Diseases of the esophagus

Disorders of esophageal motility

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Esophageal motility disorders

- Esophageal motility disorders are diseases attributable to esophageal neuromuscular dysfunctions.
- They are commonly associated with symptoms as dysphagia, heartburn and chest pain.
- The most common are achalasia, diffuse esophageal spasm and motility disorders related to GERD.
- Motility disorders can also be secondary to broader disease processes as in the case with pseudoachalasia, Chagas’ disease and scleroderma.
Diagnostic studies for esophageal motility disorders

**Endoscopy:**
- Detection of mucosal or structural lesions (hiatal hernia)
- Confirm strictures
- Detection of abnormality as Barrett’s esophagus
- Biopsy of mucosal lesions

**Radiography:**
- Detections of mucosal or structural lesions (hiatal hernia)
- Confirm strictures (sensitivity better than endoscopy)
- Assessment of esophageal function and motility
- Allows videofluoroscopic recording

**Esophageal manometry:**
- High Resolution Manometry (HRM)
- Gold standard to diagnose motility disorders
- To assess peristaltic integrity prior to the surgery for GERD
Esophageal motor disorders: esophageal manometry

Diagnostic studies

Conventional radiology
CT
MR
Endoscopy
EUS (endoscopic US)
Manometry
pH-metry
Conventional manometry
High-resolution esophageal pressure topography (right) and conventional manometry (left) of a normal swallow. UES, upper esophageal sphincter; E, esophageal body; LES, lower esophageal sphincter.
Disorders of UES
Neurological lesions causing failed UES relaxation

Failure of EUS to relax causes oro-pharyngeal dysphagia (difficulty in initiating the swallowing, passage of food in the hypopharynx and tracheal aspiration and regurgitation in the nasal cavity)

Causes are:
- Lateral medullary infarction
- Parkinson's disease
- Other extrapyramidal movement disorder
- Brainstem tumor
- Syringobulbia
- Brainstem compression secondary to cerebral haemorrhage
- Amyotrophic lateral sclerosis
- Idiopathic

Failure of UES relaxation is not a diagnosis as such, rather it is a functional abnormality caused by neuronal dysfunction within the central nervous system that may be a manifestation of a number of neurologic syndromes.

Cricopharyngeal myotomy or botulinum toxin injection remains unproven therapy
Disorders of esophageal body and LES
Achalasia

It is an incurable disease characterized by incomplete or absent relaxation of the LES and aperistalsis of the esophageal body.

Is a rare disease caused by loss of ganglion cells within the esophageal myoenteric plexus. In long-standing disease virtual aganglionosis is noted.

Population incidence: 1:100,000/year
Population prevalence: 10:100,000

Age: 25-60 yrs

Increasing evidence suggests that the ultimate cause of ganglion cells degeneration is an autoimmune process attributable to a latent infection with human herpes simplex virus 1 combined with genetic susceptibility.
Left: The normal condition includes excitatory, cholinergic (Ach) motor neurons that innervate the smooth muscle cells of the LES and contribute to the genesis of basal pressure of the LES, and inhibitory, nitric oxide (NO) motor neurons acting on the LES to produce the relaxation that accompanies a swallow.

Middle: Achalasia resulting from the loss of inhibitory neurons. In this situation, the absence of NO motor neurons results in an elevation in the basal LESP and absence of swallow induced relaxation of the LES. Esophageal aperistalsis is defined by simultaneous esophageal body contractions.

Right: Achalasia with complete loss of myenteric neurons. Here the basal LESP is below normal owing to the absent excitatory neurons, and swallow-induced relaxation is absent owing to the lack of inhibitory neurons. Esophageal body doesn’t contract.
Achalasia: Etiological classification

Idiopathic achalasia

Secondary achalasia or pseudoachalasia

Malignancy (carcinoma of the stomach, esophagus, lung, lymphoma and mesothelioma)
Paraneoplastic (pancreas, liver, colon, prostate)
Chagas' disease
Neuropathic chronic intestinal pseudo-obstruction syndrome
Eosinophilic gastroenteritis
Neurodegenerative disorder with Lewy inclusion bodies
Amyloidosis
Postvagotomy
Multiple endocrine neoplasia type IIb
AAA syndrome: achalasia associated with alachrimia (juvenile Sjögren's syndrome) and achlohydria
Von Recklinghausen's neurofibromatosis
Anderson-Fabry disease
Sarcoidosis
Achalasia: Symptoms

Clinical manifestations include:

- **Dysphagia** initially for liquid (paradoxal dysphagia) and then complete
- **Regurgitation** occurs when food, fluids and secretions are retained in the dilated esophageal lumen
- **Chest pain** as the result of esophageal spasm, described as a pressure-like retrosternal pain irradiating to the neck, arms and back
- **Hearthburn**
- **Weight loss**

Patients may also present with a complication of long standing achalasia:

- **esophageal carcinoma:** is seen in approximately 5%, and most often in the mid esophagus. It is thought to relate to the chronic irritation of the mucosa by stasis of food and secretions. The histological type is represented by squamous cell carcinoma (SCC)
- **aspiration pneumonia** and eventually **abscess formation**
- **candida esophagitis**
- **acute airway obstruction:** this is a rare complication requiring immediate esophageal decompression with nasogastric tube
Endoscopic findings of retained saliva, liquid, and food in the esophagus without mechanical obstruction from stricture or mass should raise suspicion for achalasia.
The endoscopic signs indicating an achalasia are:
(a) esophageal dilatation
(b) abnormal retention of liquid and/or food
(c) whitish change of the mucosal surface
(d) functional stenosis of the esophago-gastric junction
(e) abnormal contraction
A barium swallow is able to not only confirm that the esophagus is dilated but is also to assess for mucosal abnormalities.

Findings include:

• failure of normal peristalsis to clear the esophagus of barium when the patient is in the recumbent position, with no primary waves identified
• uncoordinated, non-propulsive, tertiary contractions
• esophageal body dilatation, which is typically maximal in the distal esophagus
• pooling or stasis of barium in the esophagus when the esophagus has become atonic or non contractile (late feature in the disease)
• when barium column is high enough (patient standing) the hydrostatic pressure can overcome the LES pressure allowing passage of esophageal content
• incomplete LES relaxation that is not coordinated with esophageal contraction
• bird beak sign
• long standing achalasia is characterized by progressive dilatation and sigmoid deformity of the esophagus with hypertrophy of the LES.
Uncoordinated, non-propulsive, tertiary contractions

Bird beak sign (a becco d’uccello - coda di topo)
Esophageal dilatation

Megaesophagus
Achalasia with esophageal dilatation, tapering at the gastroesophageal junction and an air-fluid level within the esophagus. The example on the left shows sigmoid deformity with very advanced disease.
Conventional esophageal manometry
No distal esophageal pressurization is evident and all the contractions elicited by liquid swallows have an amplitude lesser than 30 mm Hg.
Simultaneous isobaric esophageal pressurization is evident at HRM and all the contractions elicited by liquid swallows have an amplitude higher than 30 mmHg, with normal duration. Type II has the best results with treatment.
High-resolution manometric picture of rapidly propagating pressurization with spastic contractions. The high amplitude contractions of the distal esophageal body is represented by the red high-pressure area of the esophageal body contraction. (A) Conventional manometry of long-lasting, high-pressure spastic esophageal contraction.
Two classes of drugs, nitrates and calcium channel blockers, have LES muscle-relaxing effects. These drugs can decrease symptoms in people with achalasia. The drugs are usually taken by placing a pill under the tongue 10 to 30 minutes before meals.

Drug therapy is the less invasive and safest option for treating achalasia. However, most people find that long-term drug therapy is inconvenient, ineffective and often associated with unpleasant side effects, such as headache and low blood pressure. Furthermore, the drugs tend to become less effective over time. For these reasons, medications are recommended primarily for patients who are not interested in or not healthy enough for mechanical treatments such as balloon dilatation and surgery (myotomy).
Dilatation is the most common approach to treating the patient with achalasia. Pneumatic dilatation is performed endoscopically.

Patients are sedated with intravenous medications. Esophageal lavage and aspiration of gastric contents are performed prior to positioning the endoscope in the antrum. A stiff guide wire is advanced through the biopsy channel of the scope and positioned in the antrum (A). The dilator is passed over the guide wire and advanced through the gastroesophageal junction. The balloon is slowly inflated and held in position. Gradual increase in the size of the dilator may be necessary (B). The objective is to stretch the circular muscle of the lower esophageal sphincter to allow the passage of solids and liquids without subsequent reflux or perforation (C,D).
Intrasphincteric injection of the potent neurotoxin botulinum toxins a safe and effective in the majority of patients.

The procedure involves injection of the lower esophageal sphincter causing a chemical denervation of the sphincter. Twenty to 25 units of botulinum toxin are injected into each quadrant of the lower esophageal sphincter with a sclerotherapy needle passed through the endoscope. Although it is the safest of available techniques, botulinum toxin injection has a limited duration of effect, lasting on average one year. Repeat treatment is necessary to maintain the effect. Some patients may experience mild chest pain and there have been reports of skin rashes noted after treatment.
Minimally invasive surgery, using either a laparoscopic or a thorascoscopic technique has significantly decreased the morbidity associated with achalasia surgery.

A single anterior lateral myotomy or a modified Heller myotomy is typically the surgical procedure performed. A lower esophageal sphincter myotomy incises enough muscle to relieve symptoms but not enough to result in gastroesophageal reflux. In many cases, an antireflux procedure is performed at the same time.
Patients with achalasia

Low surgical risk

- Pneumatic dilatation
  - 3.0 cm
  - 3.5 cm
  - 4.0 cm

- Myotomy

High surgical risk

- Botulinum toxin

Failure

- Repeat myotomy or PD
- Esophagectomy

Nitrates
Calcium channel blockers
Diffuse esophageal spasm (DES)
Diffuse esophageal spasm (DES) is a condition in which uncoordinated contractions of the esophagus occur.

It is thought to result from abnormal esophageal contraction with normal deglutive LES relaxation. As consequence, these spasms do not propel food effectively to the stomach.

The pathophysiology and the natural history of DES are poor defined.
Diffuse esophageal spasm
Symptoms

Symptoms are chest pain, dysphagia and regurgitation.

Chest pain is the most prevalent symptom of DES and can mimic angina pectoris.

A cardiac origin of pain must be excluded.

Chest pain is usually prolonged, interrupts sleep, meal-related, relieved with antiacids, accompanied by heartburn, dysphagia and regurgitation.
Radiographically, DES has been characterized by tertiary contractions or a “corkscrew esophagus”, but in many instances these abnormalities are actually indicative of achalasia.

The characteristic “corkscrew” esophagus results from spastic contraction of the circular muscle in the esophageal wall; more precisely, this is actually a helical array of muscle. These findings are also seen with spastic achalasia.
Corkscrew esophagus

Nutcracker esophagus

a. - Immagine radiologica
b. - Immagine endoscopica
c. - Immagine 3D (tramite TC)
Esophageal pressure topography of the two major variants of esophageal spasm: spastic nutcracker (left) and diffuse esophageal spasm (right). Spastic nutcracker is defined by the extraordinarily vigorous (an amplitude > 180 mmHg) and repetitive contractions with normal peristaltic onset. DES is similar but primarily defined by a rapid propagation at the onset of the contraction.
Plots show simultaneous standard manometry and contour plot topography from two water swallows from the same patient. a: High-amplitude, double-peaked and long duration propagated esophageal body contractions with partial LES relaxation. b: Simultaneous distal esophageal body contractions of normal amplitude and failed LES relaxation. c: Barium esophagram from the patient with a corkscrew-like morphology. This case illustrates the variable motility abnormalities that can be present at any one time with overlapping features of esophageal spasm and achalasia.
Diffuse esophageal spasm: therapy

Given this vagaries of defining DES and the resultant heterogeneity of patients identified for inclusion in therapeutic trials, it is not surprising that trial results have been disappointing.

Only small, uncontrolled trials exist, reporting response to:
- Nitrates
- Calcium channels blockers
- Hydralazine
- Botulinum toxin
- Anxiolytics

Surgical therapy (long myotomy or even esophagectomy) should be considered only with severe weight loss or unbearable pain. These indications are extremely rare.
Nonspecific manometric findings

Non-specific esophageal motility disorder is not a real diagnostic entity, but only a group of manometric abnormalities.

It is uncertain that these disorders have a common etiology.

Manometric studies done to evaluate chest pain and/or dysphagia often report minor abnormalities that are insufficient to diagnose either achalasia or DES.

These include:
Abnormal peristalsis (nonperistaltic or low amplitude lesser than 30 mmHg contractions) occurring during ≥20% of wet swallows
- Retrograde
- triple-peaked contractions
- prolonged contractions >6 s
Hypertensive LES or isolated incomplete LES relaxation

Therapy should target the most common esophageal disorders, GERD, or more global conditions as depression or somatization that are found to be coexistent.
Hierarchical Analysis of Esophageal Motility

*The Chicago Classification*

1. IRP ≥ upper limit of normal AND absent peristalsis
   - No → Yes

2. IRP ≥ upper limit of normal AND some instances of intact or weak peristalsis
   - Yes
   - EGJ Outflow Obstruction
     - Achalasia variant
     - Mechanical obstruction
     - May have 1° or 2° hypercontractility
   - No

3. IRP is normal AND absent peristalsis OR reduced distal latency OR DCI > 8,000 mmHg-s-cm
   - Yes
   - Absent Peristalsis
     - Distal Esophageal Spasm (DES)
       - ≥ 20% of swallows with reduced latency
     - Hypercontractile (Jackhammer) Esophagus
       - Any swallow with DCI > 8,000 mmHg-s-cm
   - No

4. IRP is normal AND Peristaltic abnormalities
   - Yes
   - Weak Peristalsis
     - Large or small breaks in the 20-mmHg isobaric contour
   - Frequent Failed Peristalsis
     - Hypertensive Peristalsis (Nutcracker Esophagus)
   - Rapid Contraction
     - ≥ 20% of swallows with rapid contraction

Normal
<table>
<thead>
<tr>
<th>Metric</th>
<th>Description</th>
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<tbody>
<tr>
<td>Integrated relaxation pressure (mmHg)</td>
<td>Mean EGJ pressure measured with an electronic equivalent of a sleeve sensor for four contiguous or non-contiguous seconds of relaxation in the ten-second window following deglutitive UES relaxation</td>
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<tr>
<td>Distal contractile integral (mmHg-s-cm)</td>
<td>Amplitude x duration x length (mmHg-s-cm) of the distal esophageal contraction &gt;20 mmHg from proximal (P) to distal (D) pressure troughs</td>
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<td>Contractile deceleration point [(CDP) (time, position)]</td>
<td>The inflection point along the 30 mmHg isobaric contour where propagation velocity slows demarcating the tubular esophagus from the phrenic ampulla</td>
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<tr>
<td>Contractile front velocity (cm s−1)</td>
<td>Slope of the tangent approximating the 30 mmHg isobaric contour between P and the CDP</td>
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<td>Distal latency (s)</td>
<td>Interval between UES relaxation and the CDP</td>
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<tr>
<td>Peristaltic breaks (cm)</td>
<td>Gaps in the 20 mmHg isobaric contour of the peristaltic contraction between the UES and EGJ, measured in axial length</td>
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Conventional esophageal motility tracing from a patient with diffuse esophageal spasm demonstrating simultaneous contractions of the esophageal body with intact LES relaxation in >20% of swallows.