MAYO CLINIC

39-Year-Old Man With Dysphagia

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See end of article for correct answers to questions.

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A 39-year-old man with no notable medical history presented for evaluation of dysphagia. He reported a several-year history of intermittent but progressive difficulty swallowing both solids and liquids. He had been able to manage his symptoms by using water to flush foods, drinking carbonated beverages, and elevating the head of his bed. He did not experience choking or coughing with swallowing. Two weeks before presentation, he began to feel generally unwell, with worsening dysphagia and regurgitation of undigested food, chest discomfort, and decreased oral intake. He did not have nausea, abdominal pain, diarrhea, constipation, melena, hematochezia, hematemesis, odynophagia, unexplained weight loss, night sweats, exertional chest pain, dyspnea, orthopnea, neck pain, recent trauma, or recent travel outside the United States.

On physical examination, the patient's body mass index (calculated as weight in kilograms divided by height in meters squared) was 22 kg/m^2, and he was afebrile, normotensive, and in no acute distress. Cardiopulmonary examination revealed a regular heart rate and rhythm, no murmurs or gallops, no jugular venous distention or lower extremity edema, and clear lungs on auscultation bilaterally. He had moist mucous membranes, a soft nontender abdomen with active bowel sounds, no ascites, and no organomegaly. Laboratory studies revealed a hemoglobin level of 11.6 g/dL (reference range, 13.5-17.5 g/dL) with a normal mean corpuscular volume, and results of the complete blood cell count and electrolyte panel were otherwise unremarkable. Electrocardiography (ECG) identified a normal sinus rhythm with no ischemic changes, and cardiac enzymes were undetectable.

1. Based on the history and physical examination findings, which *one* of the following tests should be ordered *first*?

a. Transthoracic echocardiography (TTE)
b. Computed tomography of the neck
c. Video-assisted swallow study
d. Chest radiography
e. Barium esophagography

This patient presented with progressive dysphagia with both solids and liquids. The differential diagnosis includes an esophageal motility disorder and mechanical obstruction due to intrinsic or extrinsic compression of the esophageal lumen. With respect to the evaluation for extrinsic compression, the anatomic structures surrounding the esophagus should be considered. Causes of extrinsic compression include an enlarged left atrium, aberrant subclavian artery, cervical osteophytes, and mediastinal masses. Although TTE would help identify cardiac causes of dysphagia, the patient does not have any personal or family history of cardiac disease and has normal ECG findings and cardiac biomarkers. Therefore, TTE is not the best initial test.

Cervical osteophytes are also known to produce extrinsic compression of the esophagus. If this condition is suspected, computed tomography of the neck would be helpful, but our patient has no history of trauma or musculoskeletal disease. Video-assisted swallow studies are useful in identifying oropharyngeal dysfunction that may be leading to dysphagia. This patient's symptoms and history are suggestive of esophageal dysphagia, given his description of using water to flush down foods and no history of choking or coughing with swallowing.

Depending on the underlying cause of dysphagia, chest radiography may yield several findings, including a widened mediastinum from a dilated esophagus, absent gastric air bubble from incomplete lower esophageal sphincter (LES) relaxation, a mediastinal mass, an enlarged left atrium, or an air-fluid level in the upper chest due to retained fluid in the esophagus. Although these findings may be suggestive of underlying pathology, they would not be diagnostic. Thus, chest radiography would not be the first test used to evaluate dysphagia. Barium esophagography can identify luminal patency

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and may also provide information about esophageal motility. Therefore, it is the best initial test to evaluate our patient's dysphagia.

Barium esophagography revealed a markedly dilated esophagus with a maximum diameter of 8.8 cm (normally 2-3 cm). The esophagus had a sigmoid configuration, and a large amount of retained food and secretions was noted. Additionally, there was considerable narrowing at the gastroesophageal junction and very poor esophageal emptying.

2. In view of the findings on esophagography, which *one* of the following is the *most likely* diagnosis?

a. Primary achalasia
b. Amyloidosis
c. Eosinophilic esophagitis (EoE)
d. Chagas disease
e. Amyotrophic lateral sclerosis

Achalasia or pseudoachalasia is the most likely diagnosis in this patient on the basis of the barium esophagographic findings of esophageal dilation, poor esophageal emptying, and narrow gastroesophageal junction with the classic "bird's-beak" deformity. The patient's age, history of dysphagia with solids and liquids, and regurgitation of undigested food support this diagnosis. Gastrointestinal (GI) amyloidosis is frequently associated with GI tract dysmotility, including dysphagia, gastroparesis, and intestinal pseudoobstruction. Yet, it is uncommon for GI amyloidosis to present as achalasia, and the lack of other systemic symptoms makes amyloidosis less likely in our patient. Other systemic diseases, especially connective tissues diseases such as scleroderma, may present with dysphagia. Esophageal dysmotility is found in up to 90% of patients with scleroderma, but unlike achalasia, scleroderma results in an inadequate esophageal sphincter tone.

Eosinophilic esophagitis can present with solid food dysphagia, food impaction, esophageal strictures, and refractory gastroesophageal reflux symptoms. However, EoE is most frequently associated with narrowing of the esophageal lumen, unlike the dilation that was discovered on this patient's barium esophagography. Therefore, EoE is unlikely in this patient. Chagas disease from *Trypanosoma cruzi* infection is certainly associated with achalasia. However, this patient had no history of travel to endemic areas in Latin America. Although cases of strains of Chagas disease have been reported in the United States, it is very uncommon, and primary achalasia is a more likely diagnosis. Amyotrophic lateral sclerosis is a nervous system disorder that typically causes oropharyngeal dysphagia by affecting the neuromuscular coordination required for the pharyngeal phase of swallowing. This patient does not have symptoms of oropharyngeal dysphagia, which include coughing, drooling, and choking with swallowing, making the diagnosis of amyotrophic lateral sclerosis unlikely.

Esophagogastroduodenoscopy (EGD) revealed a large amount of food in the esophagus with friable esophageal mucosa, patchy erosions, and a vessel with adherent clot that was injected with epinephrine. Gastroscopic suction was attempted, but the food bolus could not be removed and the scope could not be passed into the stomach.

3. Which *one* of the following symptoms is *least* suggestive of achalasia in this patient?

a. Odynophagia
b. Dysphagia
c. Regurgitation of food
d. Aspiration
e. Difficulty belching

Odynophagia is typically not seen in achalasia and may be suggestive of other esophageal disorders such as infectious, pill, or reflux esophagitis. However, patients with achalasia experience chest pain on swallowing, which may be interpreted by them as odynophagia. Thus, it is important to differentiate these 2 symptoms when evaluating dysphagia. The most common clinical manifestations of achalasia include dysphagia with solids and liquids and regurgitation of undigested food. Aspiration may occur as a result of regurgitation of retained material from the esophagus, particularly if occurring while patients are lying flat. Difficulty belching is also seen in patients with achalasia, secondary to defective relaxation of the upper esophageal sphincter.[1]

The patient continued to have esophageal discomfort while swallowing. He was scheduled for repeated EGD to attempt to remove the food bolus.

4. Which *one* of the following findings is *required* for the diagnosis of achalasia?

a. Aperistalsis of the upper third of the esophagus

b. Incomplete LES relaxation
c. Incomplete upper esophageal sphincter relaxation
d. Eosinophil-predominant inflammation on esophageal biopsy
e. Diffuse ST-segment elevations in all 12 leads on ECG

Establishing the diagnosis of achalasia typically requires the presence of aperistalsis in the distal two-thirds of the esophagus and incomplete LES relaxation. Eosinophilic infiltration (>15 cells per high-power field) on esophageal biopsy is typically seen in EoE. Diffuse ST-segment elevations on ECG can be seen in acute pericarditis. In Chagas disease, there are cardiac abnormalities but no ECG findings specific to achalasia, and ECG is not utilized for the diagnosis.

The patient underwent repeated EGD. Lavage and suctioning were performed, which resulted in clearance of all debris in the esophagus. The esophageal lumen was noted to be severely dilated and tortuous. There were no appreciable esophageal contractions, and the LES was hypertonic, providing resistance to scope passage. The LES was dilated to a maximum diameter of 18 mm.

5. In view of this patient's history and esophagographic findings, which *one* of the following treatment options is *most appropriate*?

a. Pneumatic balloon dilation (PD)
b. Laparoscopic surgical myotomy
c. Calcium channel blockers
d. Botulinum toxin injection of the LES
e. Esophagectomy

Patients who are good surgical candidates should be considered for either PD or laparoscopic surgical myotomy with a partial fundoplication as initial therapy. Calcium channel blockers and botulinum toxin injections to the LES are therapeutic options that may be considered in patients who are poor candidates for invasive therapy or those unwilling to undergo surgical treatment. This patient is a healthy young man with no contraindications to surgery, making him a candidate for more invasive therapies. In patients with megaesophagus (diameter >6 cm), PD and myotomy may be less effective, and such patients should be considered for esophagectomy. This patient has a dilated and tortuous esophagus, making esophagectomy the most appropriate treatment option for him.

The patient underwent Ivor-Lewis esophagectomy, which he tolerated well, and at postoperative follow-up, his symptoms had improved considerably.

DISCUSSION

Achalasia is a primary motor disorder of the esophagus characterized by incomplete LES relaxation during swallowing. Etiologies include parasitic, autoimmune, neurodegenerative, and possibly viral causes.[2] Normal esophageal motor function is a balance of stimulatory (acetylcholine-mediated) and inhibitory (nitric oxide and vasoactive intestinal peptide) intrinsic neural activity. It is currently believed that in achalasia there is a selective degeneration of ganglion cells in the myenteric plexus of the LES and esophageal body, leading to impaired release of the inhibitory neurotransmitters nitric oxide and vasoactive intestinal peptide. Lack of inhibitor activity leads to unopposed excitatory or cholinergic activity and aperistalsis of the esophagus with incomplete relaxation of the LES.[3] However, the pathophysiology of achalasia remains poorly understood.

Primary achalasia occurs equally in men and women, most commonly between ages 30 and 60 years, with an incidence of 1 in 100,000 persons and a prevalence of 10 in 100,000 persons.[4] Patients typically present with dysphagia with solids (91% of patients) and liquids (85% of patients), as well as regurgitation of undigested food (76%-91% of patients).[5,6] There may also be weight loss, substernal chest pain with swallowing, and even the sensation of heartburn. This constellation of symptoms in otherwise young patients often leads to the misdiagnosis of gastroesophageal reflux disease and lag time of several years before appropriate diagnosis. Therefore, it is important to consider the diagnosis of achalasia in patients presenting with these symptoms in whom a trial of proton pump inhibitor therapy fails.

All patients suspected of having achalasia should undergo upper endoscopy to rule out pseudoachalasia, which can be caused by a malignant neoplasm or other forms of mechanical obstruction in the distal esophagus. Barium esophagography may reveal aperistalsis, esophageal dilation, and poor emptying of barium from the esophagus leading to the characteristic

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bird's-beak narrowing. Although these findings support the diagnosis of achalasia in patients presenting with classic symptoms, esophageal manometry is the criterion standard diagnostic test. In achalasia, esophageal manometry typically reveals impaired relaxation of the LES and aperistalsis. While impaired LES relaxation is required for the diagnosis of achalasia, other causes, such as opiates, which are known to reversibly impair LES relaxation, must be ruled out.[7] Recently introduced high-resolution esophageal manometry, with pressure transducers spaced at 1-cm intervals, has made a tremendous impact not only on the diagnosis of achalasia but also on esophageal motility disorders in general. High-resolution esophageal manometry allows classification of achalasia into 3 types, based on the contractile activity of the esophageal body.[8] Importantly, recent studies suggest that this classification system has important prognostic and therapeutic implications.[9]

Currently, there is no cure for achalasia, and thus treatment is aimed at relieving symptoms, improving esophageal emptying, and preventing dilation of the esophagus. Patients who are good surgical candidates should be offered PD or surgical myotomy as initial therapy. Both of these procedures should be performed at high-volume centers of excellence, and treatment choice should be tailored specifically for each patient. Recent data suggest that PD and Heller myotomy are equally effective at 2 years, with success rates of 86% and 90%, respectively.[10] However, for young healthy patients, Heller myotomy may provide longer-lasting relief. Botulinum toxin injections can be performed in patients who are less favorable candidates for myotomy or PD.[11] Although the initial success rate of botulinum toxin injection is comparable to that of myotomy and PD, relapses are expected, and therefore the injections are frequently repeated. Calcium channel blockers and nitrates are noninvasive but essentially ineffective and limited by adverse effects in up to 30% of patients. End-stage achalasia, as was seen in this patient, is characterized by esophageal dilation (>6 cm) and sigmoid esophagus.[2] Esophagectomy is recommended for these patients, but LES PD or myotomy may be considered initially. A newer emerging therapy for the treatment of achalasia is preoral esophageal myotomy, which uses endoscopy to perform myotomy in patients with achalasia. Early prospective studies have found that this procedure has a better than 90% success rate. Because it may allow for disruption of longer segments of the LES compared with Heller myotomy, this procedure represents a promising alternative to PD and myotomy.

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CORRECT ANSWERS: 1. e. 2. a. 3. a. 4. b. 5. e