestine

Reminder only colon

Aphthous ulcers

Cobblestone appearance

Fissures / fistulas and perforation

Strictures (due to fibrosis)

Creeping up (periserosal fat extends more than normal limit)



there's an ulceration → (liner + rigidity (cause of fibrosis) → due to inflammation

Microscoplly:(UC and CD)

Inflammatory process (mixed of lymphocytes neutrophils plasma cells) through the entire layer + ulceration (deep and transmural lead to perforation or fistulation)

Crypt abscess (Clusters of neutrophils within a crypt)

Irregular Splitting of the crypt (distortion of the crypt)

Metaplasia

- Pseudopyloric metaplasia
- Paneth cell metaplasia (in the left colon)

Granuloma (hallmark of CD) present only in 35% of the cases

Aggregation of macrophages or histiocyets

*Indeterminant colitis called when we can't distinguish between CD and UC overlapping condition

* Duration of the disease , extant of the disease and nature of the inflammatory response determine the risk of neoplasm transformation

Surveillance (the disease is a source of rectal bleeding and iron deficiency anemia and have dysplastic changes previous to cancer) and may do colectomy to the affected part (عشان ما يصير cancer)

Uc Microscoplly:

Ulcerated rectum

Granulation tissue bulging towar the surface called polyp (pseudopolyp) and mucosal bridge (polyps in each side fuse together and after fibrosis they made a bridge)

In Ulcerative pancolitis there's a Backwash iLife's (inflammatory process extend through the iliocecal valve)

Toxic megacolon (cause inflammatory process and chemical mediators affect the peristalsis and neurons lead to exaggerative dilation of the colon) ends with perforation



U.C

ulceration + Pseudo Polyps

Microscoplly : inflammation and crypt abscess limited to the mucosa

SIGMOID DIVERTICULAR DISEASE

الدكتور رجع شرح ال diverticulum نفس الكلام الي بمحاضرة ٣

Due to chronic constipation and increase intraabdominal and intraluminal pressure through the week point there's an outpouching

Diverticular disease is due to acquired pseudodiverticular outpouchings of the colonic mucosa and submucosa. these do not include all three layers of the colonic wall

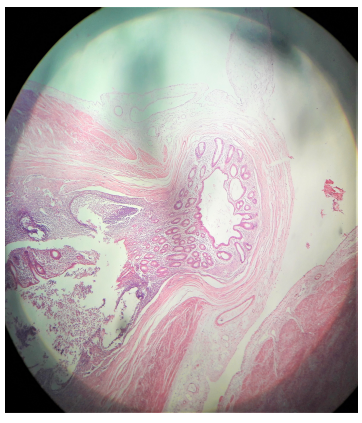
Mucosa outpouching and lined by serosa

Fragile structure not resistant to increase pressure
If the pressure continue to increase it ends by perforation or inflammatory process called diverticulitis (syptoms resemble the appendicitis

Most in right side

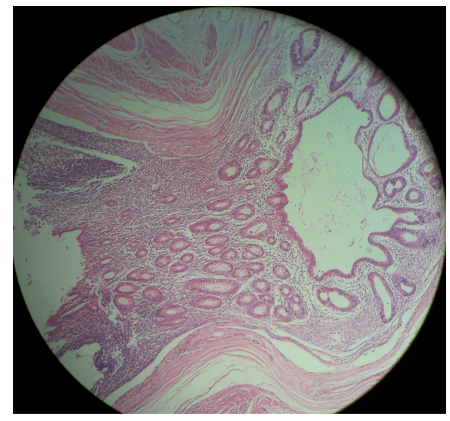
Streets play a role in diverticula diseases

the prevalence approaches 50% in Western adult populations older than age 60. Diverticulosis is less common in Japan as well as under-resourced countries, probably because of dietary differences.



lined by serosa
there's Mucosa
Submucosa +
M. propria
+
it interrubted
and then continued

out pouching
بارز
طبقة
وجود
blood vessles



Polyps

Mass over the GIT surface or lumen
May be connected to the surface through a narrow stalk or neck
Treatment: by smear around the neck and increase temperature without bleeding
Or may be have a broad base with the surface this is called sessile polyp treated by surgery
Polyp is a macroscopic detfention (is just a protrusion)
But Microscoplly you defined the type and the constant of it and determine if it's cancer or not

In general, intestinal polyps can be classified as nonneoplastic or neoplastic.

Hyperplastic polyps:
increase number of the lining surface epithelium and cause mucosal bulging
that are typically discovered in the sixth and seventh decades of life.
No clinical symptoms
Incidental findings
Not related to neoplasticism transformation
Commonly in rectosigmoid area
hyperplasia can occur as a nonspecific reaction adjacent to or overlying any mass or inflammatory lesion or cancer

Inflammatory polyps:

Pseudopolype no epithelial proliferation only increase blood vessel and inflammatory material that cause bulging

Hamartomatous-Polyps :

Hamartoma : disorganised normal tissue

Although they were originally thought to reflect development abnormalities

It associated with some syndromes lead to increase risk of cancer (it alone doesn't associated with cancer)

Juvenile Polyps

In children Younger than 6 years

Associated with rectal bleeding

Single sporadic and sometimes it's a part of syndrome called (juvenile polyposis)

Neoplasticism polyp:

Adenomas atr the most precursor of the majority of colorectal adenocarcinoma

Adenoma have a dysplastic changes

30% by age 60 in the west

Less common in Asia

Colon cancer is preventable due to that colon is easy accessible organ by endoscopy and majority of it precedes by Adenoma

A patient with family history or treated to colon cancer so the surveillance is important in them



adenoma

Smooth with Some nodularity

(تشبه الزاوية)

+

tracting the mucosa



3 sessial Polyps

Microscoplly :Adenoma is 2 types (villous or tubular) and there's combined and serrated

Villous : large size and involve the full circumference of the wall contain projections .. contain landmarks

CRC= colorectal cancer

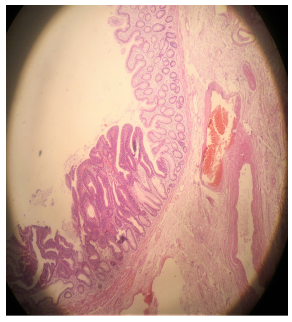
Adenoma and cancer are the same prevalence

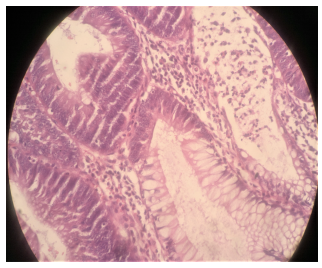
- Similar distribution in the colon
- Surveillance and polyp removal reduces the incidence of CRC
- The majority do not progress to adenocarcinoma

Till now we don't known which Adenoma produce cancer and which not

When Adenoma size increas the incidecine of high grade dysplasia increas

In Adenoma :
Nuclear size increas and stratification
Cytoplasm loss it's mucin content





Serrated adenoma:
Associated with increase risk of cancer

Intramucosal carcinoma

Mucosa between Mascularis mucosa and surface epithelium

When there's invasion inside the mucosa after the dysplasia (don't invade the muscularis mucosa)

Lamina propria in colon without lymphatics so metastasis is not present (dealer with it as carcinoma in situ)

FAMILIAL ADENOMATOUS POLYPOSIS

Patient will develop numerous amounts of Adenomas through the colon At least 100 polyps are necessary for a diagnosis of classic FAP, but thousands may be present
APC mutation (wnt pathway) .. loss of APC function lead to continuous proliferation signaling

Approximately 75% of cases are inherited, while the remainder appear to be caused by de novo mutations.

Colorectal adenocarcinoma develops in 100% of untreated FAP patients, often before age 30 and nearly always by age 50. As a result, prophylactic colectomy is the standard of care. Colectomy prevents colorectal cancer, but patients remain at risk for neoplasia at other sites. The ampulla of Vater and the stomach are common extracolonic sites of adenomas in FAP patients.

MUTYH-associated polyposis

This autosomal recessive disorder is termed MUTYH-associated polyposis, or MAP. In contrast to FAP, MAP is characterized by fewer than 100 polyps, which appear at later ages.

MYTYH associated polyposis is a pathway in colon cancer

HNPCC (lynch syndrome)

HEREDITARY NON-POLYPOSIS COLORECTAL CANCER (HNPCC)

Mismatch repair genes (MMR). (repair the mutation)

Target gene : MSH2, MLH1

If there's a mutation in MSH2, MLH1 the accumulation of mutation rate become 1000 fold of normal cell

In human Genome there's a microsatellite (repeated short segments of DNA) when mismatch repair genes mutation occur lead to mutation accumulation at the microsatellite

Lead to microsatellite instability lead to (Lynch syndrome or mismatch repair deficiency or hereditary non polyposis colon cancer) (الثلاثة نفس المعنى) (microsatellite instabilityاسمه ككل الوضع)

This pathway is the minority of colon cancer cases the majority of cases is due to APC gene (loss of function or silencing gene)

HNPCC is thought to account for 2% to 4% of all colorectal cancers, making it the most common syndromic form of colon cancer. Colon cancers in HNPCC patients tend to occur at younger ages than spo- radic colon cancers and are often located in the right colon

Patients inherit one mutant allele

Mutation later on of the second allele

FAP and HNPCC has shed light on the carcinogenesis of the sporadic cases



mucosal replaced by a number of Polyps

Adenocarcinoma

Colorectal or colon adenocarcinoma the lst in males and 2nd in females after breast

Significant mortality and morbidity

World wide 50% mortality

10% of cancer mortalitys

1200000 incidence

In USA is second only to lung cancer and 15% of cancer mortality and highest incidence

Peak age 60-70

Associated with fiber contents (poor fiber intake) and high fat intake

Associated with Apc/beta cats in pathway

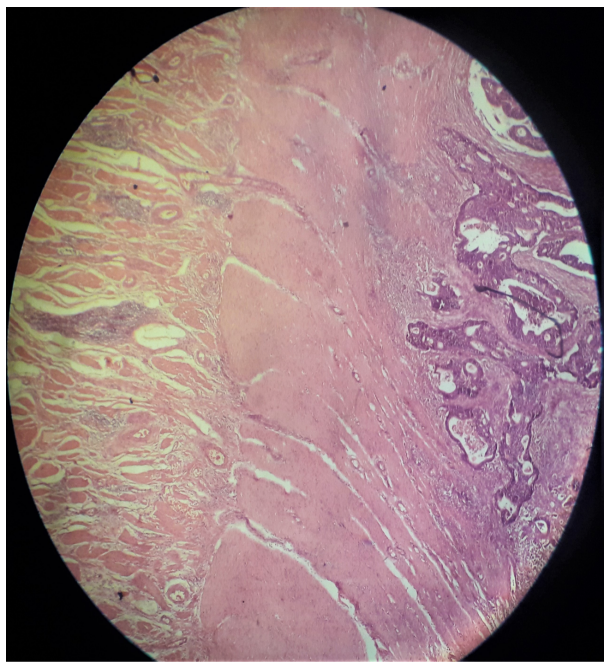
RAS mutation have a role in colon cancer but relative late event
In adenomia less than 1 cm there a KRAS mutation

Tp53 is important in colon cancer from 70-80% of adenicarcinoma

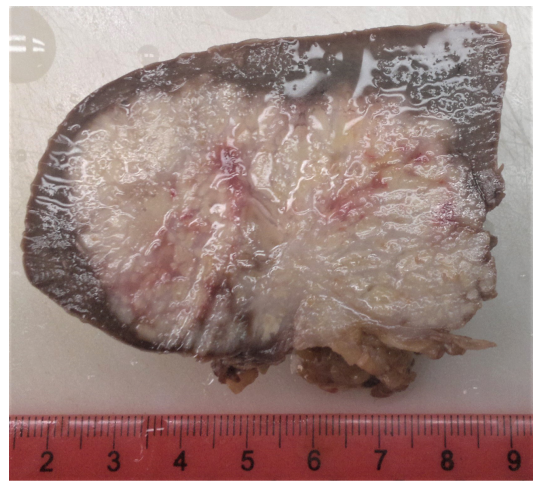
Macroscopically:
There's a round fungating regions and central necrotic



Tumor involve all layers and the periserosal fat



irregular groups of cancer cells forming glands invading through the bowel Layer



Liver metastasis Is removed called liver metastatic ectomy

Postmenopausal women with iron deficiency that mean colon cancer
Colon lymphatic drainage in portal vein so the metastasis is to liver but rectum drainage into systemic circulation so it metastasis to Lung and heart

Done ✅ 29/oct ..
12:05 Am ❤️ الحمد لله

