Approach to Patients with Esophageal Dysphagia

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Introduction

Dysphagia refers to the subjective sense that swallowing is impeded or hindered. Population studies have suggested that 16% of a Western population (Australia) has sensed this at some point over a lifetime [1]. Although the prevalence of dysphagia increases with age, it should not be attributed to a normal consequence of aging. Dysphagia can occur acutely and require immediate treatment, can be of insidious onset and progressive, or may occur chronically in paroxysms. Dysphagia is the presenting symptom of a wide range of disorders ranging from locally advanced foregut cancer, to connective tissue disorders, to benign and idiopathic gut functional disorders. Because of the consequences of delaying the diagnosis of a potentially treatable disorder or malignancy, dysphagia is an alarm symptom that cannot be ignored and must be investigated. This chapter will detail the evaluation and etiology of the symptom of esophageal dysphagia.

Presentation

Esophageal dysphagia should be considered separately from globus sensation, the sensation that there is an object remaining in the hypopharynx between meals, and odynophagia, pain with swallowing. The primary focus of the initial interview with the patient should be to determine if the dysphagia is of esophageal origin, or oropharyngeal origin. Oropharyngeal dysphagia relates to difficulty initiating a swallow in the oral preparatory phase or hypopharyngeal phase of swallowing, and generally occurs immediately on swallowing, and is associated with coughing, the sense of choking, or nasal regurgitation. Oropharyngeal dysphagia should be

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considered separately. Although some general patterns have been observed in patients presenting with esophageal dysphagia, analysis of symptoms alone is never sufficient to classify the cause of dysphagia. However, assessment of the quality of dysphagia may serve as a lead point to investigation.

Acute Dysphagia

Patients presenting with acute dysphagia may present to the emergency room. Because the esophagus is so sensitive to stretch, patients with an impacted food bolus are compelled to seek emergency treatment. Such patients may complain of needing to regurgitate and expectorate their swallowed saliva, and are aware that a food bolus has not passed into the stomach. Treatment is with immediate upper flexible endoscopy, with or without a trial of intravenous glucagon, with retrieval of the bolus or assisted transit of the bolus into the stomach. Patients presenting with a first time food bolus impaction and no prior history of dysphagia are most likely to have eosinophilic esophagitis or peptic esophageal stricture due to gastroesophageal reflux (GERD) as the etiology [2].

Chronic Dysphagia

Sensation in the esophagus is such that patients may have symptoms referred more proximally in their esophagus, but rarely will symptoms be referred distally [3, 4]. Therefore, patients presenting with discomfort in their upper thoracic or cervical esophagus may have causative pathology in any aspect of the esophagus, proximal or distal. But patients presenting with symptoms of dysphagia of the lower thoracic or distal esophagus will usually have pathology at the distal esophagus or gastroesophageal junction (GEJ).

Patients can usually discriminate whether dysphagia occurs stereotypically with a certain size bolus of food, and whether dysphagia occurs with solids or liquids or both. Generally, dysphagia to only solids implies there is a mechanical obstruction, whereas, dysphagia to solids and liquids implies an esophageal motility disorder is associated with the symptoms. Dysphagia to all solids implies a high-grade esophageal obstruction.

Patients with chronic dysphagia have usually made lifestyle and dietary changes to avoid the discomfort of dysphagia, and although weight loss is often observed with solid food dysphagia, paradoxical weight gain can occur with a change to softer high energy density foods. Dysphagia in the setting of a history of smoking and binge drinking should alert the clinician to a higher suspicion of squamous cancer of the esophagus. Dysphagia in the setting of long history of GERD should similarly raise suspicion for adenocarcinoma of the distal esophagus. However, one third of patients found to have esophageal adenocarcinoma have no history of reflux symptoms, and 40% of patients found to have achalasia have symptoms initially attributed to GERD [5]. Associated muscle weakness with dysphagia should raise suspicion for neuromuscular diseases that may also have associated oropharyngeal

swallowing disorders: ALS, polymyositis, and muscular dystrophy. And the association of connective tissue disorders with dysphagia prompts thoughts of scleroderma esophagus. Because the specificity of symptoms associations with dysphagia is so poor, further testing is required in all patients with dysphagia.

Diagnostic Testing

Contrast Esophagram

Contrast esophagram and upper flexible endoscopy (EGD) are complementary tests in the assessment of the patients with dysphagia. It has been customary teaching to have patients undergo Barium esophagram as the initial test, because knowledge of anatomical derangements found at barium swallow (Zenker's diverticulum, proximal esophageal webs and esophageal tumors or rings) may facilitate EGD or enable biopsy or treatment at the initial EGD session [6]. Barium swallow is the definitive test to identify paraesophageal hernia as the etiology of dysphagia and the most sensitive test to identify esophageal webs or rings.

Prone esophagram allows greater sensitivity in detecting subtle esophageal rings, and air contrast barium swallow may detect mucosal irregularity for future biopsy. Barium swallow with 13 mm barium tablet or barium soaked marshmallow is helpful in detecting an abnormality in solid bolus transport or mechanical obstruction of the esophagus. In patients known or suspected of having esophageal achalasia, a timed barium swallow is done by measuring the column of barium at 1, 2 and 5 min after swallowing liquid barium. This is primarily helpful in measuring progress after a procedure to improve esophageal emptying.

Upper Flexible Endoscopy—EGD

EGD is the first line test with the greatest yield in the evaluation of dysphagia and allows mucosal biopsy for the identification of Barrett's esophagus and esophageal cancer, as well as eosinophilic esophagitis. In patients with dysphagia undergoing EGD, routine biopsy should be performed in all patients, including at least four total biopsies of one proximal and one distal site down the esophageal lumen. Due to the ease and safety of through-the-scope dilation, empiric dilation of the LES should additionally be considered in patients with dysphagia. EGD is the standard for identifying or ruling out mucosal abnormalities, but is not a sensitive test for the identification of esophageal motility disorders.

Esophageal Motility Testing

High-resolution manometry and use of the Chicago classification scheme [7] to identify esophageal motility disorders has standardized the classification of esophageal motility patterns into major disorders which are always associated with

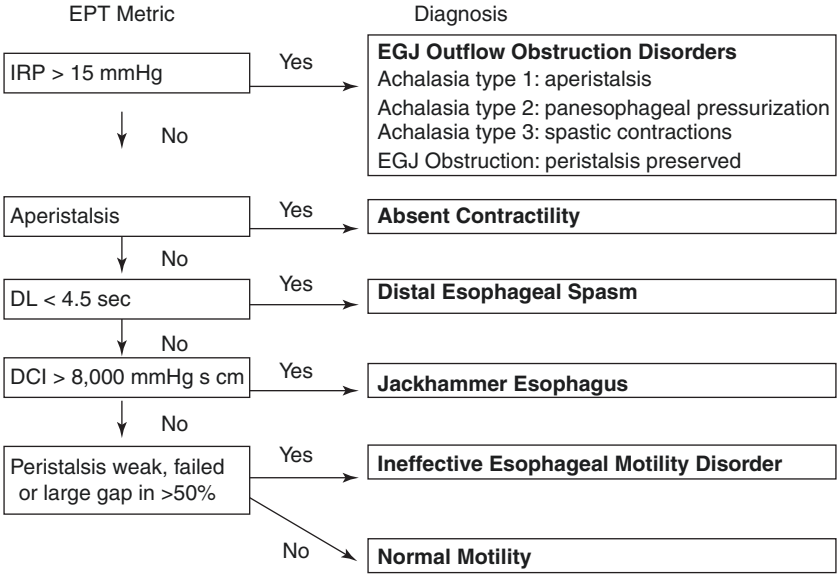

Fig. 2.1 Chicago Classification version 3. The hierarchical algorithm of the Chicago Classification is represented here, developed by the International High Resolution Manometry Working Group [8]. Abbreviations: *IRP* integrated relaxation pressure, *DL* distal latency, *DCI* distal contractile integral

symptoms. The prioritization of the Chicago classification scheme is to first identify the variants of esophageal achalasia, then to identify the other major hypermotile and hypomotile esophageal motility disorders, and finally to identify minor motility disorders [7]. Figure 2.1 diagrams the diagnostic algorithm of the Chicago Classification version 3. In those patients found to have no structural cause for dysphagia on contrast esophagram or endoscopy, motility testing identifies a causative motility disorder in 50% of patients [9].

Analysis of high-resolution manometry is performed in a systematic fashion, with the patients swallowing ten times of a 5 mL bolus of fluid. Initial assessment is of the completeness of each attempted swallow. For each complete swallow, five key metrics are measured from the esophageal topography plot (EPT). The first is the integrated relaxation pressure (IRP), measured as the mean nadir pressure of the lower esophageal sphincter (LES) in a 4 s time after swallow is initiated. This value establishes the presence or absence of achalasia variants, based on the associated findings of peristalsis, esophageal pressurization or spastic contractions.

Next, the time from initiation of swallowing to the slowing of the peristaltic wave at the esophageal ampulla (the contractile deceleration point, or CDP) is termed the distal latency (DL). This value establishes the premature- or simultaneous-nature of the peristaltic wave and is the metric used to diagnose distal esophageal spasm. The amplitude of esophageal peristalsis is measured as the integrated volume of the esophageal pressure topography map and is defined as the distal contractile integral

(DCI). The DCI metric defines both hypermotile major motility disorders (jackhammer esophagus) and minor hypomotility disorders (ineffective esophageal motility disorder). The slope of the peristaltic wave through the esophageal body is defined as the contractile front velocity (CFV) and is used as the metric to measure the rapidity of the peristaltic wave, a metric which no longer is associated with a named motility disorder. Finally, the length of any gap in the 20 mmHg isobaric curve on the peristaltic wave is measured, with a 5 cm gap signifying a fractured peristaltic wave. Simultaneous esophageal impedance testing is able to associate minor motility disturbances with incomplete esophageal emptying.

Other Diagnostic Modalities

When EGD is suspicious for vascular malformations impinging on the esophagus, a condition called dysphagia lusoria, CT scan of the chest is beneficial. Retroesophageal right subclavian artery is the most common of these malformations, but is generally asymptomatic. Impedance planimetry is used as an adjunctive test to measure esophageal compliance and can monitor progress in treating esophageal achalasia and eosinophilic esophagitis.

Differential Diagnosis of Esophageal Dysphagia

GERD Related Dysphagia

Reflux disease can be the cause of both structural- and motility-origin dysphagia and is by a considerable margin the most common cause of dysphagia. Peptic esophageal stricture is more common in elderly male patients with long reflux history, but is found in up to 10% of all patients undergoing endoscopy for evaluation of reflux symptoms. Peptic strictures occur most commonly at the squamo-columnar junction in the form of Schatzki's ring. Meat impaction is common, approaching an incidence of 13 per 100,000 population per year [10]. Short term treatment is by esophageal dilation, but long term treatment by decreasing GERD, including by antireflux surgery, reduces the incidence of repeat dilation [11].

Reflux also causes dysphagia by mechanism of ineffective esophageal motility induced by esophagitis. Gastroesophageal reflux disease is associated with hypocontractile states and GERD is likely causative of impaired peristalsis and decreased peristaltic amplitude. Hypotensive LES and inappropriate LES relaxation are similarly causative of GERD, and ineffective motility further exacerbates reflux by mechanism of delayed esophageal clearance.

Ineffective esophageal motility disorder (IEMD) is defined by the Chicago classification as greater than 50% of peristaltic waves that are failed, weak or have large gaps, but this definition does not accurately describe patients with IEMD with dysphagia [12]. As measured by HRM and a prior version of the Chicago classification, weak peristalsis has shown a higher correlation with dysphagia

than frequent failed peristalsis, but these disorders are considered together as a minor disorder because there are considerable numbers of healthy individuals who exhibit these findings.

With intensive antireflux therapy, IEMD may improve, but rarely normalizes. With antireflux surgery, partial fundoplication is associated with greater improvement in IEMD than total fundoplication and greater relief of IEMD associated dysphagia [13, 14]. Regarding surgical decision making in patients with IEMD seeking antireflux operations, it is the author's practice to consider whether the degree of IEMD is proportionate to the severity of GERD, based on degree of erosive esophagitis and pH testing. When peristaltic failure and/or dysphagia are out of proportion to the level of GERD, partial fundoplication is recommended.

Patients with aperistalsis thought due to severe GERD, without any findings consistent with connective tissue disorder, may be treated intensively with proton pump inhibitor therapy for 3–4 months and a motility study repeated. If there is significant improvement in esophageal peristalsis, then Nissen fundoplication can be considered.

Post-surgical Dysphagia

All patients undergoing fundoplication will experience immediate post-operative dysphagia related to edema of the operative site, and it is incumbent on the surgical team to prepare the patient's dietary expectations accordingly. Patients after Nissen fundoplication are usually able to return to solid food diet in a 4–8 week window after operation. However, approximately 5–10% of patients after Nissen fundoplication will be expected to struggle with the return to a solid diet. Aerophagia and early post-operative dry heaving increase post-operative dysphagia in patients otherwise expected to have routine recovery.

Postoperative dysphagia that does not improve by 8–12 weeks should be considered for esophageal dilation. This persistent postoperative dysphagia is associated with increased preoperative LES pressure and with incomplete preoperative LES relaxation [15]. Emerging use of multiple repetitive swallows during HRM has enabled some prediction of the "esophageal peristaltic reserve". When three small swallows are made in short succession, there is inhibition of esophageal body peristalsis and LES tone; this is followed in the normal state by an augmented esophageal contraction. The ratio of the DCI of the augmented contraction, relative to the average of the ten prior swallows, has predictive value for the absence of post-fundoplication dysphagia [8].

Patients undergoing magnetic sphincter augmentation are expected to experience dysphagia in the second to fourth week of recovery corresponding to the time period of maximally dense postoperative adhesive disease following operation. It is imperative that these patients persist on a solid or semi-solid diet through this period to prevent fibrotic adhesions from fusing some of the magnetic beads together. Antispasmotic medications, steroids, or even esophageal dilation can be required in this time period.

There are a small number of patients who develop worsening esophageal peristalsis after antireflux operation. When associated with hiatal stenosis or failure to pass a 13 mm barium tablet, aperistalsis in this setting can be indistinguishable from an achalasia variant. Failing esophageal dilation, remedial operation may be required to remove any foreign material at the hiatus and convert to partial fundoplication, with or without Heller myotomy.

Bariatric operations induce restriction of the upper stomach by creating stenosis via stapling (Roux en Y gastric bypass and sleeve resection of the stomach) or by extrinsic compression (adjustable gastric band). Dysphagia is not uncommon after adjustable gastric band and when associated with esophageal dilation or pouch enlargement would indicate band explant. Dysphagia can result from several different mechanisms after sleeve gastrectomy: a tight sleeve may create excessive restriction, disruption of gastric sling fibers with cardia stapling may induce spastic motility disorder, transhiatal herniation of the upper sleeve may create tortuosity of the distal esophagus, or uncontrolled GERD may induce IEMD. Although esophageal dilation for early postoperative sleeve-related dysphagia may be helpful for stenosis of the upper stomach, remedial operation with conversion to Roux en Y gastric bypass is often the best course of action.

Esophageal Cancer

Despite knowledge of the association between GERD and Barrett's esophagus and its progression to esophageal adenocarcinoma, and increasing proportion of citizens taking prescription proton pump inhibitors, the incidence of esophageal adenocarcinoma continues to increase in Western civilization. Adenocarcinomas of the gastroesophageal junction and cardia may be associated with an achalasia-like syndrome, pseudoachalasia, that be require endoscopic ultrasound to distinguish from achalasia. New onset dysphagia and rapid weight loss generally implies at least locally invasive disease that is not amenable to endoscopic resection. While long-term survival with chemo-radiation and subsequent resection has been shown to approach 50%, the overall prognosis remains dire for adenocarcinoma of the esophagus. Squamous cancer of the esophagus presents generally in the proximal to mid esophagus, is more radiation sensitive with approximately double the rate of complete response to chemoradiation, and has a higher likelihood of survival with multimodality therapy [16].

Esophageal Strictures

Approximately 75% of esophageal strictures are reflux related. These are typically passable by an endoscope, located at the squamo-columnar line, and short. Such strictures can be dilated by either freely-passed, weighted Maloney dilators, plastic Savary-Guillard over the wire bougies, or hydrostatic through-the-scope dilators. The effectiveness is based on clinician experience and generally thought to be

equivalent. Relief from dysphagia occurs with dilation to greater than 13 mm, but longer relief of dysphagia is associated with dilation to 16 mm or greater [17]. It is customary to start at the estimated stricture diameter and to dilate no more than 2 mm per session. Repeat dilation sessions approximately one-week apart may be required to achieve successful relief of dysphagia. Patients should be placed on twice daily proton pump inhibitor therapy for up to 1 year after stricture dilation, and GERD symptom control correlates with freedom from stricture recurrence [18].

Refractory or complicated strictures may require additional endoscopic techniques for successful dilation. In order of increasing invasiveness, additional techniques include: injection into the stricture of the steroid triamcinolone prior to dilation, endoscopic radial incision or biopsy of the stricture to break the mucosal ring, or placement of an expandable plastic, biodegradable, or dog-bone shaped flanged and covered metallic stent. Stents should be removed after 6–8 weeks and the stricture reassessed. An algorithm of progressive therapies for refractory strictures has not been systematically studied.

Non-peptic strictures make up the minority of esophageal strictures but account for a greater percentage of complicated strictures. Definitive chemo-radiation therapy has been proven effective for patients with squamous cancer of the esophagus exhibiting a complete pathological response to therapy; however, radiation-induced stricture is a not infrequent result of this therapy. Mucosa-limited esophageal adenocarcinoma may be treated with endoscopic mucosal dissection/resection with favorable recurrence free survival, but circumferential or near-circumferential resection is associated with up to 45% rate of esophageal stricture [19]. Other causes of non-peptic stricture include toxic ingestions of liquids such as lye. Esophageal anastomotic strictures occurring early after operation may be associated with leak, ischemia or fistula and stenting is preferable in such cases.

Esophageal Motility Disorders

With the exception of esophageal achalasia and scleroderma esophagus, disorders associated with distinct pathologic findings designating them as disease processes, all esophageal motility disorders are defined in terms of their metrics on high resolution manometry and by the current classification by the Chicago Classification v3.0.

Esophageal Achalasia

Esophageal achalasia is a disease characterized by esophageal outflow obstruction (caused by inadequate relaxation of the LES) and a pressurized and/or dilated esophagus with nonprogressive swallow responses. In achalasia, there is degeneration of ganglion cells in the myenteric plexus of the esophageal wall, related to absence in the LES of the neurotransmitters nitric oxide and vasoactive intestinal polypeptide [20]. Experimental models have long suggested that the peristaltic

abnormalities seen in esophageal achalasia are secondary to the outflow obstruction [21]. However, by the water-perfused manometry study and standard motility classification, aperistalsis was used as the most important motility abnormality identified in achalasia. Use of high-resolution manometry studies and the Chicago classification have redirected the diagnosis to reflect the pathophysiologic findings of achalasia [8]. Esophageal achalasia had previously been classified into subtypes, classic and vigorous achalasia, based on the finding in the esophageal body, of vigorous repetitive and high-amplitude swallow responses. This classification had no clinical significance, however.

The Chicago classification has refined the subclassification of achalasia into subtypes based on the finding of esophageal pressurization and premature contractions [22–24]. With type 1 representing classic achalasia and type 2 identifying patients with panesophageal pressurization (to >30 mm Hg) in 20% or greater swallows. Type 3, or spastic achalasia identifies patients who have no intact peristalsis but have the finding, in 20% or greater swallows, of premature or simultaneous contractions (with DL < 4.5 s). Further, type 3 achalasia represents patients who may have been, by classical definitions, been diagnosed as having diffuse esophageal spasm with incomplete LES relaxation. These type 3 achalasia patients are more likely to present with chest pain as a prominent symptom. Of these subtypes, type 2 seems to be slightly more common than type 1, and type 3 is infrequent in most reported series.

Additionally, the Chicago classification has allowed for the identification of patients with an achalasia variant, with the finding of incompletely- or non-relaxing LES and some preservation of peristalsis [25]. The classification EGJ (esophagogastric junction) relaxation abnormality includes patients who are found on later study to have achalasia with aperistalsis, as well as those with pseudoachalasia and postoperative (postfundoplication) states.

The development of high-resolution manometry and the Chicago classification has both broadened and simplified the definitions of achalasia and its subtypes. Additionally, the Chicago classification subtypes have some added prognostic value that may aid in the formulation of surgical planning. Type 1 achalasia seems to have better outcomes with myotomy as the initial treatment when compared with endoscopic therapies (botulinum toxin injection or pneumatic balloon dilation) [22]. Type 2 achalasia seems to have the best outcomes regardless of the initial treatment strategy and type 3 has the worst outcomes irrespective of treatment strategy (botulinum toxin, pneumatic dilation, and myotomy). Based on the reported improved response of type 2 patients to any initial treatment, there may be greater support among gastroenterologists for initial endoscopic therapy in type 2 achalasia patients, with myotomy relegated to treatment failures in type 2 patients. However, because there is a spectrum of continuity between type 1 cases with pressurization to just below 30 mm Hg and type 2 cases, and marginal differences between type 3 cases and some achalasia variants, it is unrealistic to make a firm algorithm regarding treatment based strictly on achalasia sub-types.

Although laparoscopic Heller myotomy with partial fundoplication is accessible to most patients with achalasia in North America, the diffusion of centers offering

peroral endoscopic myotomy (POEM) as a definitive treatment of achalasia has made this an option for most regions [26]. Because POEM is reflexogenic in one-third of patients without hiatal hernia, the presence of a hiatal hernia should be seen as a relative contraindication for the POEM procedure [27]. Otherwise, analysis of the outcomes for POEM based on reports from high-volume centers and the growing international experience essentially equates POEM outcomes with surgical myotomy without fundoplication by other approach [27–30].

Esophageal pulsion-type diverticula represent one of the most rare manifestations of achalasia, occurring in the author's experience in fewer than 5% of patients with achalasia. Although treatment of the underlying motility disorder yields acceptable results in most patients, the optimal surgical approach includes stapled diverticulectomy guided by intraoperative endoscopy, with Heller myotomy and partial fundoplication.

Hypercontractility States

Symptoms of dysphagia and chest pain are clinical scenarios that are suspicious for hypercontractile esophageal motility disorders. Although contrast esophagram may confirm a hypercontractile esophageal motility disorder, it is not sensitive enough to be used as a screening test. An esophageal motility study is required to establish a diagnosis and initiate treatment. Based on the Chicago classification and analysis of high-resolution manometry EPT metrics, there are two identified major hypercontractile abnormalities that are always associated with patient symptoms and never identified in normal individuals [31]. Using the new classification scheme, the number of patients diagnosed with hypercontractile motility disorders is markedly reduced and, because the most extreme cases have been selected, response to medications and natural history of the disorders as currently diagnosed are unknown.

Distal Esophageal Spasm

The name diffuse esophageal spasm has been something of a misnomer because it is the distal esophagus that is spastic [32]. DES is now the preferred terminology but both are used interchangeably. Patients with DES commonly present with dysphagia. Because of the observed response in DES patients to nitroglycerin, it is thought that DES may be pathophysiologically linked to a defect in esophageal nitric oxide production [33, 34]. Contrast esophagram may demonstrate the classic corkscrew esophagus or rosary bead esophagus; however, a normal contrast esophagram does not exclude DES. The hallmark of DES by classic esophageal motility study has been the finding of frequent simultaneous peristalsis. Classically, in one-third of patients there has been some abnormality of the LES (either hypertensive LES or incompletely relaxing LES) [35, 36]. However, with high-resolution manometry

and interpreted by the Chicago classification, some of these latter patients would be now considered to have type 3 achalasia or an achalasia variant.

High-resolution manometry diagnostic criteria rely on measurement of DL to determine whether a peristaltic contraction is considered premature or simultaneous (DL < 4.5 s). The Chicago classification designates DES as having 20% or greater of swallows with DL less than 4.5 s. This is in contrast to the characteristic manometry finding of high-velocity peristalsis (CFV > 8–9 cm/s) to identify simultaneous contractions, or the findings of repetitive contractions or contractions of long duration (>6 s) in greater than 20% of peristaltic waves that previously constituted DES. The Chicago classification requires that there also be normal LES relaxation to distinguish DES from achalasia variants. Greater than two-thirds of patients previously diagnosed as having DES will now receive a different diagnosis using the Chicago classification [37]. Rapid contraction, defined as 20% or greater swallows with CFV greater than 9 cm/s was considered borderline motility by the Chicago classification version 2 [38] but is not considered an abnormality on the current classification.

Although patients with classically defined DES followed longitudinally show that the majority improve somewhat with time without directed medical therapy, [39] there are several classes of medication that have proven to be somewhat helpful in managing the disorder. The antidepressants trazodone and imipramine were found to decrease chest pain with DES, likely by modifying esophageal sensitivity [40, 41]. The phosphodiesterase inhibitor sildenafil has been associated with symptomatic relief [42]. Botulinum toxin delivered by endoscopic injection was found to decrease dysphagia [43].

The diagnostic criteria for DES are now more restrictive and DES now refers to a more distinct clinical phenotype. With the more restrictive definition, it should be infrequent that the surgeon encounters a patient with documented GERD and DES. In a patient with documented GERD who has diagnostic criteria for DES on preoperative high-resolution manometry, the surgeon should reassess which symptoms may be due to DES and, therefore, unlikely to respond to antireflux therapy. For patients with GERD who have prominent dysphagia symptoms and DES, Nissen fundoplication is not recommended. In patients with noncardiac chest pain found to have DES and GERD that are failing medical therapy, the surgeon should consider starting an antidepressant before or after antireflux surgery.

More commonly, the surgeon encounters patients who previously would have been diagnosed with DES but are now classified as having a nonspecific spastic motility disorder because of rapid or simultaneous contractions not fulfilling criteria for DES. Expectations should be revisited as to which symptoms are likely to improve after operation. In patients presenting with DES and refractory symptoms of dysphagia and chest pain, it is reasonable to perform endoscopic botulinum toxin injection. Although there are reported small series of POEM procedure for DES [29, 44], this should be viewed with caution because of the propensity for classically defined DES symptoms to lessen over time without intervention.

Jackhammer Esophagus

The hypercontractile esophagus is characterized by high-amplitude esophageal body peristaltic contractions, associated with chest pain and/or dysphagia. Using the water-perfused manometry system, the criteria for defining the disorder as nutcracker esophagus had undergone some evolution to a higher mean amplitude (from 180 to 220 mm Hg) to decrease the number of patients diagnosed with the disorder who had reflux symptoms rather than chest pain [45]. Using the high-resolution manometry system, the Chicago classification developed an entirely new metric, the DCI, and identified the threshold for which a single swallow with elevated DCI was always associated with dysphagia (DCI > 8000 mm Hg/cm/s), and termed this disorder jackhammer esophagus. This is reflective of the finding of repetitive contractions in most spastic hypercontractile waves. Mean DCI greater than 5000 mm Hg/cm/s based on ten swallows was termed hypertensive peristalsis; however, this finding is no longer considered abnormal.

The pathophysiology of the hypercontractile esophageal disorders is thought to be due to asynchrony in the circular and longitudinal smooth muscle of the esophagus during contraction. Because this is reversible with atropine, it thought to be due, in part, to a hypercholinergic state [46]. Treatment of hypercontractile esophagus is similar to treatment of DES. Diltiazem was found to relieve chest pain in patients with nutcracker esophagus [47]. Sildenafil, trazodone, and imipramine have also been found to be helpful [40–42]. Based on the pathophysiology of the disorder, anticholinergic medications would be expected to have treatment benefit. Endoscopic botulinum toxin injection has a response rate greater than 70% and half of treated patients have, at least temporarily, complete relief of chest pain [48]. Failing medical therapy, patients with nutcracker esophagus with severe dysphagia may undergo Heller myotomy with good relief of dysphagia; however, relief of chest pain is less certain with laparoscopic Heller myotomy [49]. Small series of POEM for hypercontractile esophagus show promise, with high rates of relief of chest pain [29].

The classically described nutcracker esophagus has been associated with GERD. The finding of hypertensive peristalsis in a patient with GERD should not alter the treatment plan for antireflux surgery. Because jackhammer esophagus is a finding always associated with chest pain or dysphagia, the treatment plan should reflect the expectation that this disorder will not resolve with treatment of GERD and should be specifically addressed. However, definitive treatment studies have not been performed using these specific criteria for hypercontractile esophagus.

Hypocontractile States

There are distinct pathological findings associated with the esophageal manifestations of systemic sclerosis, or scleroderma. Scleroderma esophagus is caused by atrophy and sclerosis of the smooth muscle of the esophagus; the striated proximal esophageal muscle is spared. Thus scleroderma, mixed connective tissue disorders or collagen vascular diseases, with esophageal manifestations should be considered

separately from ineffective esophageal motility associated with GERD. Scleroderma esophagus is defined as aperistalsis with low or absent LES pressure (resting pressure < 10 mm Hg). Esophageal findings are present in over 70% of patients with the typical skin manifestations of scleroderma [50, 51]. Esophageal manometry findings similar to that found in scleroderma and the mixed connective tissue disorders may be found in other diseases, such as polymyositis, dermatomyositis, muscular dystrophy and Sjogren's. Sjogren's syndrome is also associated with the symptoms of dysphagia, and xerostomia compounds the problem of esophageal dysmotility in these patients.

The primary consideration in managing scleroderma esophagus is preventing development of peptic esophageal stricture, malnutrition, or recurrent aspiration pneumonia. Although a loose Nissen fundoplication may be used [52], more recent reports recommend partial fundoplication [53], and consideration should be given to placement of gastrostomy tube for feeding access during antireflux surgery [54].

Functional Dysphagia

Functional dysphagia was characterized by the Rome III Consensus as one of four benign functional disorders of the esophagus, along with globus sensation, functional heartburn, and functional chest pain [55]. The criteria for diagnosis include presence of the symptom of dysphagia for at least 6 months, including the last 3 months, absence of evidence that GERD is associated by both upper flexible endoscopy, contrast esophagram, and esophageal physiologic testing, and absence of histopathology-based esophageal motility disorders. Emerging reports suggest that 25% of patients with functional dysphagia have subtle esophageal motility disorders such as incomplete LES relaxation or even delayed LES relaxation (over 50% of swallows with greater than 5 s between UES and LES relaxation) [56].

Treatment is by reduction of stress that may exacerbate the sensation of dysphagia [57], desensitization of the esophagus with tricyclic antidepressants or selective serotonin reuptake inhibitors. Upper flexible endoscopy with esophageal dilation may be utilized if the lower esophageal sphincter is found to be incompletely relaxing on high-resolution motility [55] or if barium tablet is delayed on contrast esophagram.

Eosinophilic Esophagitis

The classic presentation of eosinophilic esophagitis (EoE) is dysphagia in a young male with asthma, eczema or atopic disorders and history of prior esophageal meat impaction. EGD will identify in the majority one of the characteristic findings of edema, esophageal longitudinal furrows, trachealization of the esophagus with concentric rings, or exudates, but EGD may visually be normal in up to 25% of patients with biopsy proven eosinophilic esophagitis [58, 59]. Up to 15% of all patients undergoing EGD for evaluation of dysphagia will be found to have

EoE [60]. The diagnosis is based on the finding in esophageal biopsy of greater than 15 eosinophils per high power field in the squamous epithelium of the esophagus—in EoE, the eosinophils are limited to the esophagus and persist after a two-month trial of proton pump inhibitor to exclude reflux-related eosinophilia [59]. With at least four esophageal biopsies the sensitivity of detecting eosinophils reaches 98%. When EOE is suspected in the presence of other foregut symptoms, EGD should also include gastric and duodenal biopsies to document eosinophilic gastroenteritis.

Because EoE is an antigen-mediated cellular hypersensitivity disorder, allergy testing to reduce dietary allergens can be considered for therapy. Elimination diet of allergic foods can be based on allergy testing or empirically-empiric elimination diets are generally more effective. The foods that are known to elicit the greatest IgE response and are triggers of EoE are milk, eggs, legumes and wheat. Once successful response in esophageal eosinophilia is documented by endoscopic biopsy, foods can be reintroduced sequentially with repeat endoscopic guidance. Specific validated questionnaires (MDQ-30) may be used to assess the level of dysphagia due to EoE and to guide treatment [61].

In addition, swallowed topical steroids (budesonide) have been proven effective in reducing symptoms and maintaining remission from symptoms [62], but are not as effective in patients with esophageal stricture [63]. Endoscopic dilation has classically been described as having a higher risk of perforation in patients with untreated EoE-perforation has occurred even during diagnostic endoscopy in patients with EoE. Generally, dilation is reserved for EoE related rings or strictures who are failures of first-line medical therapy and should be performed cautiously.

Conclusion

Dysphagia is an alarm symptom that the clinician should seek to explain. Upper endoscopy has the highest yield in ruling out esophageal cancer, erosive esophagitis due to severe GERD, and eosinophilic esophagitis; and endoscopic dilation may provide immediate relief from rings and strictures. Contrast esophagram can detect subtle rings and a barium pill can detect delayed esophageal emptying due to paraesophageal hernia. Esophageal motility testing is essential for diagnosing major esophageal motility disorders, and emerging refinements of the high resolution manometry are improving the diagnosis of functional dysphagia and may be predictive of post-surgical dysphagia.

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