

Pathology

● Sheet

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number

2

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Correction

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Note: I included everything in the slides.

In this lecture we will continue talking about the esophagus, specifically inflammation and tumors of the esophagus.

There are 4 types of diseases related to the esophagus:

1. Obstruction
2. Vascular diseases
3. Inflammation
4. Tumors/neoplasm

We mentioned 1 condition of inflammation which is Mallory-Weiss syndrome (MWS), it is a condition marked by a tear in the mucous membrane or inner lining, it occurs where the esophagus meets the stomach.

Inflammation of the esophagus is similar to any other organ inflammation and they include the cardinal signs of inflammation which are: redness, swelling, pain and decrease of function.

Inflammation of the esophagus also includes edema, chest pain (can mimic myocardial infarction), dysphagia (difficulty in swallowing) and odynophagia (pain in swallowing).

What are the causes of esophagitis (inflammation of the esophagus) in general?

Reflux of acid from stomach, infections, chemicals (irritants), swallowing of foreign material, swallowing of capsules (drugs) without water and heavy smoking.

1. Chemical esophagitis

Inflammation of the esophagus can result from chemicals like: drinking alcohol (an important cause), acids and bases, hot fluids (if drank too quickly) and heavy smoking, radiotherapy and chemotherapy of the chest can also cause chemical esophagitis.

Note that esophagitis caused by acids and bases is called caustic esophagitis.

Smoking (irritant) also causes harm to the lungs.

If people swallow capsules without water, it's going to lodge into the esophagus and dissolve there and causing irritation; this is called *pill induced esophagitis*.

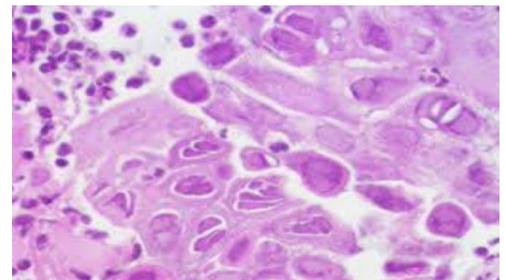
2. Esophagitis caused by infections

Infections by microorganisms can cause inflammation of the esophagus; it is mainly caused by viruses such as Herpes Simplex, Cytomegalovirus (CMV) or by fungal infections such as Candida.

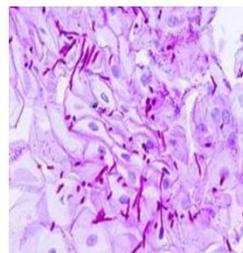
The risk of esophagitis caused by infections can increase in people with immunodeficiency.

Herpes and CMV cause punched out ulcers and shallow ulcers respectively, while candida causes white pseudo membrane formation (in the mouth) that can be scraped and removed.

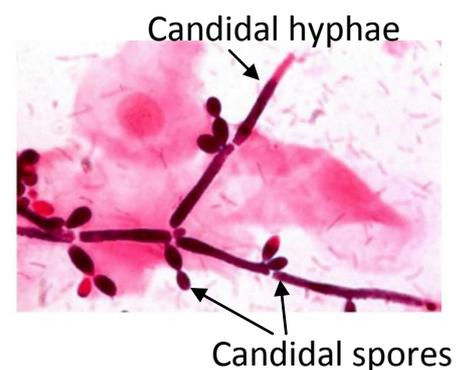
Nuclear inclusions (large bodies within the nucleus) are a characteristic of herpes as seen in the picture.



Candida (fungus/ yeast) have spores and hyphae as seen in the picture on the right.



We use PAS stain to view the Candida under the microscope.



3. Eosinophilic esophagitis

Is a recognized chronic allergic/immune condition.

Incidence of eosinophilic gastritis is increasing all over the world, including Jordan.

Symptoms include food impaction (occurs when food becomes stuck in your esophagus) and dysphagia (difficulty in swallowing), the causes are unknown but it's probably due to bad diets.

Patients with eosinophilic esophagitis also have other allergic diseases like atopic dermatitis, allergic rhinitis, asthma, eczema. And we can see high numbers of eosinophils due to allergy conditions in eosinophilic esophagitis.

Eosinophilic esophagitis is not treated with the same treatment used for acid reflux esophagitis (most common cause of esophagitis). Because in acid reflux esophagitis, we use proton pump inhibitors that work on reducing the acidity of the stomach. If you give proton pump inhibitors to a patient with eosinophilic esophagitis they will not respond, so if a patient comes to you with signs and symptoms of esophagitis, and you assumed it is reflux esophagitis and gave him proton pump inhibitors but it didn't work for him then it's probably eosinophilic esophagitis, we can take a biopsy to confirm the diagnosis

Eosinophilic esophagitis has specific treatments:

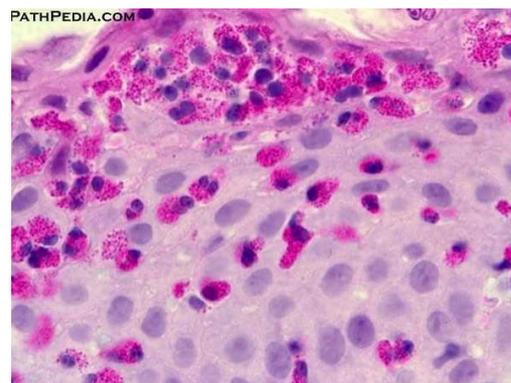
1. Dietary restriction of food allergens like milk and soy products.

2- Steroids (main treatment) are used to treat eosinophilic esophagitis because they are anti-inflammatory and decrease the allergy conditions

00:00 – 10:00.

If a patient comes to you with signs and symptoms of esophagitis, the first thing you do is that you take a biopsy by endoscopy (entering a tube

or an instrument and taking a biopsy), if you look under the microscope and find numerous eosinophils as seen in the picture, then its eosinophilic esophagitis.



4. Reflux esophagitis

Also called gastro esophageal reflux disease GERD.

GERD is the inflammation of the lower part of the esophagus due to reflux of gastric content, which are acidic, from the stomach to the esophagus causing mucosal injury in the esophagus, GERD is the most common cause of esophagitis.

Causes of this reflux:

1. **Decreased lower esophageal sphincter tone** results from relaxing and not being able to constrict the sphincter, allowing the stomach content (acidic) to go to the esophagus, this is caused by smoking and alcohol consumption.
2. **Increased abdominal pressure** caused by obesity and pregnancy by applying pressure onto the sphincter allowing of gastric content reflux.
3. **Delayed gastric emptying**, food content of heavy meals remain in the stomach for longer periods of time increasing gastric volume, this causes pressure and reflux.
4. **Over production of acids** and stomach irritation.

Note : In many cases, there are unknown causes (idiopathic)

Morphology of GERD: Hyperemia: redness seen macroscopically or during endoscopy, edema can also be seen during endoscopy.

Microscopically: eosinophils, neutrophils, basal zone hyperplasia, elongation of lamina propria papillae

Clinical features of GERD: It occurs in adults older than 40, symptoms of GERD include heartburn due to high acidity in the esophagus, dysphagia and sometimes odynophagia, regurgitation and rarely, severe chest pain that can mimic cardiac arrest .

Complications of GERD include

1. ulcerations (any severe inflammation can cause ulceration, which is a defect in the mucosa)

2. strictures (due to stenosis; cycles of inflammation, healing and fibrosis during obstruction)

3. Barrett's mucosa. (metaplastic mucosa)

5. Barrett's esophagus

Barrett's esophagus is a very important disease, it is a complication of gastroesophageal reflux (GERD) in which 10% of people with symptomatic GERD will have barrett's esophagus. Males are more affected than females, patients with barrett's esophagus have an increased risk of esophageal malignancy. (adenocarcinoma)

Barrets esophagus is when the esophagus is under infammation, chemicals or irritations, the esophageal mucosa that is normally stratified squamous undergoes metaplasia into glandular columnar epithelium, either gastric type epithelium or intestinal type epithelium.

Columnar intestinal type epithelium is characterized by the presence of goblet cells.

In barrets, we can see normal squamous epithelium (light coloured in the picture) with tongues/patches of red mucosa extending upwards (metaplastic).

If you want to take a biopsy to see barrets esophagus, you have to be away from the sphincter, because theres a transitional area where the stomach and the esophagus meet, in which the epithelium is suqamous, with columnar underneath (mixture). So to take a correct biopsy and diagnose barrett's eosphagus, you have to be 3 cm above the gastroesophageal junction (where the transitional area is).

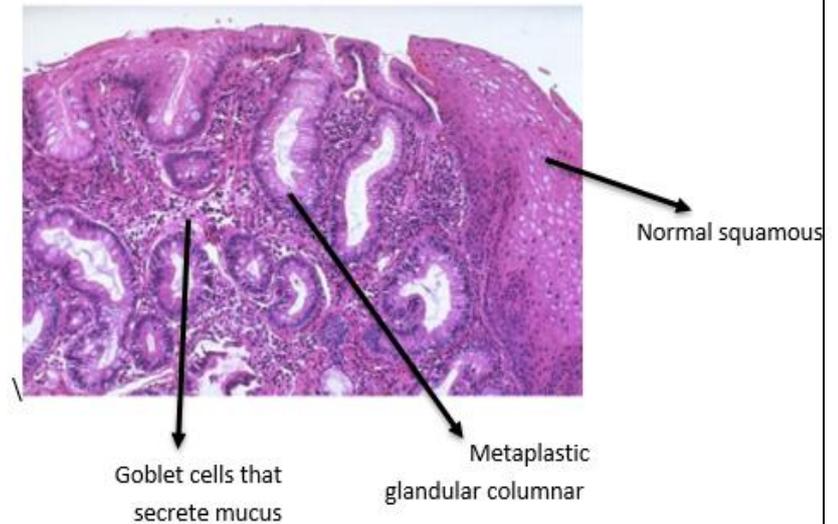


Glandular columnar metaplastic epithelium

Normal squamous

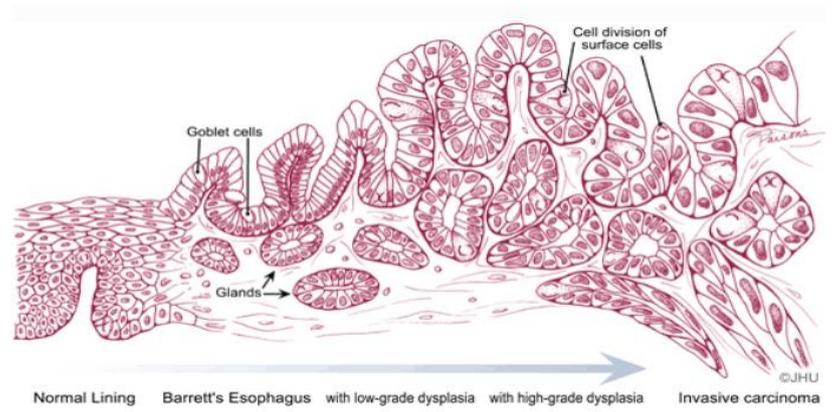
10:00 – 20:00

This is a light microscope image, note the esophageal squamous, then there is metaplastic glandular epithelium with white mucin secreting cells known as *goblet cells*. So if you see glandular mucosa especially with the presence of goblet cells then its definitely barrets metaplastic mucosa. However, we can also find barrets mucosa without goblet cells if its **gastric type**, so presence of goblet cells is an important feature but not the only one.

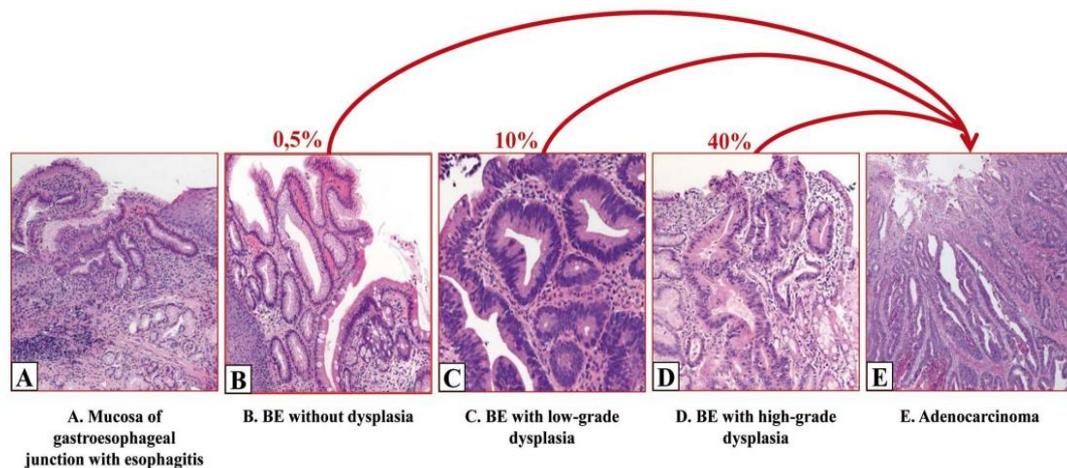


What is dangerous about Barrets Esophagus is that dysplasia can occur in barretts (around 1% of cases) as a development of metaplastic epithelium dysplasia can then develop into invasive carcinoma. thats why Barretts Esophagus can results in cancer sometimes.

Dysplasia is the abnormality in maturation of organized metaplastic cells that have cytoplasm, nucleus, goblet cells but with abnormal shape of nuclei and high rate of mitosis, stratification of nuclei. Also, the cells can not be found in any tissue of the body.



Treatment of Barretts Esophagus: ectomy of high grade dysplasia.
Following up with the patients is very important, as only 0.5% of barrett



esophagus without dysplasia can develop into adenocarcinoma. 10% of BE (barrett's esophagus) with low grade dysplasia and 40% of BE with high grade dysplasia can develop adenocarcinoma, So we must follow up with the patient and do endoscopy every 3-5 years (in early stages). Removal of the esophagus can be done, or removal of a part of it (in case of high grade).

We finished talking about inflammation, now we will talk about tumors of the esophagus.

Tumors of the esophagus.

There are 2 types of esophageal cancer:

1. Adenocarcinoma (resulting from Barretts Esophagus)
2. Squamous cell carcinoma (from normal lining)

Squamous cell carcinoma was the most common type of esophageal carcinoma until 1970, after that food habits were getting worse and barrett's mucosa incidence got higher, increasing development of adenocarcinoma. Today, adenocarcinoma is the most common type of esophageal cancers especially in the western world.

20:00-30:00

However, esophageal cancer is not very common in Jordan according to *Jordan Cancer Registry 2013 statistics*.

	number	% of overall cancers
males	13	0.5%
females	11	0.4%
overall	24	0.4%

Male to female ratio in Jordan is almost 1:1. While in the rest of the world, male to female ratio is 7:1 for adenocarcinoma.

1. Adenocarcinoma

Risk factors of adenocarcinoma include: GERD and Barrett's mucosa, smoking, alcohol, obesity, previous radiotherapy sessions taken by the patient.

Risk is reduced with diets rich in fruits and vegetables. Highest rates of adenocarcinoma can be found in USA, UK, Canada, Australia, while the lowest rates are found in Korea, Japan and Thailand.

Pathogenesis of Barrett's to adenocarcinoma:

Barrett epithelium acquires several genetic mutations over a period of time transforming into adenocarcinoma due to high proliferation of squamous stem cells to columnar, resulting in a mutation in the TP53 gene which is a common mutation of adenocarcinoma. Inflammation also enables malignant transformation from Barrett's mucosa to adenocarcinoma.

Adenocarcinoma affects the lower distal third of the esophagus near the sphincter (which is the site of Barrett).

Gross appearance: exophytic masses or ulcers.

Microscopy: tumor forming glands and producing mucin

Clinical features include: weight loss, chest pain, vomiting, dysphagia and odynophagia. (weight loss is always associated with malignant neoplasms).

Prognosis: If we diagnosed adenocarcinoma when its limited to the mucosa or submucosa (early stage), 80% of patients live for 5 years.

If we diagnosed it in the late stages (advanced disease) only 25% of patients live for 5 years.

That's why if a patient has barretts esophageus we need to follow up with him, so it depends on stage (extent of invasion and spread)

2. Squamous cell carcinoma

It affects adults older than 45, and the male to female ratio is 4:1

Risk factors of squamous cell carinoma include: alcohol, smoking, poverty, caustic injury, achalasia, frequent consumption of very hot drinks, previous radiotherapy.

Higher incidence of SSC can be found in : Iran, China, Hong Kong

Morphology

Usually in the middle third of the esophagus (recall that adenocarcinoma was in the lower part)

Under the microscope SCC appears usually as a polypoid mass. we can't see glands, we can see squamoid structures with keratin.

They spread to adjacent structures and to lymph nodes early in their development because of the rich lymphatic supply

Clinical features: dysphagia, odynophagia, weight loss.

Prognosis : 75% of patients diagnosed while the tumor is still superficial and did not spread will have 5-year survival. Much worse prognosis can be seen if diagnosed in an advanced stage. Unfortunately the overall, 5-year survival rate is 9%; as the majority of cases are discovered in late stages. (Unlike in Adenocarcinoma, in which you can follow up with patients that have Barrett's esophagus).

30:00-37:00

The End