GastroIntestinal System



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Diseases of the esophagus 2

Hello everyone 2

In this sheet we will discuss many diseases that occur in the esophagus from a pathological point of view.. Are you ready? It will be a piece of cake 22

GstroEsophygeal Reflux Disease-GERD

-Now, we come to the most frequent cause of esophagitis and the most common complaint by patients which is the reflux esophagitis or what is called the "gastroesophageal reflux disease" because it is not always associated with esophagitis.

-It starts as a reflux, then it will become complicated with esophagitis.

-It is the result of reflux of gastric acidic contents into the lower parts of the esophagus through the regurgitation through the gastroesophageal junction GEJ.

-The squamous epithelium of the esophagus is highly sensitive to acids, it is not like the gastric mucosa which is resistant to the acids, **<u>SO</u>** the lower esophageal mucosa is affected by the recurrent acidic ulceration quickly.

-The esophagus normally produces **protective forces**, which protect the esophagus from the effect of these acids.

*These forces are:

Mucin and bicarbonates these will buffer the gastric juices and decrease the effects of the acidity on the esophagus
 SO if the secretion of these forces is decreased by any reason, the problem will get worse.

-In addition to that, in normal/resting situations, the lower esophageal sphincter tone is high (is enclosed), this will prevent the passage of gastric juices from the stomach to the lower esophagus, but if there is something decreases this tone or makes it relaxed like (Medications or certain habits) this will lead to reflux of gastric contents to the lower esophagus.

So in order to have reflux, we should have:

Decreased lower esophageal tone due to predisposing factors: {alcohol, Tobacco, The use of certain drugs like CNS Depressant}

OR

We have an increased abdominal pressure which will force the gastric contents through the sphincter to the lower esophagus. This will be due to: {Obesity, pregnancy -very common-, hiatal hernia, delayed gastric emptying and increased gastric volume} - However, there is no underlying cause for many cases of gastroesophageal reflux disease, these types of cases are called: <u>idiopathic</u>

In the patient comes to your clinic complaining of symptoms of the reflux such as:

-heartburn, -sensation of sour tasting fluid in their mouth

So what the clinician does if this problem is recurrent and not responding to treatment, is **Endoscopy**. During this operation, he is going to see macroscopically many things which differ according to the severity of the case, for example:



Microscopically:

- 1) We take a biopsy from that site.
- 2) The earliest manifestation is the infiltration by eosinophils: (we are not allowed to see eosinophils in the squamous mucosa of the esophagus, so if you see them, and your patient suffers from the previous symptoms then it is the earliest sign of reflux).
- 3) After that, GERD will enter more severe phase especially if there are ulcerations and a more acute presentation, here we will have a lot of <u>neutrophils</u>.
- 4) Other features are:

 ^Dhyperplasia, proliferation of the basal zone squamous epithelium, and elongation of the papillae of the lamina propria (the lamina propria will enter the epithelium through invaginations until it reaches the surface).

During endoscopy: L) Here this is the normal 9) pinkish mucosa of the But here you can see these normal esophagus tongues of reddish in the mucosa of the esophagus, this indicates the presence of inflammation We can see the other features like: V) basal cell hyperplasia, elongation of lamina propria We see these eosinophils we have many of them The biopsy features

CLINICAL FEATURES

How do these patients present?

Usually these patients are over the age of 40 years, but it can occur in infants and children



TREATMENT:

Proton pump inhibitors

...Prevent gastric acid secretion and by this we will ameliorate the symptoms.

Complications:

Sometimes it is complicated by:

stricture formation and stenosis (esophageal narrowing accompanied with swallowing difficulty

Barrett esophagus

••This is a very important symptom to ask about, so when you find it you should suspect an upper GIT bleeding and start to find the site of bleeding Esophageal ulceration, not just redness and erythema

Hematemesis: vomiting of blood.

Melena

Which is the passage of black fatty colored stools, this discoloration of the stool usually indicates an oil bleeding, it is not a symptom for gastroesophageal reflux disease only, it can come with any ulcerations such as(gastric ulcers, duodenal ulcers) or any bleeding that comes from the upper GIT (the blood's color is modified by acids, chemicals, and enzymes in the GIT, so when it is in the stool it will be black)

The most important feared complication of gastroenterology reflux disease is <u>Barrett esophagus</u>

Which can happen in long standing gastroesophageal Reflux (metaplasia: the squamous lining of the esophagus, which can't tolerate the acidity, turns into columnar or glandular epithelium, mostly it is in an intestinal type to tolerate the acidity of gastric juices)

This type of metaplasia might be a precursor for esophageal adenocarcinoma, so these patients should be treated and followed up to avoid this complication.

Now

We will talk about a new type of esophagitis which is called:

Eosinophilic Esophagitis

It is not an infection
It is not related to chemicals
It is a chronic immune mediated disorder

Symptoms:

... May vary and sometimes they may be similar to reflux esophagitis:

Sensation of food impaction
 Dysphasia -Difficulty in swallowing- in adults

THIS disease is considered an allergic reaction in children, so it can present in children with symptoms similar to GERD, also with feeding intolerance (the patient comes with regurgitation of food, failure to thrive, allergies to certain types of food and so on).

When the doctor suspect eosinophilic esophagitis, he will go into ENDOSCOPY

One of the typical findings of eosinophilic esophagitis is <u>rings in the upper and the middle of esophagus</u> Notice that these changes are **not** in the lower esophagus. **After that:**

we take the biopsy and see it microscopically; it will show numerous eosinophils (this is why they call it eosinophilic esophagus)

Remember DIN-GERD- we see eosinophils which are in the lower part of the esophagus near the BUT here they are numerous, presented in the upper & middle of MARCENT

Endoscopic picture





We can see the rings we call them webs or rings appearance in the middle and the upper esophagus

They are characteristic if they are seen <u>but not necessarily</u> <u>seen in all cases</u>

Here is a biopsy, in which you can see a lot of **eosinophils** infiltrating the squamous epithelium.



Now, how to differentiate between eosinophilic esophagitis and GERD?

Both of them show eosinophils, so it is always important to think of clinical history, the site of biopsy and the endoscopic findings to correlate.

SOO

If the patient is in lower age and says that he has some of food allergies or peripheral blood shows eosinophilia on the CBC, and if the doctor sees webs and rings IN THE Upper and middle parts of esophagus

Then the diagnosis will be " Eosinophilic esophagitis ".

*What makes us thinking of Eosinophilic esophagitis also is Atopic dermatitis, Eczema, allergic rhinitis, asthma and peripheral eosinophilia which can be detected by complete blood count (CBC)

Tx:

It is slightly different than GERD because these patients are refractory to proton pump inhibitors -if they take PPI they don't respond-

They respond to:

Dietary restrictions because they may show cow's milk allergy or soil products allergies So patients must avoid these products especially children

They are treated by **topical or systemic corticosteroids not PPI** because the problem here is not the acidity like in GERD, it is an immune mediated disorder

BARRETT ESOPHAGUS

It is an important complication of GERD, it is defined as intestinal metaplasia within the squamous mucosa.

Because of the chronic acidic irritation, the squamous mucosa turns into intestinal type epithelium.

Usually this is the most feared complication of GERD, which develops in 10% of individuals with symptomatic GERD.

² Males are affected more than females, and usually it occurs at an advanced age (40-60) years.

2 It is important because it's considered a precursor of esophageal adenocarcinoma

-What happens is that metaplasia transforms into dysplasia in a rate of 0.2 to 1 percent per year, and once the dysplasia develops, it can transform from low grade dysplasia to high grade dysplasia then to adenocarcinoma.

-That's why patients with BARRETT ESOPHAGUS are monitored closely for the development of dysplasia to prevent the formation of adenocarcinoma -Doing intervention before the disease advances-

Morphology:

Another macroscopic picture:

What we see during endoscopy:

Red tongues extending upward from the **GEJ**-Gastroesophageal junctionslightly similar to the changes in GERD

> These are tongues extending from GEJ upward

You can see hyperemia and the red colored mucosa because normally the esophagus is pink in color

This is the esophagus and this is lower esophageal sphincteric area,

You can see here that the folds are different from the gastric folds



and this is a part from the stomach -the gastric mucosa-

endoscopies with current endoscopies

The picture is somewhat like GERD but it's more severe and usually the doctor compares previous

Here is a microscopic appearance







Management of Barrett esophagus

...Periodic surveillance endoscopy with biopsy to screen for the presence of dysplasia.

Once we have dysplasia we should decide whether it is low grade or high grade, <u>BECAUSE</u> if it is high grade dysplasia and intra mucosal carcinoma, it needs surgical interventions before it progresses into more invasive carcinoma because intra mucosal just presents in the mucosa and in the lamina propria.

<u>While if it is more advanced</u>, (reaches the submucosa or the muscularis propria), the management will be different.

The final topic is neoplasticism disorders of the esophagus and esophageal tumors.



So it is very common in males compared to females

There is a **geographic and racial variation**; it is more common in developed countries which have certain food or nutritional habits that are associated with GERD, for ex. Obesity, smoking history. 22 All these may predispose to GERD and GERD may predispose to Barrett esophagus and then to adenocarcinoma



metaplasia to dysplasia to

adenocarcinoma

This sequence happens through acquiring genetic and epigenetic changes
 The most important of these mutations is Tp53 mutation and certain chromosomal abnormalities

Morphology

How do these tumors look?

²These tumors usually occur in the distal third of the esophagus because it's the site of GERD and BARRETT esophagus.

Early on, the lesions or the tumor is a flat or slightly raised patches.
 Later on, it becomes exophytic tumor, bulky tumor with infiltration, and sometimes with ulceration.

Microscopically (Forming glands and mucin)



CLINICAL FEATURES

-How do these patients present?

Usually they present with:

-pain -Odynophygia-

Difficulty in swallowing -dysphasia-

-Progressive weight loss (cachexia), which is associated with malignancy -Chest pain

-Vomiting or regurgitation of food due to the mechanical obstruction of the esophagus.

2 The main problem in adenocarcinoma that they are **presented late** (in advanced stage), so usually when the representation occurs, the tumor will be large, invasive of the wall of the esophagus because the esophagus is devoid of serosa, which makes the invasion easier to the mediastinum area. (the 5-year survival here would be 25%)

2 The 5-year survival depends on the time of a presentation If these tumors <u>are in early stage (Barrett esophagus, dysplasia, early intramucosal</u> <u>carcinoma)</u> the 5 year survival is 80%

Another type of tumor type is squamous cell carcinoma



PATHOGENESIS:

--In western countries:

alcohol and tobacco use are the most important factors in pathogenesis which will lead to acquiring mutations in the squamous epithelium \rightarrow squamous carcinoma **--Other areas in the world :**

exposure to polycyclic hydrocarbon, nitrosamines, fungus-contaminated foods \rightarrow squamous carcinoma

Nowadays, they think that HPV infection is implicated as another cause of squamous cell carcinoma in high risk regions.

MORPHOLOGY:

-<u>The difference between squamous cell carcinoma and adenocarcinoma is that:</u> 2 the squamous cell carcinoma:

- ■-can occur in the middle third of the esophagus in 50% of cases @while adenocarcinoma:
- --occurs at the level of the lower esophageal sphincter

-<u>Squamous cell carcinoma</u> usually presents as a mass, polypoid, ulcerated or infiltrative, it can cause thickening of the wall as a result for the infiltration by the tumor, with narrowing of the lumen which will lead to difficulty in swallowing.

••They can invade the surrounding structures like bronchi, mediastinum, pericardium, and aorta, especially if the disease is advanced.

MICROSCOPICALLY:

••They have a precursor lesion, but it is not Barrett and the associated dysplasia of Barrett, it is squamous dysplasia and carcinoma in cyto -in the squamous epithelium itself-

••These tumors can be well to moderately differentiated, invasive squamous cell carcinoma or poorly differentiated.

**What distinguishes these tumors that when they are in the esophagus they form intramural tumor nodules away from the main tumor.

-Metastasis

This type of tumors is a <u>carcinoma</u>, so first the metastasis will be in the LNs through the lymphatics, and later on, the disseminated spread might occur. Uymph node metastasis depends on the site of tumor:

If it is in the upper 1/3 of the esophagus it will go to the cervical LNs in the neck
 If it is in the Middle 1/3 of the esophagus it will go to the mediastinalparatracheal and tracheobronchial LNs

If it is in the Lower 1/3 of the esophagus it will go to the gastric and celiac LNs

CLINICAL FEATURES:

You can't distinguish between adenocarcinoma and squamous cell carcinoma, because both of them will present with:

Dysphasia
 Odynoghagia -Due to the mechanical obstruction by the mass Weight loss and debilitation which is a general feature of most of malignancies
 Impaired nutrition and the tumor associated cachexia الهزال
 Hemorrhage and sepsis if ulcerated

••These tumors may form a visual fistula with the trachea -tracheoesophageal fistuladue to the invasive growth and this can lead to aspiration

-SCC has a dismal prognosis, the 5-year survival is <9%







-Abundant eosinophilic cytoplasm -pink-

*It can vary from well to moderately to poorly differentiated tumors

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