Esophageal Motility Disorders

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Preface

Board certification in gastroenterology and hepatology requires an understanding of all aspects of physiology, diagnosis, and therapy for gastrointestinal tract, liver, and pancreatic disorders. In addition to self-study of this discipline, candidates for board certification must have completed 2 years of fellowship, during which time the practical aspects of the diagnosis and treatment of gastroenterologic and hepatologic complications are learned through hands-on clinical investigation.

The Hospital Physician Gastroenterology Board Review Manual is a study guide intended to help candidates prepare for the written and oral components of this examination. The manual consists of quarterly publications that address the following areas:

- Acid peptic disease
- Acute appendicitis
- Aging and the gastrointestinal tract
- Basic biology
- Chronic cholestatic syndromes
- Cirrhosis and portal hypertension
- Diverticulosis coli
- Drug-induced and alcoholic liver disease
- Endoscopy of upper gastrointestinal hemorrhage
- Esophageal disorders
- Gallstones
- Gastrointestinal manifestations of AIDS
- Inflammatory bowel diseases and other diarrheal diseases
- Intestinal obstruction
- Irritable bowel syndromes
- Ischemic bowel disease
- Liver transplantation
- Malabsorption syndromes
- Nutritional support
- Pancreatic disease
- Small intestinal, colonic, and other tumors
- Viral and chronic hepatitis

Most of these topics are covered in the manual; however, some areas of interest are discussed in greater depth than others.

The manual presents clinical scenarios using a case-based format; questions and answers relating to the clinical presentation are provided. The editors believe that this question-and-answer format is an effective teaching tool and allows for adequate self-assessment. Each quarterly publication addresses only a few of the topics mentioned; board certification candidates should review the entire list of topics to be appropriately prepared for the examination. The Hospital Physician Gastroenterology Board Review Manual is prepared by the Series Editor and contributing authors and not in collaboration with the American Board of Internal Medicine, Gastroenterology/Hepatology.

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INTRODUCTION

The 3 classic esophageal motility disorders are achalasia, diffuse esophageal spasm, and scleroderma esophagus. Gastroesophageal reflux disease—one of the most prevalent conditions affecting the Western population—is often classified as an esophageal motility disorder because reflux events result from transient lower esophageal sphincter (LES) relaxations or in association with a hypotensive LES. Additionally, a number of disorders have been proposed to be motility disorders of the esophagus, but associations between their respective clinical presentations and the existence of motility abnormalities in the esophagus have not yet been definitively established (Table 1). Thus, it is not clear whether these candidate disorders should be considered distinct motility disorders of the esophagus or simply viewed as manometric “curiosities” or nonspecific motility abnormalities. In some instances, these disorders have been observed to transform over time into one of the classic esophageal motility disorders.

This review begins with a brief description of some of the principles of normal esophageal motility. It then provides case discussions that highlight the important pathophysiologic and clinical features of several major esophageal motility disorders: achalasia, diffuse esophageal spasm, scleroderma esophagus, and nutcracker esophagus.

NORMAL ESOPHAGEAL MOTILITY

Esophageal motility can be divided according to the functions of the esophageal body and the LES. The principal function of the esophageal body is that of peristalsis. In general, peristalsis involves the movement of material down a tubular structure by waves of muscular contractions, with each period of contraction (or excitation) being preceded by a period of relaxation (or inhibition). Peristalsis in the esophagus involves sequential contractions that propel liquids or solids from the upper esophageal sphincter through the LES and into the stomach. Peristalsis of the proximal striated muscle portion of the esophagus is regulated by the sequential activation of vagal efferent neurons. Peristalsis of the distal, smooth muscle portion of the esophagus is under the direct control of inhibitory and excitatory neurotransmitters arising from motor neurons situated in the myenteric plexus within the wall of the esophagus.

Relaxation of the distal, smooth muscle portion of the esophagus is primarily mediated by inhibitory neurotransmitters such as nitric oxide, which has recently been identified as a primary inhibitory neurotransmitter in the esophagus. Contractile distal esophageal activity is mediated by excitatory neurotransmitters such as acetylcholine.

In the esophagus, the period of inhibition increases in duration from the proximal to the distal aspects of...
the esophageal body—a phenomenon known as the latency gradient. The increasing latency gradient along the distal esophagus leads to the sequential nature of the esophageal contractions that constitute peristalsis.

Under normal conditions, the LES remains closed but opens in response to a variety of stimuli including swallowing (primary peristalsis), esophageal distension (secondary peristalsis), or gastric distension (as occurs in transient lower esophageal relaxation). The LES basal (or resting) pressure is maintained by both myogenic and neurogenic factors, whereas LES relaxation occurs in response to neurogenic factors.

Myogenic tone of the LES refers to the intrinsic ability of the smooth muscle in this region to remain contracted in the absence of external neural or hormonal influences. Neurogenic factors refer to the effects of the neurons of the myenteric plexus on the smooth muscle of the LES.

Excitatory neurons release neurotransmitters (such as acetylcholine) that play a role in the resting tone of the LES. The inhibitory neurons release neurotransmitters (such as nitric oxide and vasoactive intestinal polypeptide) that are responsible for the relaxation of the LES. These principles are illustrated in Figure 4A.

Figure 1 illustrates the normal motor pattern in response to the swallowing of a bolus of water. After its rapid transit through the pharynx, the ingested water bolus is propelled through the esophagus by wavelike, sequential contractions. At the onset of the swallow (marked by the brisk pharyngeal contraction on the uppermost row of the manometric pressure recording), the LES relaxes and remains open until the end of esophageal peristalsis. The immediate onset of LES relaxation allows for ingested material that might travel faster than peristalsis (assisted by gravity, for instance) to pass unimpeded into the stomach. Conceptualizing these normal manometric study results with the underlying control mechanisms with which they relate allows for a better understanding of the pathophysiology of esophageal motility disorders.

**IDIOPATHIC ACHALASIA**

**CASE 1 PRESENTATION AND INITIAL EVALUATION**

Patient 1 is a 73-year-old man with hypertension and a 5-year history of dysphagia: solid foods, and occasionally liquids, get stuck at the level of his upper sternum with

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**Table 1. Esophageal Motility Disorders**

**Accepted disorders**
- Achalasia
- Diffuse esophageal spasm
- Scleroderma esophagus
- Gastroesophageal reflux disease

**Candidate disorders**
- Nutcracker esophagus
- Hypertensive lower esophageal sphincter
- Ineffective esophageal peristalsis
- Lower esophageal muscular ring
- Nonspecific esophageal motility disorders
every meal. He is usually able to get the food down with repeated swallows or by drinking water. Recently, he has been spontaneously regurgitating clear, foamy liquid and undigested food into his mouth, especially after dinner, when bending over the sink to brush his teeth. His wife has noted that he has been coughing at night and that he has lost 7 to 8 lb. The patient denies heartburn or odynophagia and does report an inability to belch.

• What is the differential diagnosis for Patient 1?

DIFFERENTIAL DIAGNOSIS FOR PATIENT 1

Dysphagia for liquids and solid foods is typically indicative of an esophageal motility disorder. Two important caveats to this clinical dictum exist, however. First, difficulty with swallowing liquids at the time of a solid food impaction is common with structural esophageal lesions such as a Schatzki’s ring and should not be confused with the liquid and solid food dysphagia of patients with motility disorders. Second, patients with oropharyngeal dysphagia often report difficulty swallowing both liquids and solids. In fact, many such patients have more difficulty swallowing liquids than solids, providing the rationale for using substances that increase the consistency of liquids.

Patient 1 localizes his dysphagia to his chest region, making oropharyngeal dysphagia unlikely, since dysphagia is often referred by patients to areas proximal to the actual site of obstruction. For Patient 1, an esophageal motility disorder is the most likely diagnosis.

Although Patient 1 could have any one of the 3 classic motility disorders, his pattern of dysphagia is, for the most part, consistent with achalasia. Achalasia is manometrically defined by aperistalsis of the distal esophagus and incomplete or absent LES relaxation. Affected patients almost invariably present with dysphagia. The dysphagia of achalasia has an insidious onset, is typically chronic, relates to both liquids and solids, and is slowly progressive. It may progress to a point at which patients frequently experience episodes of spontaneous food regurgitation, nocturnal aspiration, weight loss, and malnutrition. Additionally, the inability to belch is a symptom that is reported by patients with achalasia.1

The dysphagia resulting from diffuse esophageal spasm is also chronic and occurs for both liquids and solids. However, it is generally intermittent and is not as severe as the dysphagia resulting from achalasia. The dysphagia associated with scleroderma esophagus relates primarily to solids: liquids are able to empty from the esophagus with the help of gravity.

FURTHER EVALUATION OF PATIENT 1

Patient 1 undergoes a barium swallow procedure, and the results show a dilated esophagus with tapered constriction of the gastroesophageal junction (Figure 2). An esophageal motility study is also performed (Figure 3), and the results indicate complete aperistalsis of the esophageal body and the absence of deglutitive relaxation of the LES.

• What is the most likely diagnosis for Patient 1?
DIAGNOSIS FOR PATIENT 1

The results of Patient 1’s manometric and radiographic studies point to achalasia. The classic manometric study results for achalasia are present—those that indicate aperistalsis of the esophageal body and those that indicate incomplete or absent deglutitive relaxation of the LES. Supportive manometric characteristics include those indicating low amplitude contractions of the esophageal body and hypertension of the LES. Although variants to the classic manometric findings occur, the presence of these classic manometric features is very sensitive and specific in establishing the diagnosis of achalasia.

The radiographic findings of a dilated sigmoid configuration of the esophagus with tertiary contractions and a constricted gastroesophageal junction are classic for achalasia. However, barium esophagrams may be interpreted as normal in one third of patients with newly diagnosed achalasia.

In most instances, as for Patient 1, achalasia occurs as a primary disease of unknown cause. The possibility of secondary achalasia (addressed further in the next case) should be considered in all patients newly diagnosed with the disorder.

• What is the pathophysiology of achalasia?

PATHOPHYSIOLOGY OF ACHALASIA

Histopathologic studies performed on samples of smooth muscle tissue from the esophagi of patients with achalasia have shown the marked paucity—and often the complete absence—of neurons from the myenteric plexus. Such findings led to a working model of the pathophysiology of achalasia in which inhibitory, nitric oxide neurons and excitatory, cholinergic neurons are absent from the myenteric plexus (Figure 4C).

A number of physiologic studies have demonstrated intact cholinergic innervation to the esophagus in some patients with achalasia. In these studies, patients were administered substances that would have an effect only if the target nerve cells were present. In one study, the acetylcholinesterase inhibitor, edrophonium, was shown to significantly increase the LES pressure in patients with achalasia. In a study examining the effects of the anticholinergic agent, atropine, in patients with achalasia, researchers demonstrated a 30% to 60% reduction in LES pressure with atropine in patients with achalasia. Recently, botulinum toxin has been introduced as a novel treatment for achalasia. Botulinum toxin acts to inhibit the release of acetylcholine from cholinergic nerve endings. Studies using botulinum toxin have found a significant symptomatic response and some reduction in LES pressure. The fact that these substances had an effect on the LES supports the concept of the preservation of cholinergic innervation to the esophagus in patients with achalasia.

The preservation of the excitatory, cholinergic innervation to the esophagus implies that the neuronal loss that characterizes achalasia may be selective for inhibitory neurons (Figure 4B). Studies have provided indirect evidence for this through the use of cholecystokinin. Cholecystokinin has excitatory effects on smooth muscle, as well as indirect inhibitory effects via postganglionic inhibitory neurons. In patients with achalasia, cholecystokinin has been shown to induce LES contraction, whereas in control patients, it has been shown to induce LES relaxation, providing evidence for impaired postganglionic inhibitory nerves in patients with achalasia. More recent evidence comes from in vitro studies examining the responses to electrical stimuli of preparations of LES tissue specimens from patients with achalasia. Muscle strips of the LES from control subjects characteristically relax in response to electrical...
field stimulation—owing to predominant activation of the nitric oxide–containing inhibitory neurons. Paradoxically, LES strips from patients with achalasia were found to contract in response to electrical field stimulation. Such findings can be readily explained by the absence of inhibitory neurons.

Direct evidence to support the concept of inhibitory neuron loss in the pathophysiology of achalasia came from immunohistochemical studies that demonstrated the absence of vasoactive intestinal polypeptide inhibitory neurons, as well as nitric oxide synthase (the enzyme responsible for producing nitric oxide), in LES tissue specimens of patients with achalasia. Other studies have demonstrated a deficiency of inhibitory neurons in patients with achalasia by using radioimmunoassay procedures involving antibodies directed against the neuronal form of nitric oxide synthase.

Moreover, a number of studies have shown that selective inhibition of nitric oxide synthase leads to an elimination of the latency gradient in the esophageal body, which in turn leads to aperistalsis of the esophagus. An increase in the resting tone of the LES and an inhibition of LES relaxation lead to a hypertensive LES that impairs bolus transit. This overall motility pattern of an aperistaltic esophageal body and a nonrelaxing, hypertensive sphincter mimics the motility pattern of achalasia and lends further credence to the model of the pathophysiology of achalasia that incorporates the loss of inhibitory neurons.

**What treatment options for idiopathic achalasia are available?**

**TREATMENT OF IDIOPATHIC ACHALASIA**

Treatment options for idiopathic achalasia include endoscopic pneumatic dilation, surgical myotomy, endoscopic botulinum toxin injection, and medical therapy.
The goal of all the treatment options is to reduce the LES pressure to allow for esophageal emptying.

Endoscopic pneumatic dilation provides symptom relief in approximately 70% to 80% of patients with achalasia. Larger balloon diameters provide greater response rates but also increase the risk of perforation, which is generally less than 5%.

Surgical myotomy was first performed via thoracotomy by Heller in 1913. The operation is now performed both thoracoscopically or laparoscopically with much shorter lengths of hospitalization (1 to 3 days in most series), compared with open procedures, and is associated with excellent outcomes. Retrospective studies and one randomized trial reported better outcomes in patients treated surgically as compared with those treated with pneumatic dilation. Furthermore, perforations that occur as a result of pneumatic dilation require repair via open thoracotomy, necessitating a much longer recovery period, as compared with laparoscopic or thoracoscopic approaches to surgical myotomy. As in many decisions in medicine, the experience of locally available specialists is an important consideration in the choice of initial therapy for achalasia.

Botulinum toxin injection, introduced by Pasricha et al in 1995, is a novel therapeutic option for achalasia. The technique involves the injection of botulinum toxin into the region of the LES through endoscopic guidance. Studies by multiple groups have now demonstrated significant symptom relief in approximately two thirds of patients treated with botulinum toxin in the LES. The toxin works by preventing the release of acetylcholine from neurons within the myenteric plexus. This therapeutic option does have limitations, however. Long-term studies using botulinum toxin have shown the need for repeated injections to maintain symptom relief. Vaezi et al, who performed a randomized controlled trial studying botulinum toxin and pneumatic dilation in 42 patients with achalasia, found at a 12-month follow-up that 70% of the patients treated with pneumatic dilation and only 32% of patients treated with botulinum toxin were in symptomatic remission. Of greater concern was the finding that while providing symptom relief, botulinum toxin failed to significantly reduce LES pressure or barium retention on a quantitative barium swallow study.

Medical therapy involves the use of smooth muscle relaxants such as calcium channel antagonists, nitrates, and anticholinergic agents. Small, randomized, controlled trials using sublingual nifedipine and isosorbide dinitrate have demonstrated a significant reduction in LES pressure and notable symptom relief. A single Italian study randomized 30 patients with achalasia to receive either pneumatic dilation or sublingual nifedipine and found comparable efficacy. However, concerns over adverse cardiovascular effects relating to the use of short-acting nifedipine have limited its regular use. In general, the long-term effectiveness of medical therapy has been limited by adverse side effects and efficacy that is usually less substantial than that of the more invasive therapies.

First-line therapy for achalasia is best accomplished by either endoscopic pneumatic dilation or surgical myotomy. Given the limitations of both medical therapy and therapy with botulinum toxin, such treatments are generally reserved for patients who are poor candidates for more invasive interventions or as temporizing measures while patients await more definitive treatment.

**Treatment of Patient 1**

After detailed discussions on the various treatment options, Patient 1 undergoes an uneventful laparoscopic Heller myotomy with Dor fundoplasty. He is discharged on postoperative day 1. On follow-up 4 weeks later, the patient reports substantial improvements in his dysphagia but does note some delay in the transit of solid food in his lower chest region. The food usually passes after several seconds, and it helps when he drinks liquids. He denies experiencing heartburn, although he has been experiencing nocturnal coughing and postprandial regurgitation after any feeding. He has been taking a proton-pump inhibitor since the surgery. His nocturnal coughing and postprandial regurgitation have completely resolved, and he has been gradually gaining weight.

- **Why does Patient 1 continue to experience dysphagia?**

**DISCUSSION**

Persistent dysphagia after treatment of idiopathic achalasia can have several possible causes. One is incomplete or ineffective therapy. In the case of either an open or minimally invasive Heller myotomy, an incomplete myotomy can occur but is uncommon. This can be detected via an esophageal manometric study as a residual high-pressure zone. Also, in a patient who has undergone surgery, there may exist a mechanical obstruction related to the creation of a fundoplasty or fundoplication, which commonly is performed to prevent gastroesophageal reflux after the myotomy. Another cause of persistent dysphagia, which can occur after any form of treatment for achalasia has been used, relates to the esophageal body aperistalsis that characterizes the disease. The low or absent esophageal body contractions characteristic of achalasia do not normalize after treatment. As such, mild dysphagia to solids often persists after effective therapy. In addition, owing to the
sigmoid deformity and massive dilation of the esophagus that results from long-standing achalasia, emptying of the esophagus can be difficult despite an adequate myotomy. Persistent dysphagia may also be caused by gastroesophageal reflux disease and peptic stricture formation, which can complicate endoscopic or surgical disruption of the LES. Finally, there are several delayed complications of achalasia that present with dysphagia. For example, cancer that develops secondary to achalasia can present with dysphagia.

• What are the significant, long-term complications of achalasia?

LONG-TERM COMPLICATIONS OF ACHALASIA

The primary complications of achalasia are related to the functional obstruction rendered by the non-relaxing LES and include progressive malnutrition and aspiration. Aspiration can be a substantial cause of morbidity; in particular, patients with aspiration are at risk for nocturnal coughing and choking, as well as aspiration pneumonia.

Uncommon but important complications of achalasia include the formation of epiphrenic diverticula and esophageal cancer. Epiphrenic diverticula are commonly associated with esophageal motility disorders, presumably as a result of increased intraluminal pressures. Also, the incidence of esophageal cancer is increased in patients with idiopathic achalasia. The cancers that most commonly develop are squamous cell carcinomas, although adenocarcinomas have also been reported. A large cohort study in Sweden examining patients with achalasia found a 16-fold increased risk of esophageal cancer during years 1 through 24 after initial diagnosis.20 Cancers detected in the first year after diagnosis of achalasia were excluded to eliminate prevalent cancers that may have presented as secondary achalasia or pseudoachalasia.20 Nevertheless, because the incidence of esophageal cancer is generally low among patients with achalasia, routine endoscopic screening of these patients is not recommended.

It is generally thought that successful treatment of achalasia may reduce the risk of cancer, but this has not been proven and several case studies have reported carcinoma arising after treatment of the disorder.20 Therefore, continued clinical follow-up of patients with achalasia is reasonable regardless of the treatment modality used.

FOLLOW-UP OF PATIENT 1

A follow-up barium swallow study is performed for Patient 1 and shows free passage of barium through a patent gastroesophageal junction. There is no evidence of a peptic stricture, and the fundoplasty is intact. The patient is reassured and scheduled for follow-up in 6 months.

SECONDARY ACHALASIA AND PSEUDOACHALASIA

CASE 2 PRESENTATION AND INITIAL EVALUATION

Patient 2 is a 57-year-old man who was referred for evaluation of a 6-month history of dysphagia. His dysphagia relates to both liquids and solids, and he localizes it to his lower sternal region. He notes difficulty lying flat at night after meals because of spontaneous regurgitation. He has lost over 15 lb since his symptoms began. His heartburn, which was quite common in the past, has notably improved since his dysphagia began. His past medical history is unremarkable, and he is taking no medications. He is originally from Bolivia but moved to the United States more than 25 years ago. The results from his physical examination are unremarkable. The results from an esophagogastroduodenoscopy (EGD) show a dilated esophagus with a large amount of retained solid and semisolid debris (Figure 5). Results from an esophageal manometric study indicate complete aperistalsis of the esophageal body. The LES is hypertensive with a resting pressure of 45 to 60 mm Hg. No relaxation of the LES is detected with swallowing.

• What is the cause of Patient 2’s dysphagia?

DISCUSSION

This patient’s presentation is quite similar to that of the first case patient. Patient 2’s dysphagia has been present for only 6 months, which, in an older person, raises the concern for pseudoachalasia secondary to cancer, ie, cancer that mimics achalasia. With such concerns, close endoscopic inspection of the gastroesophageal junction and gastric cardia is necessary. Diagnostic imaging with computed tomography (CT) scans may be required in some cases. Although the patient’s endoscopic and manometric study results are characteristic of achalasia, they do not distinguish between primary (idiopathic) achalasia or secondary achalasia.

CANCER AS A CAUSE OF SECONDARY ACHALASIA AND PSEUDOACHALASIA

Cancer is an important cause of secondary achalasia and pseudoachalasia. A common mechanism by which it leads to pseudoachalasia is by direct mechanical obstruction of the distal esophagus. A number of cancers have been observed to do this, particularly distal esophageal
and proximal gastric carcinomas (Table 2). Cancer can also infiltrate the submucosa of the LES and thereby disrupt the myenteric neurons, resulting in an achalasia-like condition. Submucosally infiltrating malignancies may not always be apparent on endoscopic evaluation because of the absence of mucosal abnormalities.

Tumors remote from the esophagus can lead to secondary achalasia via a paraneoplastic syndrome that is an unusual but important complication of small cell lung cancer. Type I antineuronal nuclear (ANNA-1 or anti-Hu) autoantibodies recognize proteins expressed in small cell lung cancer tissue as well as neurons of the central, peripheral, autonomic, and enteric nervous systems.21 The manifestations associated with ANNA-1 positivity include achalasia and gastroparesis, and pseudo-obstruction can precede the diagnosis of the cancer.

CONTINUED EVALUATION OF PATIENT 2

No tumor is observed in Patient 2 by endoscopic techniques. Further evaluation may involve the use of CT scans and endoscopic ultrasonographic techniques. Patient 2’s history of residence in South America leads to serologic testing for Chagas’ disease, and the result is markedly positive.

- Why does Patient 2’s residence in South America raise the possibility of Chagas’ disease?

CHARACTERISTICS OF CHAGAS’ DISEASE

Chagas’ disease is one of the many causes of secondary achalasia (Table 2). It is a parasitic infection caused by Trypanosoma cruzi, which is endemic to regions of Central and South America and Mexico. T. cruzi is transmitted from person to person via the blood-sucking Triatominae (reduviid) insects. Approximately 10% to 30% of infected individuals develop symptoms of chronic infection that present years or even decades after initial infection. The heart is the most commonly affected organ. Although any portion of the gastrointestinal tract may be involved, the esophagus is most commonly affected, manifesting as secondary achalasia. Secondary achalasia develops in 7% to 10% of chronically infected individuals.22 Recently, antibodies directed at targets within the myenteric plexus have been noted in patients with Chagas’ disease and achalasia.23 The treatment of Chagas’ disease–induced achalasia is identical to treatment of idiopathic achalasia. Treatment of the chronic parasitic infection is controversial and does not appear to affect the organ damage already inflicted.

FOLLOW-UP OF PATIENT 2

Patient 2 undergoes an uneventful laparoscopic Heller myotomy and continues to do well 1 year later.
CASE 3 PRESENTATION AND INITIAL EVALUATION

Patient 3 is a 72-year-old man with dysphagia and a history of hypertension and peptic ulcer disease. He has had intermittent dysphagia for the past 6 years. It is characterized by the feeling of food sticking in his lower sternum region. The dysphagia is primarily for solids but has also occurred when he rapidly drinks liquids. He occasionally forces himself to regurgitate food that has become trapped in his esophagus. Over the years his dysphagia has gradually worsened; he has episodes several times a week. He underwent an EGD procedure 1 year ago, at which time a Schatzki’s ring was detected and dilated with a 17-mm Savary dilator. After the dilation, he continued to have dysphagia and was told he was not chewing his food well. One year later, owing to worsening symptoms, a second EGD and dilation was performed, although no clear stricture was identified on this examination. Several weeks after this, the patient returned to his primary care physician complaining of persistent dysphagia.

• What is the differential diagnosis for Patient 3?
• Why is a Schatzki’s ring unlikely to be causing this patient’s dysphagia?
• What diagnostic testing is appropriate for this patient?

DIFFERENTIAL DIAGNOSIS FOR PATIENT 3

The differential diagnosis for Patient 3 is the same as that presented in the first case and includes the classic esophageal motility disorders. A Schatzki’s ring and peptic stricture are unlikely, given the history of dysphagia for liquids. Furthermore, the lack of symptomatic benefit from esophageal dilation is an important clue to the presence of a problem other than a Schatzki’s ring: a single endoscopic dilation is very effective in relieving the dysphagia from the mechanical obstruction caused by such rings. Schatzki’s rings are very prevalent and are reported in approximately 4% to 14% of radiographic studies. Hence, the presence of a ring itself should not necessarily implicate it as the cause of dysphagia. The internal diameter of the ring is the most important factor determining whether or not it will lead to dysphagia, with rings smaller than 13 mm producing symptoms in most patients.

FURTHER EVALUATION OF PATIENT 3

Appropriate diagnostic testing at this point for Patient 3 would include an upper gastrointestinal series and esophageal motility test. Both a barium swallow study and an esophageal motility test are performed for the patient, and the results are depicted in Figures 6 and 7.

• What is the diagnosis for Patient 3, and how should his condition be managed?

DIAGNOSIS FOR PATIENT 3

In the barium study, multiple, simultaneous, tertiary
contractions of the distal esophageal body are evident. The manometric test results indicate simultaneous and repetitive esophageal body contractions. LES relaxation is preserved: the results of these diagnostic studies illustrate classic characteristics of diffuse esophageal spasm.

CHARACTERISTICS OF DIFFUSE ESOPHAGEAL SPASM

Diffuse esophageal spasm is a rare condition and was first described by Osgood in 1889. The diagnosis relies on the finding of simultaneous esophageal body contractions. Although high-amplitude, repetitive contractions of long duration may be present, they are not necessary for a diagnosis of diffuse esophageal spasm. Intermittent preservation of esophageal peristalsis should be observed, also. If esophageal contractions are simultaneous with every swallow sequence, or if failed LES relaxation is noted, the diagnosis of achalasia needs to be entertained.

specific for diffuse esophageal spasm and have been reported in patients with diabetes, connective tissue disorders, amyloid, alcoholism, and gastroesophageal reflux disease.

A number of similarities exist between achalasia and diffuse esophageal spasm. Both conditions appear to result from a defect in the inhibitory neurotransmission of the esophagus, presumably at the level of the myenteric plexus. Because of the rarity of cases of diffuse esophageal spasm and the even less common need for surgical intervention, histopathologic data are lacking. A few studies have demonstrated degeneration of vagal fibers, inflammatory infiltration of the myenteric plexus, and hypertrophy of smooth muscle. These features have also been described with idiopathic achalasia. Furthermore, several cases have been reported in which the transformation from diffuse esophageal spasm into achalasia has been observed.

MANAGEMENT OF DIFFUSE ESOPHAGEAL SPASM

The management of the patient with diffuse esophageal spasm consists primarily of medical therapy. Both calcium channel antagonists and nitrates have been shown to be beneficial in uncontrolled trials. No data exist on the use of oral anticholinergic agents, although recent preliminary studies have found botulinum toxin injections in the LES or distal esophageal body to be somewhat efficacious.
In patients with DES and dysfunction of the LES, endoscopic dilation therapy has been effective in relieving dysphagia. Such cases may represent early or variant forms of achalasia. Finally, in severe cases, surgical therapy consisting of a longitudinal myotomy of the distal esophagus may be considered.

Management of Patient 3

Patient 3 is treated with oral nitrates and has a good response.

SCLERODERMA ESOPHAGUS

CASE 4 PRESENTATION AND INITIAL EVALUATION

Patient 4 is a 45-year-old woman with a history of connective tissue disease who was referred for evaluation of dysphagia. For several months, she has experienced difficulty swallowing solid foods. She notes that there is usually a delay in the transit of food through her midsternal region. She takes all her meals in an upright position, which improves her ability to swallow. She denies experiencing food impactions or nausea and vomiting. She also denies heartburn but has experienced reflux of bitter-tasting fluid on a frequent basis. On physical examination, multiple telangiectasias are noted on her fingers, and skin tightening is present over her hands and wrists. Although these findings are consistent with scleroderma, additional skin findings are present that raise the diagnostic possibilities of polymyositis. An EGD procedure is performed, which shows mild, erosive, distal esophagitis. Manometric findings relating to this disorder include weak or absent distal esophageal body contractions and a hypotensive LES.

• What is the most likely diagnosis for Patient 4?
• How should Patient 4 be treated?

DIAGNOSIS FOR PATIENT 4

The results of the esophageal motility study indicate the presence of preserved esophageal body contractions in the proximal esophagus with absent contractions in the distal esophagus. The LES is markedly hypotensive. Relaxation of the LES is not seen, as the basal LES pressure is almost nonexistent. These findings are characteristic for scleroderma esophagus. In polymyositis, peristalsis in the proximal, striated muscle portion of the esophagus is affected while the function of the distal, smooth muscle esophagus and LES are intact.

CHARACTERISTICS OF SCLERODERMA ESOPHAGUS

Scleroderma is a connective tissue disease of unknown etiology. It is a prototypic myopathic motility disorder involving smooth muscle atrophy and fibrosis. Esophageal dysmotility complicates up to 90% of cases of this disease and manifests as gastroesophageal reflux and dysphagia. Manometric findings relating to this disorder include weak or absent distal esophageal body contractions and a hypotensive LES. Proximal esophageal body function should be preserved, except in cases of mixed connective tissue disorders that share features of polymyositis, with involvement of the skeletal muscle of the esophagus. These results, although classic for scleroderma, are not specific for the disease, however. Patients with a number of other connective tissue and metabolic disorders, such as severe gastroesophageal reflux disease, may have similar results. Therefore, manometric findings of scleroderma esophagus need to be put in the context of the clinical scenario.

Regardless of the underlying cause, the abnormal manometric study results point to a predisposition for severe gastroesophageal reflux. This is because of the
increase in reflux events and inadequate acid clearance mechanisms that are consequences of the diminished LES pressure and impaired esophageal peristalsis, respectively. Peptic strictures often complicate the course of scleroderma esophagus and can confuse the presentation of dysphagia. Other portions of the digestive tract are frequently affected in patients with scleroderma, leading to problems of delayed gastric, small bowel, and colonic transit. Wide-mouthed, small bowel diverticula are seen in patients with scleroderma and may lead to bacterial overgrowth.

TREATMENT OF SCLERODERMA ESOPHAGUS

Treatment options for esophageal dysmotility in scleroderma are limited. Swallowing in an upright position allows for gravity to assist in the emptying of the weakened esophagus. Modest improvements in esophageal symptoms and function have been demonstrated using prokinetic agents such as metoclopramide and cisapride. Potent acid suppressant therapy with proton-pump inhibitors should be strongly considered in all patients with scleroderma esophagus to prevent reflux symptoms as well as peptic stricture formation.

The use of esophageal manometry in the evaluation of patients with scleroderma or other connective tissue diseases is not recommended unless their detection through this means helps in establishing a more definitive diagnosis or aids in disease management.27

Treatment of Patient 4

Patient 4 is placed on a combination of metoclopramide and lansoprazole with reduction of the bitter refluxate, but continues to experience mild dysphagia.

NUTCRACKER ESOPHAGUS

CASE 5 PRESENTATION AND INITIAL EVALUATION

Patient 5 is a 42-year-old man with a complaint of chest pain, which he describes as a sharp pain in the midsternal region that typically occurs during meals and with stressful situations. Drinking cold liquids sometimes precipitates the pain. There has been no association with physical exertion and no progression of the pain since it began 9 months ago. He denies dysphagia, odynophagia, or heartburn. His weight has been stable. An exercise stress test with thallium imaging shows normal results.

The patient is referred to a gastroenterologist who orders an ambulatory pH study. An esophageal manometric test is performed before the pH study for the purpose of localizing the LES to allow for positioning of the pH sensor. However, the technician is concerned by several abnormalities in the manometric recording (Figure 9).

• Based on the manometric study results, what is the most probable diagnosis for Patient 5, and how should his condition be managed?

DIAGNOSIS FOR PATIENT 5

The results of the motility study indicate very high amplitude esophageal body contractions with distal esophageal contractions exceeding 200 mm Hg. The contractions are peristaltic, and the LES relaxation is normal. These results are consistent with the diagnosis of nutcracker esophagus, defined as the presence of esophageal contractile amplitudes exceeding 180 mm Hg.

CHARACTERISTICS OF NUTCRACKER ESOPHAGUS

Nutcracker esophagus is one of the most common disorders involving esophageal motility. In one study series, nutcracker esophagus was found in 48% of...
patients who presented with noncardiac chest pain and abnormal esophageal motility.29 In general, symptoms that have been observed in patients with nutcracker esophagus include chest pain and dysphagia. However, studies have demonstrated poor direct correlation between the existence of these symptoms and the abnormal manometric study results relating to nutcracker esophagus. Furthermore, treatments documented to improve the abnormal motility have not led to symptom improvement in patients.29 Additionally, therapies using low-dose antidepressants have improved patients’ symptoms while having no effect on their abnormal manometric results.30,31 Thus, it presently appears that nutcracker esophagus may represent a manometric “curiosity” rather than a true esophageal motility disorder. The manometric aberrations do not appear to be the cause of symptoms of chest pain in such patients.

**TREATMENT OF NUTCRACKER ESOPHAGUS**

The routine use of medications directed at the abnormal motility test results, for the purpose of relieving chest pain, is not supported by the available data. Likewise, the routine use of esophageal manometry in the initial evaluation of patients with noncardiac chest pain is not recommended.27 Instead, it is important to first exclude other reversible causes, including gastro-esophageal reflux disease, in patients presenting with noncardiac chest pain. Manometry would have a role in the evaluation of patients with chest pain and dysphagia who have normal results on endoscopic evaluation. If reflux disease is excluded, patients with noncardiac chest pain may benefit from the use of low-dose antidepressant therapy.

**REFERENCES**