Revisiting Achalasia and Esophageal Squamous Cell Carcinoma

INTRODUCTION

Achalasia is a rare, chronic esophageal motility disorder with an estimated annual prevalence of 1 per 100,000 subjects in the western populations. The disease can occur at all ages but the incidence increases with age. Achalasia results from progressive degeneration of ganglion cells in the myenteric plexus of the smooth muscle of the lower esophageal sphincter and the lower two-thirds of the esophagus, resulting in failure of relaxation of the lower esophageal sphincter, accompanied by a loss of peristalsis in the distal esophagus. Predominant symptoms are dysphagia and regurgitation. Treatment is purely symptomatic as the etiology of achalasia is still unclear. Treatment aims at lowering the lower esophageal sphincter (LES) pressure to improve the passage of food. Even after treatment there is continued aperistalsis and delayed transit, so sufficient symptom control does not prevent patients from having persistent retention of foods and fluids in the esophagus. This is associated with degrees of bacterial degradation of the retained contents and impaired clearance of regurgitated acid gastric contents. These factors can result in chronic inflammation of the esophageal mucosa, which potentially increases the risk of development of hyperplasia, dysplasia, and esophageal cancer. In addition, lowering of LES pressure does facilitate chronic acid gastroesophageal reflux which in a small percentage of patients leads to Barrett’s metaplasia and adenocarcinoma. Currently there are no specific guidelines for cancer surveillance in long term follow up of patients with achalasia.

Case Report
A 58 year-old Caucasian male presented with dysphagia. He had the history of heavy alcohol use (four drinks daily for 35 years). Previously (continued on page 32)
diagnosed with achalasia, he underwent pneumatic balloon dilation in 2012. He experienced an esophageal perforation requiring an open repair and myotomy without any accompanying fundoplication. After surgery, he experienced constant reflux but no achalasia symptoms. He was started on a proton pump therapy immediately after surgery. He noticed weight loss and difficulty swallowing in July 2017, with a 20-pound weight loss and progressive dysphagia to solid food, unable to tolerate anything but a pureed diet.

On physical examination the patient had facial thinning, firm hepatomegaly and scoliosis. There were no Virchow lymph nodes palpable in the neck. His laboratory evaluation was unremarkable, including albumin and hemoglobin. Liver enzymes were also within normal limits.

Barium swallow with a 13 mm barium tablet revealed a tight stricture with a suggestion of “shouldering” in the proximal esophagus, 15 cm proximal to the gastroesophageal (GE) junction, and delay of the barium tablet at the stricture (Figure 1). Distal to the stricture there were no radiographic findings of achalasia. Upper endoscopy revealed that the upper third of the esophagus was normal. A stricture was found 25 cm from the incisors and the endoscope would not pass (Figure 2). Savary dilation was performed at 7 mm, 9 mm, 11 mm and 14 mm. The endoscope could then traverse the stricture after dilation. The stricture extended from 25 to 35 cm from the incisors. Its mucosa was nodular, friable, irregular and polypoid, suspicious for esophageal cancer (Figure 3). Biopsies of stricture showed moderately differentiated squamous cell carcinoma. The biopsies of the esophagus distal to the stricture showed changes of reflux esophagitis but no Barrett’s esophagus.

Subsequent computed tomography (CT) imaging of the chest revealed a circumferential, mass-like thickening of the proximal esophagus, approximately 7.5 cm in length. There was a loss of the fat plane with the aortic arch, proximal ascending aorta, lower trachea and left mainstem bronchus, concerning for tumor infiltration. There were no pulmonary nodules but a couple of small mediastinal lymph nodes were noted (Figure 4).

The patient was referred for chemotherapy and radiation. The esophageal stricture was re-dilated to a 17mm diameter size in preparation for the initiation of the radiation treatment. In addition, a percutaneous gastrostomy tube was placed to ensure adequate nutrition maintained through the treatment course.

Discussion

Esophageal cancer has been a very infrequent complication in the long term follow up of achalasia. Among a large case series, it ranges from 0.4% to 9.2%.

One review found that the prevalence of esophageal cancer in achalasia was 3% in the long term follow up (five to 20 years), corresponding to a 50-fold increased risk. Most cases of esophageal cancer in patients with achalasia are squamous cell carcinoma located in the middle third of the esophagus. It is proposed that, although improved symptomatically by medical or surgical therapies, there is continuing stasis of food in the esophagus promoting lactic acid production and fermentation, inducing slow and continuous damage to the esophageal mucosa. Conversely, adenocarcinoma may occur after treatment for achalasia, almost invariably arising from Barrett’s esophagus due to longstanding gastroesophageal reflux. Alcohol use also places patients at higher risk for squamous cell cancer. A combination of the factors described above along with the long history of alcohol abuse may have been the main triggers for squamous cell carcinoma.
Currently there are no guidelines for monitoring squamous cell carcinoma or other late complications such as esophageal and peptic stenosis or megaesophagus. Whether surveillance endoscopy should be generally recommended for all patients with esophageal achalasia is still controversial due to the long interval between the initial symptoms and diagnosis of achalasia and the development of carcinoma. Studies have indicated an interval between the diagnosis and treatment of achalasia and the diagnosis of esophageal cancer of at least 15 years. Its opponents contend that, even under surveillance, mortality from esophageal cancer in achalasia patients resembles the general population with a survival rate of 40% after year two of diagnosis while similar surveillance programs for Barrett’s esophagus improve survival to 73–85% within two years of diagnosis. One other consideration is the large cost of such surveillance programs. One study in 1995 has estimated that about 732 endoscopic procedures were needed to detect three cancers over a 15-year study period costing $585,000 thus averaging $195,000 per cancer detected. This is contrasted to $31,000 in similar adenocarcinoma surveillance program for patients with Barrett’s esophagus. On the other hand, its proponents for surveillance argue that without strict endoscopy surveillance, esophageal malignancies will be detected very late and in an advanced stage. This is thought to be due to residual dysphagia which can mimic esophageal cancer and recurrent achalasia. In a recent study in 2016, Ota...
et al. performed annual endoscopies follow-up in 32 patients over a mean period of 14 years (range 5-40 years) after successful achalasia surgery treatment. They were able diagnose 6 of 32 patients with esophageal cancer at early stage. All six patients were alcoholic drinkers and three had smoking habit. This suggests follow-up endoscopy with biopsy is important in early cancer diagnosis as the risk for malignant transformation still persist even after successful achalasia treatment.

Overall, we suggest to identify a risk assessment profile score in individual achalasia patients based on the type of treatment they initially underwent, esophageal pH data, previous endoscopy biopsy results, barium swallow and other known independent risk factors for squamous cells carcinoma such as age, alcohol, tobacco use and male gender. In high risk patients, we should consider endoscopy with biopsy beginning within five years after diagnosis and possibly every three to five years thereafter.

**Take Home Messages**
When following patients who have been treated for achalasia, the initial treatment is key. It is expected that after pneumatic dilation there may be recurrence of dysphagia and repeated pneumatics over the next five to 20 years. With a successful myotomy and partial fundoplication there should be minimal or no recurrence of the achalasia.

However, when the myotomy surgery is incomplete, typically because the myotomy is not extended at least 2cm into the stomach, recurrence of “achalasia” dysphagia will occur within the first one to two years. When there is no fundoplication accompanying the Heller myotomy then the scenario for complications of long term reflux are also in the equation, specifically a peptic stricture as witnessed in our case. Finally, there

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**Figure 4.** CT scan of the chest: Esophagus: There is a circumferential mass like thickening of the mid esophagus measuring up to 2.3 cm in maximum thickening and over a length of approximately 7.5 cm. There is mild stagnation of the contrast in proximal dilation of the esophagus without complete obstruction. There is loss of the fat plane between the thickened esophagus and the medial portion of the aortic arch and anterior wall of the proximal ascending aorta without evidence of intraluminal filling defects. In addition, anteriorly the mass is adherent to the lower trachea above the tracheal bifurcation on the left side and posterior wall of the left mainstem bronchus. These latter observations raise concern for the possibility of local invasion by the esophageal cancer.
remains a background incidence for squamous cell esophageal cancer in all patients, particularly with age, heavy alcohol intake and or cigarette smoking. The bottom line is to be aware of the different possibilities in the long-term follow-up of achalasia patients.

References


Johns Hopkins University School of Medicine, Division of Gastroenterology is looking for a gastroenterology hospitalist with experience in ERCP, EUS, and enteroscopy. Applicants should have at least five years of post fellowship experience in gastroenterology and have completed a two year advanced interventional endoscopy fellowship. Experience in motility and fluency in Spanish helpful.

For further information please contact:
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