Benign Esophageal Tumors

CrossMark

Cindy Ha, MD[a], James Regan, MD[a], Ibrahim Bulent Cetindag, MD[a],
Aman Ali, MD[b], John D. Mellinger, MD[a],*

KEYWORDS

- Leiomyoma • Gastrointestinal stromal tumor • Mediastinal cyst

KEY POINTS

- Endoscopic evaluation including endoscopic ultrasonography is foundational to the evaluation of benign and indeterminate esophageal pathology.
- Leiomyomas have distinctive distributions, behavior, and entailed therapeutic significance in pediatric patients.
- Immunohistochemical analysis is an important adjunctive diagnostic tool in distinguishing noncarcinomatous tumors of the esophagus.
- Symptomatic lesions and those with rapid change in size dictate surgical management.
- Endoscopic, thoracoscopic, and laparoscopic techniques including enucleation are widely used in the management of benign tumors of the esophagus.

INTRODUCTION

Unlike esophageal carcinoma, benign esophageal tumors and cysts are rare. Multiple autopsy series have been performed in the past, and although the specific results vary, the overall incidence is less than 1%. In addition, benign tumors account for less than 5% of all surgically resected esophageal tumors.[1] Nevertheless, the past century has shown an increasing trend in the incidence of these lesions, most likely a reflection of improving diagnostic methods,[2] and continued advancements in the understanding of their natural history and management. Benign esophageal tumors are often asymptomatic and typically require only close surveillance. If surgery is indicated because of symptoms or diagnostic uncertainty, many of these tumors can be successfully resected with excellent long-term outcomes. Because these lesions are rare, the general or gastrointestinal (GI) surgeon should have a strong foundation in their diagnosis and treatment.

[a] Department of Surgery, Division of General Surgery at SIU, Southern Illinois University School of Medicine, 701 North First Street, Springfield, IL 62794, USA; [b] Department of Internal Medicine, Division of Gastroenterology, Southern Illinois University School of Medicine, 701 North First Street, Springfield, IL 62794, USA
* Corresponding author. PO Box 19638, 701 North First Street, Springfield, IL 62794.
E-mail address: jmellinger@siumed.edu

HISTORY

The first documented record of a benign esophageal tumor was in 1559 by Sussius. The tumor was discovered on autopsy, located in the distal esophagus, and has been cited as a leiomyoma, although histologic confirmation is lacking.[3] In 1763, Dallas-Monro performed one of the first treatments of a benign esophageal tumor when he excised a pedunculated esophageal mass using a snare from a 64-year-old man who had regurgitated the mass into his mouth. The first successful surgical treatment of a benign esophageal tumor is generally credited to Sauerbach, who performed a partial esophagectomy with esophagogastrostomy in 1932 for a myoma, most likely a leiomyoma. One year later, Oshawa performed the first open enucleation of an esophageal leiomyoma, and in 1937, Churchill performed the first open enucleation of a benign esophageal tumor in the United States for what was initially described as a neurofibroma but later reclassified as a leiomyoma.

According to Storey and Adams[4] in their case report and review of leiomyoma of the esophagus, only 16 documented surgical cases were found up until 1948, but between then and time of their publication in 1956, they found an additional 94 cases described, including 4 cases of their own. Since then, there have been many more recorded surgeries for benign esophageal tumors, and within the past 2 decades, there has been a shift toward minimally invasive approaches, specifically via thoracoscopy and endoscopy.

INCIDENCE

Several autopsy series and medical literature reviews have been performed in the past, searching for the true incidence of benign esophageal neoplasms. In 1932, Patterson[5] reported a total of 62 benign esophageal tumors during a 215-year period from 1717 to 1932. In 1944, Moersch[6] found 44 benign tumors and cysts in 7459 autopsy examinations, for an incidence of 0.59%. Plachta[7] in 1962 reviewed 19,982 postmortem examinations and found a total of 505 esophageal neoplasms, 90 of which were benign, resulting in an overall incidence of 0.45% with approximately 18% of all esophageal tumors being benign. In 1968, Attah and Hajdu[8] found 26 benign tumors among 15,454 autopsies during a 30-year period, for an incidence of 0.16%. Allowing for some variation among these studies, the overall incidence is cumulatively documented as less than 1%.[1] By way of comparison, malignant esophageal carcinoma is approximately 50 times more common.[9] The mean age of presentation for benign lesions is between the third and fifth decade of life, much younger than the mean age of presentation for esophageal carcinoma, and studies suggest a slight male predominance with an average ratio of 2:1.[1]

Unlike other benign tumors, esophageal duplications and cysts are more common in children. Accordingly, although such lesions are estimated to comprise only 0.5% to 3.3% of all benign esophageal masses in adults, they account for approximately 12% of all mediastinal tumors in the pediatric population. Between 25% and 35% of all esophageal duplications first become manifest in adults, and of these, most present in adults younger than 50 years.[10]

CLINICAL FEATURES

Benign esophageal tumors are generally slow-growing masses, and they may remain stable without any change in size for many years. At least 50% of benign esophageal masses are asymptomatic,[7] and they are frequently diagnosed incidentally on imaging or endoscopy performed for other reasons.[2] Choong and Meyers[1] broadly categorized

the clinical presentations of benign esophageal neoplasms into 5 groups: asymptomatic, obstruction from intraluminal growth, compression of adjacent tissue by extraluminal tumor, regurgitation of a pedunculated tumor, and ulceration with bleeding.

The most common presenting symptom is dysphagia, and the degree of severity varies between patients. Because of the compliance of the esophagus, symptoms often occur late in the disease process as the lesions grow enough to cause luminal obstruction or compression. Typically, a size of 5 cm or more correlates with the likelihood of such symptoms developing.

The next most common symptoms are pain, usually retrosternal or epigastric in location, and pyrosis. Obstructive symptoms more commonly occur with intraluminal tumors,[1] and rarely, these tumors can present with ulceration,[11] bleeding, or regurgitation. Circumferential or annular involvement has been described, causing luminal narrowing and obstruction,[11] but this is an uncommon presentation.[1]

Respiratory symptoms may occur as well. Storey and Adams[4] found that 10 of the 110 reviewed patients presented with predominately respiratory symptoms, which were thought to be the result of tracheal or bronchial compression by the tumor. Presenting respiratory complaints are more common in the pediatric population.

In contrast to patients with malignant esophageal carcinomas, patients with benign tumors often present with multiple symptoms of long duration. Seremetis and colleagues[12] in their analysis of 838 cases of esophageal leiomyoma found that 30% of symptomatic patients reported a symptom duration of more than 5 years; another 30%, 2 to 5 years; and the remaining 40%, an average of 11 months.

DIAGNOSIS

Frequently, the diagnosis of a benign esophageal tumor or cyst is made incidentally on imaging or endoscopy performed for other indications. A plain chest radiograph may reveal a posterior and/or middle mediastinal, paraesophageal mass. However, the sensitivity and specificity of a plain radiograph is low, and the mass must reach a significant size before it becomes apparent on a chest radiograph.[4]

A contrast swallow study is most likely the best initial test to obtain in the evaluation of a symptomatic patient. Esophagography is usually performed in a biphasic manner with upright double-contrast views with high-density barium suspension and prone single-contrast views with low-density barium suspension. The former allows for evaluation of the mucosa, and the latter facilitates evaluation of any areas of luminal narrowing. Benign esophageal tumors usually are manifest as mobile lesions with smooth contours. Occasionally, altered peristalsis is seen with intraluminal tumors.[13]

Computed tomography (CT) of the chest is helpful in the evaluation of extraesophageal tumors and exclusion of other mediastinal masses that could lead to similar clinical presentations. The relationships between the esophageal tumor and surrounding tissues are also better defined with CT, which may be invaluable in preoperative planning when indicated by symptoms or diagnostic uncertainty.[14]

Endoscopy and endoscopic ultrasound (EUS) imaging are mandatory in the evaluation of a symptomatic esophageal tumor. In addition to excluding malignant carcinomas, endoscopy allows for visualization of the mucosa and biopsy of intraluminal and submucosal tumors. Although intramural tumors are not visualized on endoscopy, it is essential to confirm an intact mucosa if an intramural tumor is suspected. EUS imaging provides visualization of the esophageal layers and defines which layers are involved with the tumor, which is invaluable in perioperative planning and surveillance. In addition, EUS imaging can reveal certain unique sonographic characteristics that can aid in the diagnosis of the tumor. Lack of enlarged lymph nodes, smaller size,

homogeneous echo pattern, and smooth borders favor a benign lesion on EUS imaging.[2] EUS imaging also allows needle biopsy of these lesions and any associated pathology including lymph nodes, which is more often diagnostic than simple endoluminal biopsy for lesions beyond the confines of the mucosa.[14]

MANAGEMENT

In the past, surgical resection was recommended for most esophageal neoplasms, including benign ones. However, recent advances have shown that most benign esophageal tumors are slow growing,[15] and with the exception of esophageal gastrointestinal stromal tumors (GISTs) and adenomas, malignant transformation is rare.[16] Accordingly, many of these lesions can be followed with serial studies if asymptomatic.[14] Historically, if surgery was indicated, an open approach was advocated. However, in the past 2 decades there has been an increasing shift toward minimally invasive techniques with endoscopic, laparoscopic, or thoracoscopic resections.[17] These methods are discussed in greater detail as they apply to each individual type of lesion in the following sections.

CLASSIFICATION

Benign esophageal tumors can be classified in several ways, and various classification schemes have been proposed in the past based on esophageal layer of origin, histologic cell type, and location as well as clinical appearance. Many of the histologic tumor types can occur in multiple and varying layers of the wall. Rice[2] described the 5 discrete esophageal layers seen on EUS imaging, specifically the superficial mucosa, deep mucosa, submucosa, muscularis propria, and paraesophageal tissue. As a way of characterizing layer of origin and relationship to adjacent structures, EUS imaging has become a practically essential tool in the diagnosis and characterization of these benign esophageal tumors. Having weighed all these variables, classification by location is probably the most practical method, primarily because it dictates the treatment strategy. A summary of a location-based classification scheme is given in **Box 1**.

Box 1
Classification of benign esophageal tumors

Intramural

Leiomyoma

Gastrointestinal stromal tumor

Schwannoma

Intraluminal

Epithelial polyps (adenomatous and inflammatory)

Lipomatous polyps

Fibrovascular polyps

Papilloma

Hemangioma

Granular cell tumor

Extraesophageal

Duplications and cysts

INTRAMURAL TUMORS
Leiomyoma

Leiomyoma is a benign smooth muscle tumor found throughout the GI tract, and although only 10% of all GI leiomyomas are located in the esophagus,[11] they are the most common benign esophageal masses, accounting for approximately two-thirds of all benign esophageal tumors.[14] Morgagni provided the first description of a GI leiomyoma in 1761.[4]

Many autopsy reviews have been performed to assess the incidence of benign esophageal tumors as documented earlier, and in regards to leiomyomas specifically, the general incidence ranges from 0.006% to 0.1%.[9] The incidence of clinically significant leiomyomas is much lower, as at least half of these lesions are asymptomatic and diagnosed incidentally. There has been an increase in incidence during the past few decades because of improved and more widespread use of endoscopy.[2]

Leiomyomas can arise from smooth muscle in the muscularis propria or muscularis mucosae, but the latter is much less commonly encountered, presenting as an intraluminal polypoid lesion in 7% of documented cases based on a review by Hatch and colleagues.[15] Most lesions arise from the muscularis propria, with 80% being found in intramural and 7% in extraesophageal positions. Most are solitary and involve a localized area of the esophageal wall. Less than 2.4% of documented cases reported multiple tumors, and 10% to 13% were annular with circumferential involvement.[14]

Anatomically, leiomyoma is found most often in the middle and distal thirds of the esophagus, which reflects the increasing proportion of smooth muscle as opposed to striated muscle within the esophageal wall. In their review of 838 cases, Seremetis and colleagues[12] found that 56% were found in the distal third, 33% in the middle third, and 11% in the upper third. Furthermore, approximately 6.8% also involved the gastroesophageal junction and/or proximal stomach.

These benign esophageal smooth muscle tumors can occur at any age, but more than 80% are found between the second and sixth decades, with the peak time of presentation between ages 30 and 50 years. It is also more commonly seen in adult men, with an overall 2:1 male to female ratio.[14] The natural history of the esophageal leiomyoma reflects an overall slow, indolent progression, and malignant transformation is extremely rare. There have only been 4 documented cases in the past of progression to leiomyosarcoma, and each case was heralded by a preceding change in size.[12,14,15]

Esophageal leiomyoma has rarely been found in the pediatric population.[11] In contradistinction to adults, leiomyomas in the pediatric population are twice as common in girls. Furthermore, 91% of cases show multiple tumors and/or diffuse involvement, with 35% involving the entire length of the esophagus. Individuals with this more diffuse form of involvement typically require more aggressive surgical management strategies, as outlined further in the discussion.[18]

Leiomyoma has been associated with a variety of other benign esophageal conditions such as achalasia, other dysmotility disorders, esophageal diverticulum, and gastroesophageal reflux. The most commonly associated condition is hiatal hernia, found in 4.5% to 23% of patients with leiomyoma.[14]

In the past, leiomyoma was considered apart of a spectrum of mesenchymal tumors, which also included GISTs. However, studies have shown that these 2 tumors are distinct entities in regards to ultrastructure, histology, and genetic and immunohistochemical markers.[16,19]

In regards to gross appearance, leiomyomas are firm, rubbery, well-encapsulated masses with smooth surfaces. They range from white, gray, tan, or yellow in color and often have a whorled appearance on cut section.[12] Although shapes vary, smaller

ones tend to be oval or spherical and larger ones, horseshoe or dumbbell-like in shape. Most are small in size as well, likely reflecting the more slow-growing natural history, with approximately 50% less than 5 cm and 93% less than 15 cm.[14] On histologic examination, leiomyomas are characteristically composed of uniform spindle cells arranged in fascicles or whorls with eosinophilic cytoplasm and surrounding hypovascular connective tissue, few to no mitotic figures, bland cigar-ended nuclei, minimal to no cellular atypia, and overall hypocellularity.[12,14,16]

The description of GISTs in regards to gross, histologic, and immunohistochemical characteristics are discussed in more detail in a separate section, but in brief comparison for the sake of review of leiomyomas, GISTs grossly appear soft with fish flesh–like consistency and histologically appear overall basophilic with high cellularity and increased mitotic figures and cellular atypia. The histologic features in turn reflect the higher malignant potential and more aggressive nature of GISTs vis-à-vis leiomyomas.[16,19]

Although gross appearance and histology can help differentiate leiomyoma from GIST, the definitive foundation for distinguishing between these 2 entities lies in 4 immunohistochemical markers. Leiomyoma is typically positive for desmin and smooth muscle antigen (SMA) and negative for CD117 and CD34. By way of contrast, GISTs are uniformly positive for CD117 and almost uniformly positive for CD34, and usually negative for desmin and SMA. The most specific of these markers is CD117, which corresponds to the c-kit protein.[16]

These histopathologic and immunohistochemical characteristics are essential to differentiate leiomyoma from GIST, which in turn becomes important in defining management and surveillance strategies.

Approximately 50% of leiomyomas are asymptomatic and incidentally diagnosed, which likely reflects the smaller average size of these masses. Although not absolute, the presence of symptoms seems to trend directly with the increase in size, with symptoms usually presenting once the leiomyoma reaches a dimension of 5 cm.[1] Overall, symptoms tend to be vague and nonspecific in nature and develop over a longer duration than in the case of malignant esophageal lesions. Seremetis and colleagues[12] found that 30% of reviewed cases reported symptoms for more than 5 years and another 30% for 2 to 5 years; of the remaining 40%, the average length of symptom duration was 11 months. In addition, most present with multiple symptoms rather than 1 predominant one.[3]

The most common initial symptoms are dysphagia and/or chest pain. The pain is located usually in the epigastrium and/or retrosternal region and described as a pressurelike pain. The level of the dysphagia and pain vary widely, but in general, these symptoms are less severe and present less acutely compared with esophageal carcinomas.[15] Other frequently encountered symptoms include pyrosis, mild and gradual weight loss (rarely more than 20 lb [9.1 kg]), and nausea.[12] Respiratory symptoms such as dyspnea, recurrent respiratory infections, and cough can occur as well but are uncommon, occurring in approximately 10% of cases.[3] Hemorrhage and ulceration rarely occur with esophageal leiomyomas and constitute an indication for removal.[15]

In regards to the pediatric population, esophageal leiomyomas are more often symptomatic in contrast to adults. In addition, although dysphagia is still the most common presenting symptom in children, unlike in adults, the second most common symptom in pediatric patients is dyspnea, with respiratory symptoms in general being more often encountered.[18]

It is important to distinguish leiomyoma from leiomyomatosis, a benign condition characterized by diffuse smooth muscle proliferation. In leiomyomatosis, there is

typically involvement of muscularis propria and muscularis mucosae along the entire length of the esophagus. Most patients, approximately 95%, are symptomatic, and it is often associated with Alport syndrome or other smooth muscle hypertrophy disorders affecting multiple organs.[20]

Although not particularly sensitive or specific, plain chest radiographs are often the first diagnostic modalities to suggest the presence of leiomyoma, leading to its incidental diagnosis. These lesions can be missed if they are small, but if large enough, an esophageal leiomyoma may appear as a smooth, round hyperdense mass in the posterior mediastinum.[3]

Because of its high sensitivity and noninvasive nature, barium swallow study is the best initial diagnostic test. Leiomyoma classically is seen as a smooth, well-defined filling defect with approximately half of the submucosal mass protruding into the lumen as a convex mass and the other half within the esophageal wall. It is often half-moon or crescent shaped and characteristically forms right or slight obtuse angles with the adjacent esophageal wall when seen on lateral view. The mass is usually mobile and nonobstructing, rarely presenting with proximal esophageal dilatation. Over the mass itself, flattened mucosal folds are classically described.[14]

In addition to barium swallow, endoscopic evaluation is mandatory (**Fig. 1**). Although leiomyomas, in the absence of ulceration, would be characterized by normal overlying mucosa and as such would not be well visualized by endoscopy, it is necessary to rule out mucosal abnormalities, which would point toward another cause. The presence and location of the tumor should also be identified.[12] The 4 characteristic endoscopic findings of leiomyoma according to Postlethwait are (1) intact, normal overlying mucosa; (2) tumor projecting into the lumen at varying degrees; (3) tumor mobility with overlying mucosa sliding easily over the mass itself; and (4) possible luminal narrowing but rarely any findings of stenosis or obstruction.[21]

If leiomyoma is suspected, blind endoscopic biopsy is not recommended as it increases the risk for perioperative complications and rarely obtains adequate tissue for diagnosis because of the submucosal location. In regards to the former, endoscopic biopsies increase the risk for adhesions to the mucosa during healing and as a result may complicate surgical enucleation, increasing the risk for violation of the mucosa at the time of resection via that technique.[22]

EUS imaging is emerging as an essential test in the diagnosis and management of leiomyoma. Although esophagoscopy is limited to partial mucosal visualization, EUS imaging allows evaluation of all esophageal layers. As described by Rice[2] and
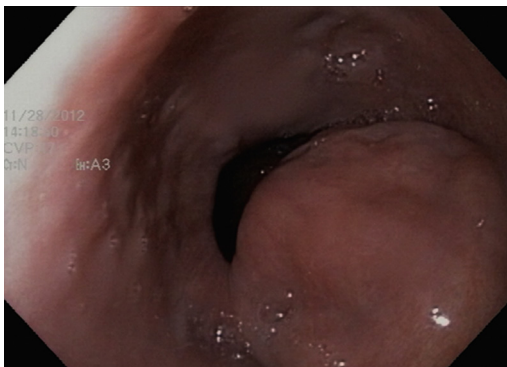

Fig. 1. Endoluminal endoscopic view of leiomyoma.

mentioned earlier, there are 5 alternating hyperechoic and hypoechoic layers visualized on EUS imaging, which in turn represent the mucosal, deep mucosal, submucosal, muscularis propria, and surrounding connective tissue layers, respectively. In the evaluation of an esophageal mass, EUS imaging provides the ability to determine the layer of origin as well as the ability to evaluate for other features such as size, borders, regional lymphadenopathy, echoic pattern, and local invasion.

On EUS imaging, leiomyoma appears as a well-circumscribed, homogenous, hypoechoic mass with smooth borders, arising from the third submucosal layer. There is no regional lymphadenopathy. Findings of size greater than 4 cm, irregular borders, invasion into other layers, and/or regional lymphadenopathy are atypical[14] and would require further workup to rule out malignancy, such as endoscopic biopsy,[22] fine-needle aspiration (FNA) via EUS imaging, and/or surgical enucleation or resection to rule out other causes.[14]

EUS-FNA may be used in conjunction with EUS imaging to obtain cytology and possibly more definitive diagnosis of leiomyoma (Fig. 2).[14] Cytology would allow for immunohistochemical analysis as well, which as described earlier, would help differentiate leiomyoma from GIST and leiomyosarcoma. Although EUS-FNA has not been proved more accurate than EUS imaging alone in terms of esophageal submucosal tumors specifically, it has been proved to improve diagnostic accuracy for similar gastric and duodenal tumors, and, accordingly, is worthy of consideration if more definitive diagnosis is needed.[23]

CT may also be performed to evaluate a possible esophageal leiomyoma with an estimated sensitivity of 91%. It is most helpful in evaluating for invasion, the presence of extrinsic compression, and anatomic relationships to nearby structures.[14] Leiomyoma classically appears as a smooth, well-demarcated, round or lobulated mass with homogenously low or isoattenuation. CT scanning does not typically differentiate cystic from solid masses and is therefore limited in its utility for evaluation of intramural pathology.[13]

The treatment of symptomatic leiomyoma is surgical enucleation, either via an open or a thoracoscopic approach (Fig. 3) or via laparoscopy for lesions in the distal esophagus or gastroesophageal junction area.[22] The management of asymptomatic leiomyoma, however, is more debatable as suggested by the natural history studies outlined earlier. In the past, the recommendation was to excise every esophageal leiomyoma diagnosed.[3,15] However, it has been demonstrated that leiomyoma rarely progresses to malignant leiomyosarcoma and often remains stable in size for years.[1]
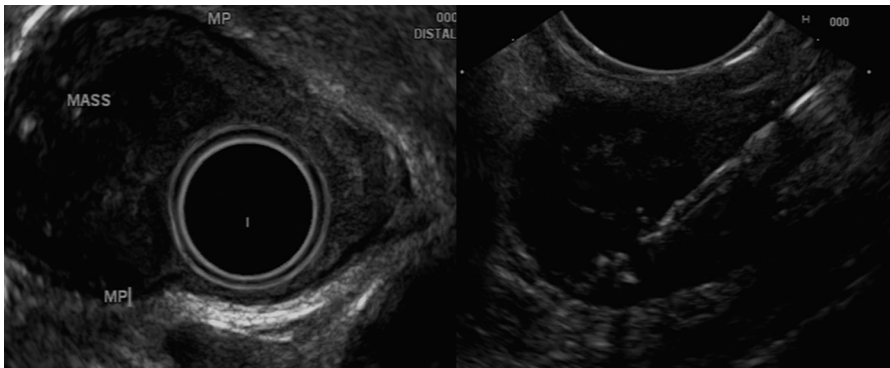

Fig. 2. EUS view of leiomyoma (*left*) and FNA needle in same under EUS guidance (*right*).
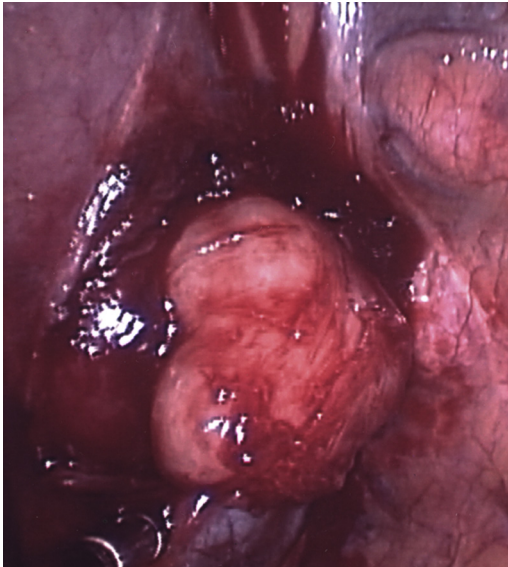
Fig. 3. Esophageal leiomyoma undergoing thoracoscopic enucleation. (*Courtesy of* Stephen R. Hazelrigg, MD, Department of Surgery, Southern Illinois University School of Medicine, IL.)

In general, the indications for surgery for leiomyoma is the presence of symptoms; size greater than 4 cm[14]; atypical findings on studies concerning for malignancy such as the presence of irregular borders, regional lymphadenopathy, heterogenous echoic pattern, or mucosal abnormalities; ulceration; and increase in size.[22] If the leiomyoma is small and asymptomatic, it may be followed with surveillance endoscopy and EUS imaging with or without chest CT every 6 to 12 months and perhaps at longer intervals if stability is demonstrated over time along with continuing asymptomatic clinical status.[14]

The technique for surgical removal of leiomyoma is enucleation via an open or a minimally invasive approach. In the past, thoracotomy or laparotomy was the standard approach.[9] The first documented thoracoscopic enucleation was by Everitt in 1992,[22] and since then, there has been a shift toward minimally invasive techniques. Multiple studies have been performed comparing open and minimally invasive approaches, and the overall mortality is not significantly different between the 2 approaches.[24–26] Minimally invasive techniques are associated with decreased postoperative respiratory complications, shorter hospital stays, and improved postoperative pain control and hence have become more standard as skills and instrumentation appropriate for such strategies have evolved.[25,26]

For the open technique, the approach depends on the location of the tumor. A right thoracotomy would be indicated to reach tumors of the upper two-thirds of the esophagus and left thoracotomy for those of the lower one-third and of intrathoracic location. For tumors of the intra-abdominal portion of the esophagus, including those involving the gastroesophageal junction, laparoscopy or laparotomy may be indicated. Intraoperative endoscopy and ultrasonography can be used to facilitate identification of the tumor and also to evaluate for possible intraoperative mucosal injury.[17]

The specific techniques in regards to right or left thoracoscopy or laparoscopy are generally the same with minimally invasive techniques. The placement of the trocars depends on the location of the lesion, and as in most minimally invasive strategies,

the lesion should be in the base of a baseball diamond trocar configuration with the camera on the opposite corner of the diamond and working ports at the other angles of the same. Single lung ventilation is crucial for exposure of the mediastinum if a thoracoscopic approach is used.[25,26]

Regardless of open or minimally invasive technique, the key principles regarding the surgical enucleation of leiomyoma are largely the same. A longitudinal myotomy is created just over the tumor itself, taking care to stay over its apex, and after splitting the muscular coat, the tumor is visualized, often as a well-circumscribed, avascular mass. Blunt dissection is used to separate the tumor from the mucosa, often with the placement of a traction suture in the mass to facilitate the process, with the goal of avoiding violation of the mucosa itself.[22] This procedure can usually be accomplished without difficulty, noting that the risk of mucosal injury may be increased if preoperative endoscopic biopsy was performed.[17] If there are dense adhesions between the tumor and mucosa, possible malignancy must be considered as well, in which case frozen section may be indicated, recognizing that it may or may not be conclusive.[27]

After completing enucleation of the tumor, the presence of mucosal injuries can be evaluated with the use of intraoperative endoscopy and insufflation, and any injuries should be repaired with interrupted absorbable sutures.[17] Finally, it is recommended to reapproximate the myotomy muscle edges at the end to avoid possible postoperative mucosal bulging, diverticulum formation, and associated dysphagia and/or gastroesophageal reflux disease (GERD) symptoms.[9,17,22,24,25]

Variations of surgical enucleation include the balloon push-out method, a thoracoscopic approach with assistance of a balloon-mounted endoscope to promote intraluminal expulsion of the tumor from the esophageal wall,[14] and robotic-assisted thoracoscopic enucleation.[27,28]

Up to 10% of esophageal leiomyomas may require esophagectomy. In general, the indications for esophagectomy are size greater than 8 to 10 cm, annular morphology, multiple or diffuse involvement, extensive damage and/or ulceration to the mucosa, or presence of or suspicion for leiomyosarcoma.[12] Esophagectomy is more commonly required in the pediatric population because of the increased incidence of multiple tumors and diffuse esophageal involvement as detailed earlier.[18]

The mortality associated with open esophagectomy is 10.5% in adults[22] and up to 21% in children[18] and is primarily related to the risk of anastomotic leak and associated sepsis as well as pulmonary complications. The mortality of open enucleation is approximately 1.3%. There have been no reported deaths with patients treated with minimally invasive enucleation.[22]

Most patients treated with enucleation report complete resolution of their symptoms. According to a retrospective review by Jiang and colleagues[24] of 40 cases of thoracoscopic enucleation of leiomyoma, all patients had complete resolution of their symptoms at a mean follow-up of 27 months. In addition, there have been no documented cases of recurrence of leiomyoma after surgical removal. Postoperative complications are uncommon but include esophageal leak due to mucosal injury and GERD. The development of postoperative GERD is most likely due to a disturbance of esophageal motility or lower esophageal sphincter function and may require future fundoplication; however, it is overall uncommon and, as such, routine fundoplication with enucleation is not recommended.[17]

Endoscopic excision of leiomyoma is possible. This strategy may be especially appropriate for the occasional leiomyoma of muscularis mucosal origin with an intraluminal or polypoid growth pattern. In general, pedunculated lesions of this type are removed via endoscopic snare techniques. Endoscopic mucosal resection (EMR)

has also become more popular in recent years for a variety of mucosal and submucosal pathologic conditions. As pertains to leiomyomas, submucosal saline injection followed by cap-fitted endoscopic snaring typical of EMR methodology has been described for more wide-based yet smaller lesions up to 2 cm in size. Ethanol injection also has been used as a tool for facilitating lesion necrosis and involution, yet the experience in the United States is limited.[9,14] Finally, endoscopic submucosal dissection (ESD) techniques continue to evolve and may become a more prevalent option for enucleation via an endoluminal approach in years to come, particularly again for lesions originating from the muscularis mucosa.

Gastrointestinal Stromal Tumor

The second most common esophageal mesenchymal tumor is the GIST. Even though these lesions have malignant potential, many behave in a benign manner, and these lesions are thought to be worthy of discussion for several reasons, including their similarities to other mesenchymal benign tumors, as well as the fact that GISTs must be distinguished from other lesions to make appropriate treatment decisions. Less than 5% of GISTs are found in the esophagus compared with 60% in the stomach and 30% in the small intestine.[19]

Based on the finding of shared expression of CD117 and CD34, GISTs are thought to arise from the interstitial cells of Cajal, also known as the GI pacemaker cells, and/or the intestinal mesenchymal precursor cells.

Most of these tumors present between the fifth and seventh decades of life. In a review of 17 esophageal GISTs by Miettinen and colleagues, the median age of presentation was 63 years, with a range from 49 to 75 years.[19] These tumors are rarely found before the age of 40 years, and the diagnosis of a GIST in a younger patient may suggest a lesion of particularly malignant potential. Like leiomyomas, approximately half are asymptomatic. Of the remaining, the most common presenting symptom is dysphagia followed by chest discomfort. Other less common symptoms include cough, gradual mild weight loss, and GI bleeding.

Similar to most other benign esophageal tumors, GISTs of the esophagus are most often located in the distal third and may extend to involve the gastroesophageal junction.[16,27] Sizes are widely variable. In a series by Miettinen of 17 esophageal GISTs, most were less than 10 cm, with a median size of 8 cm and range from 2.6 to 25 cm.[19]

The characteristic histologic findings include overall basophilic appearance with high cellularity and mild-to-no nuclear pleomorphism on hematoxylin-eosin staining. Like gastric GISTs, approximately 70% to 80% of esophageal GISTs are spindle cell tumors and the rest, predominately epithelioid tumors. The spindle cell form can present histologically with growth of tumors cells in solid sheets or in myxoid, pseudo-organoid, palisading, or perivascular collar patterns. Coagulation necrosis may be seen as well, but lymphatic or vascular or diffuse mucosal invasion is uncommon. Mitotic figures are more often found in GISTs than in leiomyomas, where they are quite rare. However, mitotic activity can still vary widely among GISTs and plays a key role in predicting malignant potential, as described in more detail later in discussion.[16]

As mentioned in the leiomyoma section, GISTs previously were classified alongside leiomyoma, schwannoma, and other mesenchymal tumors, but recent studies and discoveries have shown GISTs to be distinct from these other mesenchymal tumors. Although gross and histologic features may help differentiate GISTs from other similar tumors, the best method of distinction is immunohistochemical testing. The most reliable marker is the expression of c-kit protein, CD117, which is uniformly seen in GISTs. In addition, the vast majority also express CD34. In turn, GISTs are almost never positive for desmin, and most do not stain positive for α-smooth muscle actin

(SMA) either. Most studies show an approximately 20% to 40% frequency of SMA positivity in all GISTs throughout the GI tract, and the expression is usually partial and focal in comparison with the diffuse reactivity seen in leiomyomas.[16] Furthermore, GISTs are negative for S-100 as well in comparison with schwannomas.[19] These markers are invaluable in distinguishing these lesions and guiding decisions regarding management that are linked to underlying histology and the associated potential for future malignant behavior, which is significantly higher for GISTs.[16]

Because GISTs are also intramural esophageal tumors, the diagnostic workup is similar to that of leiomyoma. Typical workup includes a contrast swallow study, EGD, and EUS imaging, and findings are usually similar to leiomyoma, which makes distinguishing between the 2 tumors difficult based solely on such criteria.

Overall, approximately 70% of all GISTs are benign. In the past, these tumors were classified as benign or malignant based on mitotic activity and size, but studies have shown that prediction and classification of GISTs into those with benign versus malignant behavior can be challenging.[29] As a result, the National Institutes of Health (NIH) developed a classification scheme for GISTs in general, categorizing these tumors into 4 categories of risk for recurrence and metastasis, specifically very low risk, low risk, intermediate risk, and high risk, based on mitotic activity and size (**Table 1**).[30]

Although the NIH classification can provide some guidance in distinguishing low- and high-risk GISTs in regards to malignant potential, small size and/or low mitotic activity does not guarantee benign behavior. Other favorable prognostic factors include gastric location, low proliferation index, absence of infiltration to adjacent organs, DNA diploidy in G2 peak on flow cytometry, and possibly female gender and younger age.[19] In regards to esophageal GISTs in particular, mitotic index and size are not proven prognostic factors, possibly in part due to the low incidence.[31] Esophageal GISTs are more commonly aggressive and malignant histologically. Miettinen and colleagues reported in their series of 17 esophageal GISTs a mortality rate of 59% with a median survival of 27 months. One disease-associated death occurred in a patient with a mitotic rate less than 5 mitoses per 50 high-power field (HPF), again underlining the inconsistent relationship between malignant behavior and mitotic rate.[17]

Although it is important to differentiate GIST from leiomyoma for the reasons outlined, it is often difficult because the findings of the typical diagnostic studies of contrast swallow, EGD, and EUS imaging frequently overlap between the 2 entities. Occasionally, mucosal changes may be seen with GISTs in a manner less common with leiomyomas, which rarely are associated with such findings as mentioned previously. The appearance of ulceration, Barrett esophagus, and/or esophagitis accordingly calls for further investigation to rule out GIST as well as other possible malignant tumors such as carcinoma. However, mucosal changes are still uncommon.

Table 1 Risk classification for GIST tumors	
Classification	**Size and/or Mitotic Activity**
Very low risk	<2 cm and <5 mitoses/50 HPF
Low risk	2–5 cm and <5 mitoses/50 HPF
Intermediate risk	<5 cm and 6–10 mitoses/50 HPF 5–10 cm and <5 mitoses/50 HPF
High risk	>5 cm and >5 mitoses/50 HPF >10 cm and mitotic rate any size and >10 mitoses/50 HPF

Abbreviation: HPF, high-power field.

Consequently, the addition of a PET scan[29] and/or FNA via EUS imaging may provide further assistance in distinguishing between GISTs and leiomyomas.[31]

GISTs are PET-avid, especially malignant GISTs, in comparison with leiomyomas.[29] Furthermore, FNA may be performed under EUS guidance and provide adequate tissue for immunohistochemical testing for CD117, CD34, and other markers. Blum and colleagues[27] recommended addition of EUS-FNA for any intramural esophageal tumor larger than 2 cm, demonstrating positive growth on serial surveillance examination and/or manifesting increased PET scan activity.

Although initially small GISTs may be observed with serial examinations similar to leiomyoma, once the actual diagnosis of GIST has been made, the management changes and usually entails a combination of medical and surgical treatments, specifically with complete resection of the mass.[23]

The management of GISTs has significantly changed in recent years because of introduction of imatinib, a monoclonal antibody inhibiting the tyrosine-kinase c-kit protein. Imatinib use is indicated for unresectable, recurrent, or residual GISTs and, in turn, can be used as primary, adjuvant, or neoadjuvant treatment. Its addition has led to a significant increase in median survival of patients with advanced GIST from approximately 20 to 60 months. Adjuvant imatinib is recommended for most patients for 2 years, including those with residual disease after resection or larger primary tumors. Serial CT and/or PET scans can help track disease response, which may be manifest as a decrease in tumor attenuation more so than size and decrease in maximum standard uptake value on PET.[32]

Along with the use of imatinib, complete surgical excision is recommended whenever possible and is still associated with the best chance for survival. Although the standard of surgical treatment is complete excision,[23,27,32] the optimal extent of surgery with regards to margin sizes and approaches has not yet been well defined[23]; however, negative margins without lymphadenectomy is generally considered an adequate resection.[27] Enucleation may be performed via open or minimally invasive approaches for smaller tumors of low malignant potential.[23] In general, an open approach may be preferred in the setting of known preoperative diagnosis of GIST because of the poor integrity of the tumor and high frequency of adhesions to the mucosa or submucosa,[27] but personal surgical experience may also play a role in determining the approach in such settings.

For larger tumors, esophagectomy with gastric tube reconstruction is recommended. The specific size threshold for enucleation versus esophagectomy has also not been well established. Blum and colleagues[27] recommended esophagectomy for GISTs greater than 2 cm, whereas Lee and colleagues[23] reported safe excision via enculeation of tumors up to 5 cm in size. The concurrent findings of mucosal and/or muscular invasion, involvement of the gastroesophageal junction, and other features relating to risk of malignant behavior as outlined play a role in determining the best approach and extent of resection. The techniques of enucleation and esophagectomy otherwise are similar to those described for leiomyomas. In comparison with leiomyoma, it is frequently difficult to assess adequacy of the resection intraoperatively because of the occasional presence of adhesions to surrounding layers blurring anatomic planes and the unreliability of frozen section to assess adequate margins. The adequacy of resection can only be assessed with immunohistochemical staining, which determines the presence or absence of tumors cells along the excised borders.

In the past, esophageal GISTs have been associated with poor prognosis with high mortality and recurrence rates. Blum and colleagues[27] cited only a 14% 5-year survival rate, but the addition of imatinib has significantly changed the outcomes and prognoses. Shingare and colleagues[33] in a series of 7 patients, all treated with imatinib

and 3 with surgical excision, found no disease progression or metastasis in all patients at the end of mean follow-up of 26 months. The availability of newer-generation tyrosine kinase inhibitors for patients not responding to imatinib, such as gefitinib, erlotinib, and sunitinib, offers hope for alternative therapies focused on underlying tumor biology with these lesions.

Schwannoma

Schwannoma is the least common esophageal mesenchymal tumor. In general, they are uncommonly found in the GI tract, and of these, most occur in the stomach.[33] Esophageal schwannoma is extremely rare, with less than 30 reported cases in the literature.[34]

These submucosal tumors arise from the Schwann cells of the neural plexus within the GI tract wall, and although they can occur at any age, they most commonly present during middle age, between 50 and 60 years.[35] In a literature review of 19 reported cases, Murase and colleagues[37] reported a median age of 54 years, with a range from 10 to 79 years. In addition, there is a mild female predominance, with reported male to female ratios ranging from 1:1.6 and 1:2.8.

Unlike other benign esophageal tumors, schwannomas are located most frequently in the upper esophagus, specifically the cervical and upper thoracic regions. Size varies widely, ranging from less than 0.5 cm to up to 15 to 16 cm. Similar to leiomyoma and GIST, schwannoma is often asymptomatic, and if symptomatic, the most common presenting symptoms are dysphagia and chest discomfort.[36]

Grossly, these tumors are yellow-white to tan and appear rubbery and/or firm with glistening, smooth surfaces. They may appear trabeculated without necrosis or hemorrhage on cut surface. Histologically, schwannomas feature peripheral lymphoid cuffs composed of lymphoid follicles, moderate cellularity, and broad bundles, interlacing fascicles, or whorls of elongated cells.[37] Additional histologic characteristics also include nuclear palisading, intermixing collagen fibers, nuclear pleomorphism with evenly distributed chromatin, and inflammatory cell infiltrates composed of plasma cells and lymphocytes. The presence of the distinctive peripheral lymphoid cuff ranges from complete to partial between tumors, and may be missed depending on sectioning, but when seen, is pathognomonic for schwannoma.[36,37]

The diagnostic workup for schwannoma is similar to that of leiomyoma and GIST, consisting of contrast swallow study, EGD, and EUS imaging. CT and PET scans can also be added for further details, as mentioned previously.[36] Schwannomas characteristically appear homogenous on postenhanced CT images.[34] However, the findings from these diagnostic tests for schwannoma usually overlap with those of other submucosal tumors, including GIST, and immunohistochemical testing is required for definitive diagnosis. Adding EUS-FNA or proceeding to surgical excision may provide adequate tissue for such testing, and schwannomas characteristically express S-100 protein as well as vimentin and glial fibrillary acidic protein. On the other hand, they are negative for CD117, CD34, desmin, and SMA, thus allowing for differentiation from GISTs and leiomyomas.[16,38,39]

The management of schwannomas is similar to that of leiomyomas. Smaller, asymptomatic ones may be observed with serial examinations.[38] Indications for excision include larger size (generally >2 cm), the presence of symptoms, and/or the findings of growth on serial examinations. Schwannomas less than 2 cm may be safely excised endoscopically.[36] Larger ones may be enucleated through thoracotomy or thoracoscopy.[34,35,39]

There is a malignant potential associated with schwannomas as well with 3 to 4 reported cases of malignant schwannoma in the literature. The malignancy criteria

are histologic and based on mitotic activity, cellularity, nuclear atypia, and presence of tumor necrosis. Of these, mitotic rate is the most reliable. The presence of 5 or more mitotic figures per 50 HPF correlates most strongly with malignancy. In the setting of malignant disease, complete surgical excision is necessary, and although some studies suggest enucleation may be adequate for smaller tumors with intact mucosa and absent local invasion, the standard is still esophagectomy.[39]

Granular Cell Tumor

Granular cell tumors (GCTs), historically known as granular cell myoblastomas, were first described by Abrikossoff in the 1920s. They are soft-tissue neoplasms that have a neural origin located in the submucosa. The exact cell type that they originate from is thought to be a Schwann cell because of staining characteristics; however, there is still some debate.

GCTs are mostly benign, but it is reported that 1% to 2% of cases are malignant.[40] GCTs are found in many different tissues, with approximately 1% to 8% located in the GI tract and around one-third of these localized to the esophagus.[41–43] Most of these are found in the distal esophagus.

GCTs are usually asymptomatic and found incidentally during radiological evaluation or endoscopy. When symptomatic they tend to be larger.[44] GCTs present similar to leiomyomas. The most common symptom accordingly is dysphagia; however, they may present with chest pain, cough, nausea, or gastroesophageal reflux. GCTs are often found on contrast radiography or during endoscopy. On endoscopy they appear as pale yellow wide-based polypoid lesions with intact thin mucosa protruding into the lumen. EUS imaging is useful in that it can help determine the size, location, and invading layer of the tumor. The tumor looks hypoechoic and is surrounded with hypoechoic mucosa. Definitive diagnosis can be difficult, and tissue is typically required. Tissue is usually obtained during endoscopy with multiple biopsies taken from the same site to reach the submucosal position. Histologic evaluation and immunostaining are performed to help differentiate malignant from benign tumors.

At present, there is no consensus on the treatment. But if the tumor is determined as benign, there are no instances of malignant transformation reported. However, there is 1% to 3% malignancy rate, and if the malignancy is suspected, resection is indicated. It has been suggested that symptomatic tumors, tumors larger then 10 mm, rapidly growing lesions, and those with histologic features concerning for malignancy be resected.[44,45] Conversely, small, asymptomatic tumors may be biopsied and followed up.[46,47] Historically, surgical treatment when dictated has been a transthoracic approach. However, EMR (Fig. 4) has been successful for lesions that do not extend beyond the submuscosal layer.[48–56]

Inflammatory Pseudotumor

Inflammatory pseudotumors are generally localized masses found in the distal esophagus. They arise from the mucosal layer and often appear as pedunculated lesions. It is thought that they originate from underlying injury such as mechanical injury or from ulceration as a result of chronic reflux. Infection with Epstein-Barr virus has been suggested as a cause, as has autoimmune disorders. These lesions can be mistaken for malignancy, so it is important to biopsy them when found for histologic characterization.

Histology of inflammatory pseudotumors show inflammatory changes and are composed of mostly fibroblasts, inflammatory cells, and blood vessels. Once these lesions are determined to not be a malignancy or other pathology mandating other
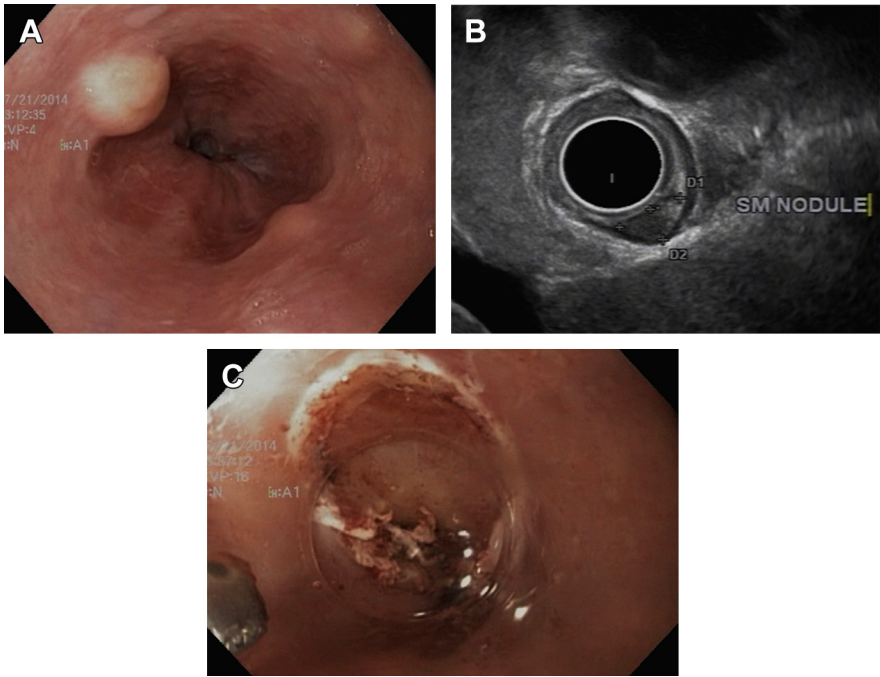
Fig. 4. Granular cell tumor of distal esophagus. (*A*) Endoscopic appearance (*upper left panel*); (*B*) EUS appearance (*upper right panel*); (*C*) after EMR using cap fitted endoscopic band and snare technique (*lower left panel*).

intervention, no specific treatment is required. If chronic reflux is suspected as the cause, treatment of reflux is suggested.

Hemangioma

Hemangiomas are benign vascular tumors that arise from the submucosal layer in the esophagus as a localized hypertrophy of blood vessels. They are benign tumors and represent approximately 3% of all benign tumors of the esophagus.[7] Given their rarity there are no data regarding their demographics. They can be found in the distal esophagus and can present as a solitary lesion or as multiple lesions in association with Rendu-Osler-Weber syndrome. As with other benign tumors of the esophagus, they are often asymptomatic. When symptomatic, their most common symptoms are dysphagia and hematemesis. Hematemesis is often the result of mucosal ulceration overlying the lesion and, given the vascular nature of the lesion, can be minimal or life threatening.

These tumors can be evaluated by several different techniques. On barium esoph-agography they appear as well-defined submucosal lesions. Endoscopy is often used, and they appear as bluish, polypoid submucosal lesions that are compressible. As opposed to some of the other submucosal lesions mentioned earlier, CT with contrast is particularly useful in confirming a diagnosis and delineating further characteristics.[57] MRI as well as radionuclide study or angiography may also be useful. EUS imaging has started to play an increasing role as it provides further characterization of the lesion including confirming the absence of continuity with major blood vessels.[58,59] Finally, a tissue biopsy may allow a tissue diagnosis; however, this should generally be

avoided because of concern for inducing hemorrhage. If a bluish submucosal lesion is found on endoscopy, contrast-enhanced CT scan, radionuclide study, or angiography can establish the diagnosis. Generally, observation of asymptomatic lesions with no occult blood loss is an acceptable option, and signs of ongoing active or otherwise unexplained occult blood loss dictates intervention.

For symptomatic lesions several options have been reported. More recently, hemangiomas have been treated with endoscopic resection, sclerotherapy, radiation, laser fulguration, and video-assisted thoracoscopic resection.[60–63] However, both esophagectomy and tumor enucleation have been performed as well. Given their rarity and an increasing number of options described in their management, a multidisciplinary treatment discussion for symptomatic or bleeding lesions would seem appropriate.

Adenoma

Adenomatous polyps of the esophagus are the result of a benign neoplastic proliferation of columnar cells. They often occur in the distal esophagus and may share the same dysplastic characteristics as colonic adenomas. In the esophagus they have also been found to be associated with Barrett esophagus.[64,65] These polyps may harbor high-grade dysplasia or carcinoma or progress into the same over time. As such, it is recommended that they be removed endoscopically or rigorously sampled and ablated if documented as benign. If high-grade dysplasia or cancer is found, then aggressive surgical resection has historically been advised. EMR may be used for smaller lesions, recognizing that increasingly large lesions are being approached with techniques such as EMR and ESD after careful histologic and EUS evaluation, when appropriate. For sessile or wide-based lesions, aggressive sampling and excisional therapy treatment is indicated, with surgical resection still representing an appropriate consideration for patients of acceptable risk status who exhibit foci of invasive disease or high-grade dysplasia. When associated with Barrett esophagus, focal lesional treatment endoscopically with management of underlying GERD is appropriate, but presence of dysplasia or high-risk markers dictates mucosal ablative therapy.

Papilloma

Squamous papillomas of the esophagus are extremely rare. Their incidence was found to be 0.01% on an autopsy series and 0.07% in an endoscopy series.[66,67] They are more common in older individuals. The exact cause is unknown; however, it is thought that their development is related to chronic gastroesophageal reflux or infection with human papilloma virus or possibly a combination of the two. These lesions tend to be small and solitary and are found most often in the distal esophagus.[66] Rarely, multiple papillomas can be found, which may be associated with a rare condition known as esophageal papillomatosis.[68]

The lesions are generally asymptomatic and identified incidentally on endoscopy. Rarely, they may cause dysphagia. They are generally small, less than 1 cm, solitary, sessile projections that are generally pink and appear fleshy on endoscopy. Often they can be confused with squamous carcinoma, so it is imperative that they be biopsied. EUS imaging may be performed to determine the noninvasive nature of the lesion, but once diagnosed by biopsy, further workup is not indicated. There has only been one case of malignant transformation of an esophageal papilloma.[69] Resection of a papilloma is indicated if it is symptomatic due to obstruction, if it has atypical histologic features, or if malignancy cannot be ruled out. Endoscopic resection (EMR) is the treatment of choice. However, if this is not possible or cancer is still a concern after resection, then an esophagotomy with local resection can be performed.

Fibrovascular Polyp

Fibrovascular polyps are the most common benign intraluminal tumor of the esophagus. They are mostly located in the upper esophagus, generally located distal to the cricopharyngeus in the posterior midline above the confluence of the longitudinal layer of esophageal muscle called Lamier triangle. These lesions are the product of submucosal thickening that progresses to polypoid formation. They can be long because of peristalsis and its effect on the lesion once it develops.[70] They may have spectacular presentations, such as regurgitation from the mouth or even causing sudden death due to asphyxia.[11] It is most likely the aforementioned first case of resection of an esophageal tumor by Dallas-Monro was of this type, since the description was of a regurgitated, pedunculated tumor.

Contrast esophagography shows a large sausagelike elongated tumor.[11] CT and MRI may demonstrate heterogenous attenuation based on the relative amount of adipose and fibrous tissue.[71] Endoscopy demonstrates a fleshy, sausagelike elongated lesion typically arising from the postcricopharyngeal, posterior location outlined earlier.[70]

Once diagnosed, removal is recommended because of the risk for fatal airway complications. The resection planning is developed by information obtained by endoscopy and EUS imaging. The vascularity of the stalk, location, and size dictate the method of resection.[52] Smaller lesions are easily removed endoscopically with either direct snare or EMR techniques. It is recommended to have airway control during endoscopic procedures performed for this pathologic condition to minimize the risk of airway complications during the procedure. Larger lesions or those with abundant blood flow in the stalk demonstrated on EUS imaging require longitudinal esophagotomy on the opposite side of the tumor origin. The tumor stalk is ligated and resected, followed by 2-layer closure of the esophagotomy.[72]

EXTRAESOPHAGEAL TUMORS
Cysts and Duplications

Cysts and duplications are not neoplasms but malformations of the esophagus. They can cause symptoms similar to those of the lesions already discussed by creating mass effects and collectively constitute the second most common tumorlike condition of the esophagus. They can originate not only from the foregut itself but also from developmental aberrations of the trachea that may manifest with dysphagia, hemorrhage, and infection. Other cystic lesions besides congenital developmental cysts and duplications can include inclusion and neuroenteric cysts.

Histologically, esophageal duplication cysts have muscular and epithelial layers and an intramural component. Bronchogenic cysts originate from lung primordia and typically have cartilage in them. Inclusion cysts conversely have similar epithelial lining as esophageal duplications, yet there is no muscle or cartilage. The neuroenteric cysts are malformations resulting from aberrant separation of the foregut from the primitive spinal column. They are posterior in location and often associated with other spinal abnormalities such as spina bifida.[10]

Presenting symptoms in younger patients can include dysphagia or airway symptoms such as wheezing and stridor. In older patients, these lesions may present with infection, dysphagia, chest pain, hemorrhage, fistulization, and malignant transformation.[70]

Diagnosis is made by a combination of esophagography (**Fig. 5**), endoscopy and EUS imaging, and CT (**Fig. 6**) or MRI. These lesions are generally not biopsied because the resulting scar tissue from these biopsies may make future resection more challenging. If a smooth lesion is seen on endoscopy and EUS imaging documents the fluid-filled nature of the lesion (**Fig. 7**), a cross-sectional imaging study is typically obtained next to

Fig. 5. Extrinsic compression of esophagus due to adjacent cystic lesion on barium study. (*Courtesy of* Stephen R. Hazelrigg, MD, Department of Surgery, Southern Illinois University School of Medicine, IL.)

further delineate the characteristics and extent of the pathology for operative planning purposes. On cross-sectional imaging, the fluid-filled nature of the lesion is typically confirmed, although previous infections can make this determination difficult because the attenuation of the fluid is thicker in such cysts. In those situations, the findings on EUS imaging are used in a complimentary manner for establishing the diagnosis. As for all posterior mediastinal tumors, if the cyst appears to be neuroenteric, an MRI and neurosurgical consultation may be appropriate in preoperative planning.

Fig. 6. Posterior mediastinal cyst compressing esophagus. (*Courtesy of* Stephen R. Hazelrigg, MD, Department of Surgery, Southern Illinois University School of Medicine, IL.)
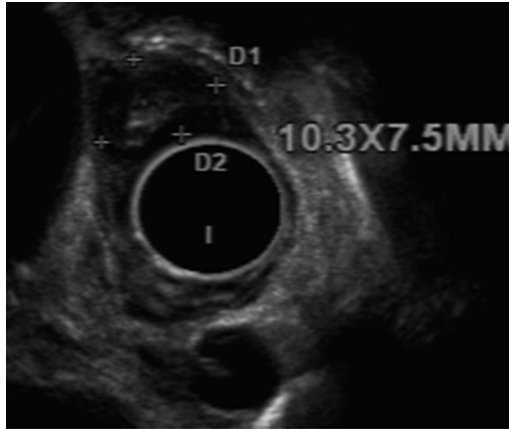
Fig. 7. Radial EUS image of intramural duplication cyst of esophagus.

Once diagnosed, resection is recommended, and thoracoscopy is typically successful with intraoperative endoscopic assistance.[73] A history of previous biopsies and/or infection may make the surgical resection challenging, and in such instances, thoracotomy should be more strongly considered.

SUMMARY

Given the rarity of benign esophageal tumors, the clinician must have a thorough grasp of their causes, behaviors, and respective management strategies. Many of these lesions may be safely observed if they are asymptomatic and stable on serial assessment. Symptomatic and larger or growing lesions require more careful characterization by EUS imaging, FNA, and cross-sectional imaging to guide therapeutic decision making. A familiarity with related medical conditions such as GERD and Barrett esophagus, with the distinctive patterns of disease characterizing pediatric and adult patient groups, and with the biologic complexities characterizing behavior and treatment of pathologies such as GISTs, is a requisite cognitive skill set for the managing provider. Removal of symptomatic lesions can be approached increasingly by minimally invasive methods and with some pathologies with advancing endoluminal resective techniques. Surgeons managing these patients should either have the current skills necessary for their management, including skills in minimally invasive thoracoscopic and laparoscopic surgery as well as therapeutic endoscopy and EUS imaging, or participate in multidisciplinary treatment teams that include individuals with these skills. With appropriate characterization of the pathologic condition, these lesions are increasingly able to be appropriately managed with techniques that can optimize outcomes and limit both short- and long-term morbidity and risk for the patient.

REFERENCES

1. Choong CK, Meyers BF. Benign esophageal tumors: introduction, incidence, classification, and clinical features. Semin Thorac Cardiovasc Surg 2003;15: 3–8 No. 1. WB Saunders.
2. Rice TW. Benign esophageal tumors: esophagoscopy and endoscopic esophageal ultrasound. Semin Thorac Cardiovasc Surg 2003;15:20–6 No. 1. WB Saunders.

3. Watson RR, O'Connor TM, Weisel W. Solid benign tumors of the esophagus. Ann Thorac Surg 1967;4(1):80–91.

4. Storey CF, Adams WC Jr. Leiomyoma of the esophagus: a report of four cases and review of the surgical literature. Am J Surg 1956;91(1):3–23.

5. Patterson EJ. Benign neoplasms of the esophagus: report of a case of myxofibroma. Ann Otol Rhinol Laryngol 1932;41(3):942–50.

6. Moersch HJ. Benign tumor of the esophagus. Ann Otol Rhinol Laryngol 1944;53:800–17.

7. Plachta A. Benign tumors of the esophagus. Review of literature and report of 99 cases. Am J Gastroenterol 1962;38:639–52.

8. Attah EB, Hajdu SI. Benign and malignant tumors of the esophagus at autopsy. J Thorac Cardiovasc Surg 1968;55(3):396.

9. Mutrie CJ, Donahue DM, Wain JC, et al. Esophageal leiomyoma: a 40-year experience. Ann Thorac Surg 2005;79(4):1122–5.

10. Arbona JL, Fazzi JG, Mayoral J. Congenital esophageal cysts: case report and review of literature. Am J Gastroenterol 1984;79(3):177–82.

11. Levine MS, Buck JL, Pantongrag-Brown L, et al. Fibrovascular polyps of the esophagus: clinical, radiographic, and pathologic findings in 16 patients. AJR Am J Roentgenol 1996;166:781–7.

12. Seremetis MG, Lyons WS, deGuzman VC, et al. Leiomyomata of the esophagus. An analysis of 838 cases. Cancer 1976;38:2166–77.

13. Levine MS. Benign tumors of the esophagus: radiologic evaluation. Semin Thorac Cardiovasc Surg 2003;15:9–19 No. 1. WB Saunders.

14. Lee LS, Singhal S, Brinster CJ, et al. Current management of esophageal leiomyoma. J Am Coll Surg 2004;198:136–46.

15. Hatch GF III, George F, Hatch KF, et al. Tumors of the esophagus. World J Surg 2000;24:401–11.

16. Miettinen M, Sarlomo-Rikala M, Sobin LH, et al. Esophageal stromal tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 17 cases and comparison with esophageal leiomyomas and leiomyosarcomas. Am J Surg Pathol 2000;24:211–22.

17. Kent M, d'Amato T, Nordman C, et al. Minimally invasive resection of benign esophageal tumors. J Thorac Cardiovasc Surg 2007;134:176–81.

18. Bourque MD, Spigland N, Bensoussan AL, et al. Esophageal leiomyoma in children: two case reports and review of the literature. J Pediatr Surg 1989;24:1103–7.

19. Miettinen M, Lasota J. Gastrointestinal stromal tumors–definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis. Virchows Arch 2001;438:1–12.

20. Calabrese C, Fabbri A, Fusaroli P, et al. Diffuse esophageal leiomyomatosis: case report and review. Gastrointest Endosc 2002;55:590–3.

21. Postlethwait RW. Benign tumors and cysts of the esophagus. Surg Clin North Am 1983;63:925–31.

22. Samphire J, Nafteux P, Luketich J. Minimally invasive techniques for resection of benign esophageal tumors. Semin Thorac Cardiovasc Surg 2003;15:35–43 No. 1. WB Saunders.

23. Lee HJ, Park SI, Kim DK, et al. Surgical resection of esophageal gastrointestinal stromal tumors. Ann Thorac Surg 2009;87:1569–71.

24. Jiang G, Zhao H, Yang F, et al. Thoracoscopic enucleation of esophageal leiomyoma: a retrospective study on 40 cases. Dis Esophagus 2009;22:279–83.

25. Von Rahden BH, Stein HJ, Feussner H, et al. Enucleation of submucosal tumors of the esophagus: minimally invasive versus open approach. Surg Endosc 2004;18: 924–30.

26. Zaninotto G, Portale G, Costantini M, et al. Minimally invasive enucleation of esophageal leiomyoma. Surg Endosc 2006;20:1904–8.

27. Blum MG, Bilimoria KY, Wayne JD, et al. Surgical considerations for the management and resection of esophageal gastrointestinal stromal tumors. Ann Thorac Surg 2007;84:1717–23.

28. Bodner JC, Zitt M, Ott H, et al. Robotic-assisted thoracoscopic surgery (RATS) for benign and malignant esophageal tumors. Ann Thorac Surg 2005;80:1202–6.

29. Chang WC, Tzao C, Shen DH, et al. Gastrointestinal stromal tumor (GIST) of the esophagus detected by positron emission tomography/computed tomography. Dig Dis Sci 2005;50:1315–8.

30. Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor. Hum Pathol 2008;39:1411–9.

31. Emory TS, Sobin LH, Lukes L, et al. Prognosis of gastrointestinal smooth-muscle (stromal) tumors: dependence on anatomic site. Am J Surg Pathol 1999;23: 82–7.

32. Portale G, Zaninotto G, Costantini M, et al. Esophageal GIST: case report of surgical enucleation and update on current diagnostic and therapeutic options. Int J Surg Pathol 2007;15:393–6.

33. Shinagare AB, Zukotynski KA, Krajewski KM, et al. Esophageal gastrointestinal stromal tumor: report of 7 patients. Cancer Imaging 2012;12:100–8.

34. Kwon MS, Lee SS, Ahn GH. Schwannomas of the gastrointestinal tract: clinicopathological features of 12 cases including a case of esophageal tumor compared with those of gastrointestinal stromal tumors and leiomyomas of the gastrointestinal tract. Pathol Res Pract 2002;198:605–13.

35. Yoon HY, Kim CB, Lee YH, et al. An obstructing large schwannoma in the esophagus. J Gastrointest Surg 2008;12:761–3.

36. Kobayashi N, Kikuchi S, Shimao H, et al. Benign esophageal schwannoma: report of a case. Surg Today 2000;30:526–9.

37. Murase K, Hino A, Ozeki Y, et al. Malignant schwannoma of the esophagus with lymph node metastasis: literature review of schwannoma of the esophagus. J Gastroenterol 2001;36:772–7.

38. Iwata H, Kataoka M, Yamakawa Y, et al. Esophageal schwannoma. Ann Thorac Surg 1993;56:376–7.

39. Hou YY, Tan YS, Xu JF, et al. Schwannoma of the gastrointestinal tract: a clinicopathological, immunohistochemical and ultrastructural study of 33 cases. Histopathology 2006;48:536–45.

40. Fanburg-smith JC, Meis-Kindblom JM, Fante R, et al. Malignant granular cell tumor of soft tissue: diagnostic criteria and clinicopathologic correlation. Am J Surg Pathol 1998;22:779–94.

41. Lack EE, Worsham GF, Callihan MD, et al. Granular cell tumor: a clinicopathlogic study of 110 patients. J Surg Oncol 1980;13:301–16.

42. McSwain GR, Colpitt R, Kreutner A, et al. Granular cell myoblastoma. Surg Gynecol Obstet 1980;150:703–10.

43. Johnston J, Helwig EB. Granular cell tumors of the gastrointestinal tract and perineal region: a study of 74 cases. Dig Dis Sci 1981;26:807–16.

44. Coutinho DS, Soga J, Yoshikawa T, et al. Granular cell tumors or the esophagus: a report of two cases and review of the literature. Am J Gastroenterol 1985;80:758.

45. Percinel S, Savas B, Yilmaz G, et al. Granular cell tumor of the esophagus: report of 5 cases and review of diagnostic and therapeutic techniques. Dis Esophagus 2007;20:435–43.
46. Voskuil J, Van Dijk MM, Wagenaar SS, et al. Occurrence of esophageal granular cell tumors in the Netherlands between 1988 and 1994. Dig Dis Sci 2001;24:1610–4.
47. Mineo TC, Biancari F, Francioni, et al. Conservative approach to granular cell tumor of the esophagus: three case reports. Scand Cardiovasc J 1995;29:141–4.
48. Hyun JH, Jeen YT, Chu HJ, et al. Endoscopic resection of submucosal tumor of the esophagus: result in 62 patients. Endoscopy 1997;29:165–70.
49. Fujiwara Y, Watanabe T, Hamasaki N, et al. Endoscopic resection of two granular cell tumours of the oesophagus. Eur J Gastroenterol Hepatol 1999;11:1413–6.
50. Fotiadis C, Manolis EN, Troupis TG, et al. Endoscopic resection of a large granular cell tumor of the esophagus. J Surg Oncol 2000;75:277–9.
51. van der Peet DL, Berends FJ, Klinkengerg-Knol EC, et al. Endoscopic treatment of benign esophageal tumors: case report of three patients. Surg Endosc 2001;15:1489.
52. Kinney T, Waxman I. Treatment of benign esophageal tumors by endoscopic techniques. Semin Thorac Cardiovasc Surg 2003;15:27–34.
53. Wehrmann T, Martchenko K, Nakamura M, et al. Endoscopic resection of submucosal esophageal tumors: a prospective case series. Endoscopy 2004;36:802–7.
54. Bataglia G, Rampado S, Bocus P, et al. Single-band mucosectomy of granular cell tumor of the esophagus: safe and easy technique. Surg Endosc 2006;20:1296–8.
55. Zhong N, Katzka DA, Smyrk TC, et al. Endoscopic diagnosis and resection of esophageal granular cell tumors. Dis Esophagus 2011;24:438–543.
56. Kahng DH, Kim GH, Park DY, et al. Endoscopic resection of granular cell tumors in the gastrointestinal tract: a single center experience. Surg Endosc 2013;27:3228–36.
57. Taylor FH, Fowler FC, Betsill WL, et al. Hemangioma of the esophagus. Ann Thorac Surg 1996;61:726.
58. Tominaga K, Arakawa T, Ando K, et al. Oesophageal cavernous haemangioma diagnosed histologically, not by endoscopic procedures. J Gastroenterol Hepatol 2000;15:215–9.
59. Cantero D, Yoshida T, Ito M, et al. Esophageal hemangioma:endoscopic diagnosis and treatment. Endoscopy 1994;26:250–3.
60. Yoshikane H, Suzuki T, Yoshioka N, et al. Hemangioma of the esophagus. Endoscopic imaging and endoscopic resection. Endoscopy 1995;27:267.
61. Shigemitsu K, Naomoto Y, Yamatsuji T, et al. Esophageal hemangioma successfully treated by fulguration using potassium titanyl phosphate/yttrium aluminum garnet (KTP/YAG) laser: a case report. Dis Esophagus 2000;13:161.
62. Aoki T, Okagawa K, Uemura Y, et al. Successful treatment of an esophageal hemangioma by endoscopic injection sclerotherapy: report of a case. Surg Today 1997;27:450.
63. Ramo OJ, Salo JA, Bardini R, et al. Treatment of a submucosal hemangioma of the esophagus using simultaneous video-assisted thoracoscopy and esophagoscopy: Description of a new minimally invasive technique. Endoscopy 1997;29:S27–8.
64. Lee RG. Adenomas arising in Barrett's esophagus. Am J Clin Pathol 1986;85:629–32.
65. McDonald GB, Brand DL, Thorning DR. Multiple adenomatous neoplasms arising in columnar-lined (Barrett's) esophagus. Gastroenterology 1977;72:1317–21.

66. Weitzer S, Hentel W. Squamous papilloma of esophagus. Case report and review of the literature. Am J Gastroenterol 1968;50:391.
67. Mosca S, Manes G, Onaco R, et al. Squamous papilloma of the esophagus: long-term follow up. J Gastroenterol Hepatol 2001;16:857–61.
68. Sandvik AK, Aase S, Kvberg KH, et al. Papillomatosis of the esophagus. J Clin Gastroenterol 1996;22:35–7.
69. Van Cutsem E, Geboes K, Vantrappen G, et al. Malignant degeneration of esophageal squamous papilloma associated with the human papillomavirus. Gastroenterology 1992;103:1119.
70. Pitichote H, Ferguson MK. Minimally invasive treatment of benign esophageal tumors. Surgical management of benign esophageal disorders. Springer-Verlag; 2014. p. 181–99.
71. Ascenti G, Racchiusa S, Mazziotti S, et al. Giant fibrovascular polyp of the esophagus: CT and MR findings. Abdom Imaging 1999;24(2):109–10.
72. Solerio D, Gasparri G, Ruffini E, et al. Giant fibrovascular polyp of the esophagus. Dis Esophagus 2005;18(6):410–2.
73. Hirose S, Clifton MS, Bratton B, et al. Thoracoscopic resection of foregut duplication cysts. J Laparoendosc Adv Surg Tech A 2006;16(5):526–9.