

Lec 6

Gastrointestinal Stromal Tumor (GIST)

Incidence between 11 and 20 per 1 million people.

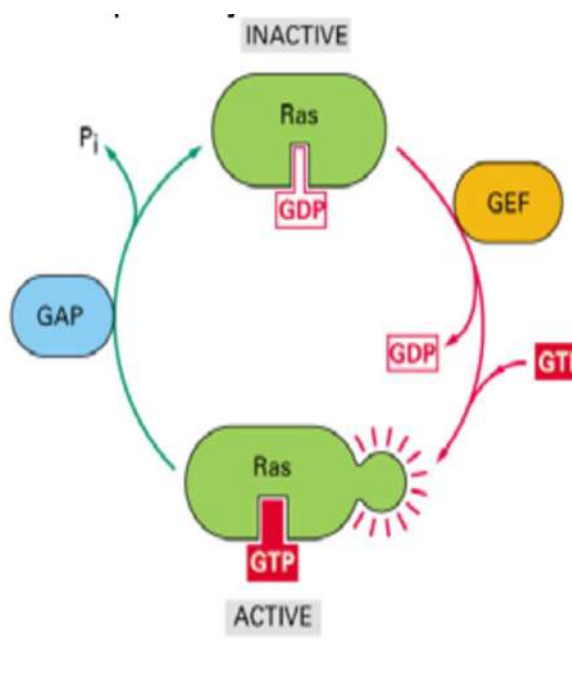
More than half of these tumors occur in the stomach.

arise from the interstitial cells of Cajal, or pacemaker cells.

Peak age => 60 year

some are related to the Carney triad, a nonhereditary syndrome of GIST, paraganglioma, and pulmonary chondroma

There is also an increased incidence of GIST in individuals with neurofibromatosis type 1. (NF1) ... patients with NF1 will have cafe au lait spots [they have a defect of neurofibromine , a gene that involved in RAS pathway , it's on of GAP activating protein]



Approximately 75% of all GISTs have oncogenic, gain of function mutations in the receptor tyrosine kinase KIT. Another 8% of GISTs have mutations that activate the related receptor tyrosine kinase, platelet-derived growth factor receptor α (PDGFR α).

Rare individuals with germline mutations of these genes have diffuse hyperplasia of Cajal cells and develop multiple GISTs.

The most useful diagnostic marker is KIT (CD117) which is immunohistochemically detectable in Cajal cells

When AB bind to the specific protein a brown Color appear (chromogin) مادة ملونة

Morphology :

It's a mass imbedded in the wall beneath the mucosa and sub mucosa difficult to have a biopsy by endoscope so by needle and ultrasound or CT guided the biopsy will be taken or by surgery

Tumor caused bulging toward the lumen and the bulging is ulcerated and central mucosa will have necrosis

Behaviour and prognosis:

It depends on

1-**size of the tumour** (when the size increased the risk of recurrence and metastasis increase)

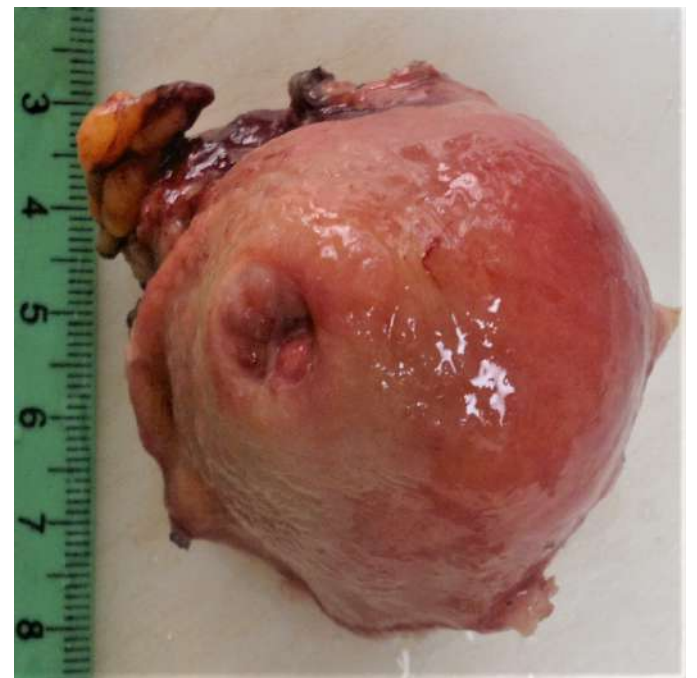
2- **mitotic activity** (more mitotic activity more recurrence and metastasis)

By the 2 factors a score determines the chance of recurrence and metastasis

*Treatment: The molecular phenotype is an important consideration in the treatment of patients with unresectable, recurrent, or metastatic GISTs. Tumors with mutations in KIT or PDGFRA often respond to the tyrosine kinase inhibitor imatinib, whereas tumors without these mutations are generally resistant.



*multiple masses
in stomach*

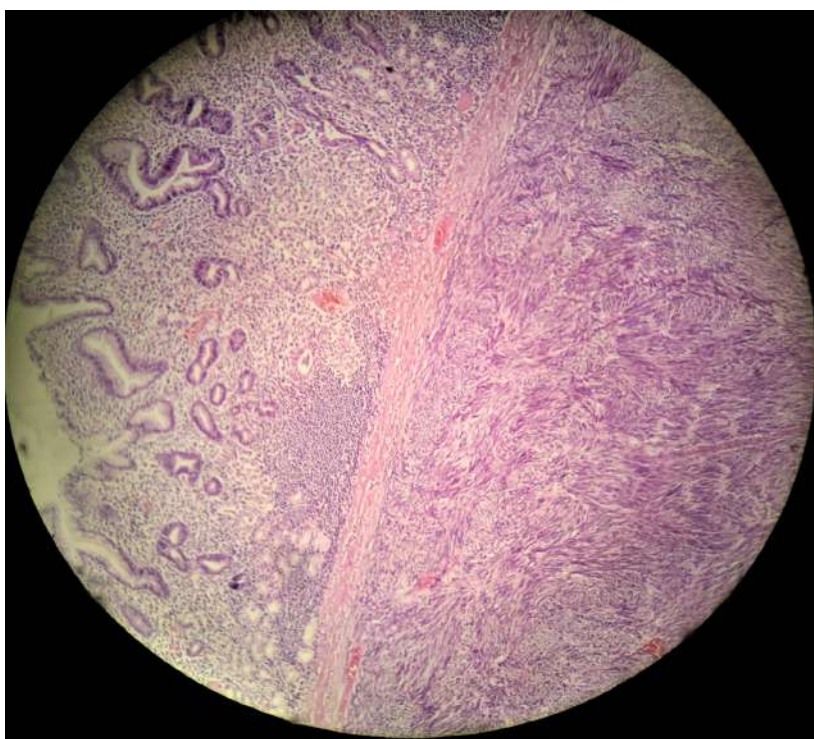


*tumor under the
stomach mucosa
+
ulceration*



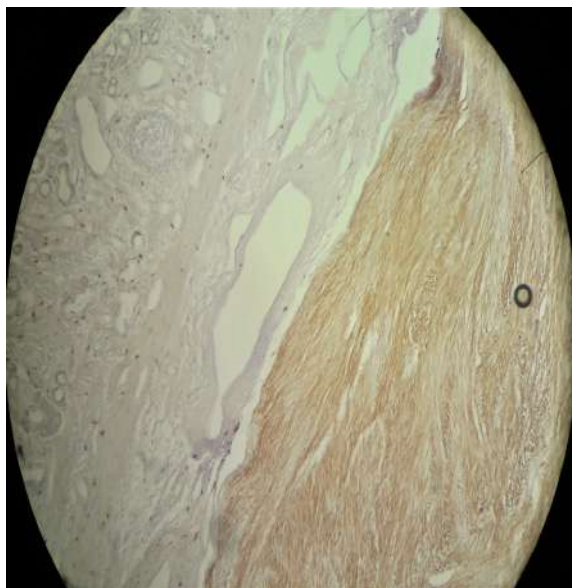
GIST in
Small intestine
mesentery

[solid + fibrily texture]

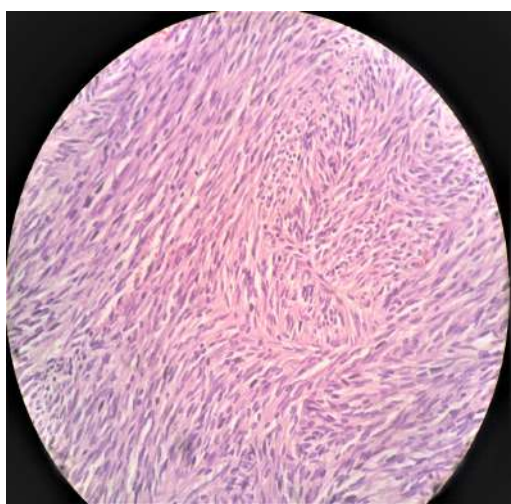


Stomach
GIST

muscularis
mucosa



brown
color
by
KIT
(CD117)



spindle cell type

=
elongated

no nuclear atypia

+ intersecting
vasicles
attached
to
each
other

Small intestine diseases

INTESTINAL OBSTRUCTION

Obstruction of the GI tract may occur at any level, but the small intestine is most often involved because of its relatively narrow lumen.

obstruction include abdominal pain and distention, vomiting, and constipation

80% of mechanical obstructions caused by :

1- hernias [Obstruction usually occurs because of visceral protrusion (external herniation)]

2- intestinal adhesions [Surgical procedures, infection, or other causes of peritoneal inflammation with fibrosis and fibre bands between bowel segments.. These fibrous bridges can create closed loops through which other viscera may slide and become entrapped, resulting in internal herniation.]

,
3- intussusception [one segment telescoping in another segment it take the mesentery lead to blood vessel comprising and ischemia]

4- volvulus [loop of bowel twists about its mesenteric point of attachment and results in both luminal and vascular compromise]

Tumors, infarction, and other causes of strictures, for example, Crohn disease, make up the remainder.)

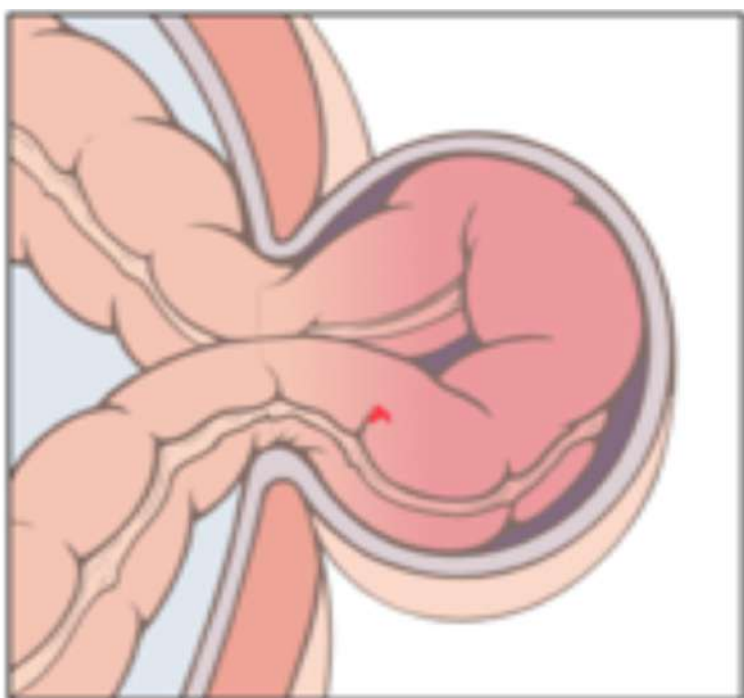
Hernias are the most frequent cause of intestinal obstruction worldwide and the third most common cause of obstruction in the United States.

Most commonly inguinal hernia

Occur in abdominal weak points (inguinal canal , femoral canal , around the umbilicals) and may after a surgery (iatrogenic)

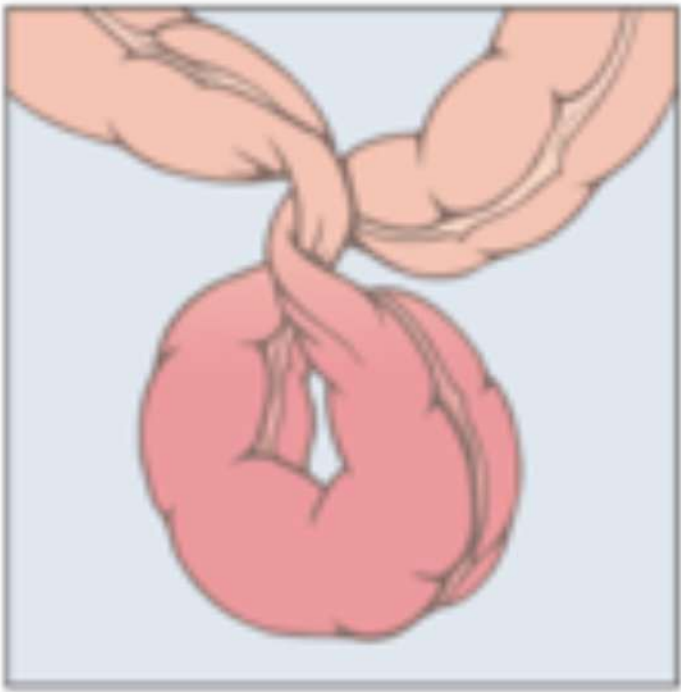
Inguinal canal internal opening is narrow bowel and scrotum pass through this narrow

Small bowel loops are typically involved, but omentum or large bowel may also protrude, and any of these may become entrapped lead to edema and congestion of the herniated part . Pressure at the neck of the pouch may impair venous drainage of the entrapped viscus. The resultant stasis and edema increase the bulk of the herniated loop, leading to permanent entrapment (incarceration) and, over time, arterial and venous compromise (strangulation) and infarction



*Small bowel inside
the hernial sac
+
discoloration due
to ischemic changes
and partial infarction*

Adhesions :loop trapped between the wall and the fibrous band lead to edema and emergency condition



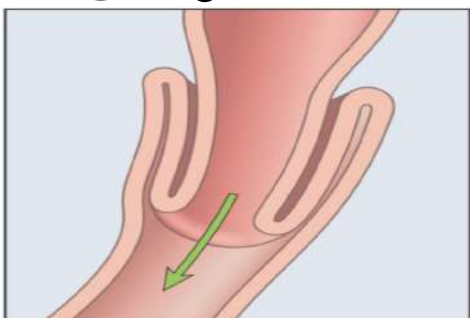
Volvulus

volvulus
+
luminal obstruction
+
ischemic changes

Intussusception is idiopathic in newborn but in children or adult it's caused by leading point as a mass, polyp , tumor that always induce peristalsis
(هي كتلة مش حتتحرك ومع الزمن حتسبب Intussuception)

In children vaccines and viral infection may be a cause for Intussusception due to induction of MALT and hyperplasia and form a modular structure (a leading point . In adult the cause may a polyp or tumor

Treatment surgery but in children may be enema



intussusception
٠

ISCHEMIC BOWEL DISEASE

Common in old age it's associated with atherosclerosis or blood vessel problems

Blood supply in small bowel (due to its length and movements) when the artery closer to the bowel wall is formed arcades and sent straight small blood vessel and there's a anastomoses and connection between the arcades in normal conditions there's no ischemia

The arteries of GUT have anastomosis normally if a sudden obstruction occur it lead to infraction because there's the collaterals can't compensate the fraction But the gradual obstruction (as in atherosclerosis) the collateral branches will develop induced by reduced blood supply

Ischemia has grades so it may involve mucosa only (mucosal ischemic changes) or mucosa and submucosa (mural ischemic changes) and called (transmural)when the muscularis propria is involved

Transmural is an acute and sudden obstruction Muscularis propria may resist the ischemia due the high proliferating rate but the mucosa has ischemia easily

In acute ischemic injury the causes may be

1- sever atherosclerosis => injury => trigger thrombus formation and lead to complete obstruction

The abdominal aorta and iliac bifurcation one of the preferred locations of atherosclerosis
So ischemic bowel diseases is one of the most common and frequent condition in old ages

2- embolus : dislodge part of thrombus when reach an area with same size it block it

It's origin often from the aorta or atheroma plaque or cardiac mural thrombi (as in arterial fibrillation thrombus)

3- mesenteric venous thrombosis : thrombosis in venous system as in Deep venous thrombosis

Deep venous thrombosis predisposing factors :
Inherited or acquired hypercoagulability

- Invasive neoplasm (a leukaemia type release substance ther increase coagulability)
- Cirrhosis (coagulation factor synthesised in liver)
- Trauma
- Abdominal masses and pregnancy in last months (because it lead to venous system stasis)

4- non obstructive settings

Normal blood vessels but there's a hypotension and bleeding and shock

5- sever dehydration (due to sever hypotension)

6- vasoconstrictive drugs

Pathogenesis of ischemic bowel disease:

First step / Obstruction and ischemic changes and tissue or cell degeneration or cell death

Second step/ reperfused injury (when the obstruction become opened again(iatrogenic) after it degenerate and have ischemia) lead to additional tissue damage due to that the cellular disruption allow the bacteria and its substance to reach the cell as the lipopolysaccharide which is a toxic material and cause tissue damage and blood supply full of O₂ to a cell with damaged mechanisms (ATP problems and other systems) so the O₂ react and form a free radicals and there's no anti-free radical mechanism So reperfused lead to form more free radicals which is a harmful substances +++ blood will contain neutrophil leukocytes which contain granular (inside the granules there's an anti microbial material so it's harmful for the surrounding tissue) +++ inflammatory mediators

Infarction severity depends on:

- 1- obstructed blood vessel (يعني هل هو فرع صغير ولا trunk)
- 2- duration of action (sudden more harmful than gradual)
- 3-degree of obstruction (complete or partially)

Distribution associated with the anatomy

Watershed zones (the area where supply ends [for example the point where SMA end and IMA begins]) this area is more sensitive to ischemic changes than other areas so in hypotension or shock this area is the most affected area [splenic flexure is a watershed area]

Ischemic change :

Tissue and cell necrosis

Inflammatory process will be added to the picture

**When there's an inflammatory process in the splenic flexure the Ischemic bowel diseases may be the cause
Or if the patient is old age or have a surgery or accident**

Crypts/villous circulation

there's a capillary system in the villi make a vascular hairpin [stem cell in crypts] so the basal part will receive more blood supply so morphologically when there's a crypts hyperplasia and the epithelial lining degenerated or have necrosis [these are an ischemic changes]

Ischemic bowel disease; morphology

- Colon is the most common
- Continuous or patchy (according to the anatomy blood supply)

Thickening of the wall + degenerative changes of the blood vessel wall

Note 🤔

If there's a transmural infarction (coagulation necrosis the cell architecture is normal but the nuclei is degenerated)

More sever in right sided cases (damaged part is colon and part of the small bowel so the consequences is more sever

May first as limited zones may progress to more extensive

CMV cause Ischemia

Radiation cause ischemia

Necrotizing enterocolitis (in children)

Angiodysplasia

Angiodysplasia is characterized by malformed submucosal and mucosal blood vessels that are dilated, tortuous and thin walled.

The most common cause of rectal massive serous bleeding in old ages

Pathogenesis: the movement and contractions of the organ and pressure differences lead to dilation and tortuosity so it's a mechanical function of the digestive system defect more than pathological cause

MALABSORPTION AND DIARRHEA

Carbohydrate, lipid, protein and vitamins should be absorbed in small bowel

If there is a defect in the absorption function => malabsorption syndrome (it's not a single dish but it's multiple causes and mechanisms)

steatorrhea, characterized by excessive fecal fat and bulky, frothy, greasy, yellow or clay colored stools

The chronic malabsorptive disorders most commonly encountered in the United States are pancreatic insufficiency, celiac disease, and Crohn disease

Malabsorption results from disturbance in at least one of the four phases of nutrient absorption:

- Intraluminal digestion, in which proteins, carbohydrates, and fats are broken down into forms suitable for absorption**
- Terminal digestion, involving hydrolysis of carbohydrates and peptides by disaccharidases and peptidases in the brush border of the small intestinal mucosa (enzymes at the surface in glycocalyx structure)**
- Transepithelial transport, in which nutrients, fluid, and electrolytes are transported across and processed within the small intestinal epithelium**
- Lymphatic transport of absorbed lipids**

Diarrhea is defined as an increase in stool mass, frequency, or fluidity, typically greater than 200 g per day.

Diarrhea types:

- Secretory diarrhea is characterized by isotonic stool and persists during fasting. May be caused by microorganisms as cholera .. secretion of fluid and electrolyte toward the stool (stop intake will not stop the diarrhea due to the microorganism)
- Osmotic diarrhea, (a material inside the lumen with high osmolarity that take water from the tissue) such as occurs with lactase deficiency the condition called lactose intolerance , is due to the excessive osmotic force exerted by unabsorbed luminal solutes. (occur in children who depends on milk) (stop intake will stop diarrhea)
- Malabsorptive diarrhea follows generalized failure of nutrient absorption, is associated with steatorrhea, and is relieved by fasting. It will affect the mass of stool and frequency of defecation
- Exudative diarrhea due to inflammatory disease is characterized by purulent, often bloody stools that continue during fasting. Caused by microorganisms as shigella and entamoeba histolytica