Advanced Esophageal Squamous Cell Dysplasia and Early Carcinoma Detected After Remote Esophagectomy for Adenocarcinoma

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Abstract

We present a case of squamous dysplasia and early squamous carcinoma of the esophagus after esophagectomy for esophageal adenocarcinoma. We briefly discuss mucosectomy and ablative therapy as potential treatment options.

Introduction

Esophageal adenocarcinoma and squamous cell carcinoma have varying risk factors. While Barrett's esophagus is a known precursor to adenocarcinoma, it has not been associated with squamous cell cancer of the esophagus. It is unclear whether the presence of 2 cancers of different cell lines in the same patient are incidental and mutually exclusive, or possibly a long-term sequela of one condition.

Case Report

A 59-year-old man was referred for evaluation of a new esophageal nodule found during surveillance endoscopy. At the time of referral, he was asymptomatic. He had a prior history of Barrett's esophagus and esophageal adenocarcinoma in situ at the gastroesophageal junction, for which he had undergone an Ivor-Lewis esophagectomy 20 years prior. The esophagectomy was uncomplicated and he had been taking once daily acid suppression with various proton pump inhibitors for many years. Although he had a history of alcohol and tobacco use prior to his surgery, he had abstained for over 20 years.

At the time of his first endoscopy in 2009, the esophagogastric anastomosis was seen 28 cm from the incisors, and at this site, cobblestone-appearing mucosa with raised nodularity was noted (Figure 1). Biopsies from the nodules came back as reactive atypia with papilloma-type changes. Given the patient's prior history of cancer with concern for recurrent cancer at this site, a repeat endoscopy with endoscopic ultrasound was performed, which only revealed patchy wall thickening in the esophagus, mainly involving the deep mucosa, with an overall thickness of 4.6 mm. The esophagogastric anastomosis was diffusely thickened (9.3 mm in total thickness), which was not concerning for a malignant invasion. A repeat sampling of this tissue only revealed reactive atypia with squamous papilloma changes. He subsequently underwent annual surveillance endoscopy by his community gastroenterologist.

In 2013, due to concerns that the findings had changed, examination of the squamous mucosa of the distal remnant esophagus proximal to the nodules revealed several new whitish granular plaques (Figure 2). The biopsy results from these plaques revealed high-grade dysplasia with squamous carcinoma in situ. Immunohistochemical staining was positive for p63, suggesting high proliferation and a highly dysplastic pattern in these areas. High-risk human papilloma...
Hpv virus (Hpv) infection was excluded from these areas using in situ hybridization. Chromoendoscopy using Lugol's solution to assess for voiding areas revealed focal non-staining areas just proximal to the nodules in the distal remnant of the esophagus, with more extensive non-staining areas in the mid-esophagus, 25-27 cm from the incisors (Figure 3).

The non-staining regions were initially removed by mucosectomy using the band ligation technique. This endoscopic mucosal resection was performed for removal of nodularity as well as for deeper tissue resection of the carcinoma in situ. Several mucosectomy sections were obtained during this endoscopy. Three follow-up endoscopic sessions have been performed to ablate residual non-staining and flat lesions using radiofrequency ablation, and to adequately treat the areas of dysplasia. The patient is currently undergoing close endoscopic follow-up with biopsies to assess final clearance of dysplasia.

Discussion

Squamous papillomas of the esophagus are benign, rare, and usually found incidentally during endoscopy. They are generally located in the distal esophagus. The natural history of esophageal squamous papilloma is variable, and, currently, no clear association between esophageal squamous cell cancer and squamous papilloma can be made. In the medical literature, there is no clear case of a patient with a history of early esophageal adenocarcinoma with Barrett's esophagus that subsequently developed either squamous papillomas or advanced esophageal squamous cell dysplasia. Only 1 case of adenocarcinoma of the esophagus has been reported within a squamous papilloma that was removed endoscopically. Although there is association between transcriptionally active high-risk Hpv with Barrett's dysplasia, this case did not reveal any evidence of high-risk Hpv to explain the finding. There may be several possible explanations for this presentation. It may be related to reflux causing chronic mucosal irritation, given the persistent exposure of acid without the presence of an esophageal sphincter in a patient with partial esophagectomy. It is also possible that this condition may have been related to a non-malignant form of a Hpv that is currently not associated with malignancies, which was exacerbated by an exuberant inflammatory response secondary to severe post-esophagectomy gastroesophageal reflux.

While attempts should be made at therapy of dysplasia, no definitive treatment can be indicated for the squamous papillomas at the esophagogastric anastomosis. Due to paucity of cases, no definitive therapeutic or surveillance recommendation exists. If dysplasia exists, similar to treatment of superficial adenocarcinoma and Barrett's esophagus, endoscopic mucosectomy (for nodularity) followed by ablation may serve as an appropriate therapeutic plan for these squamous lesions. While radiofrequency ablation has been reported as treatment for flat high-grade dysplasia in
Barrett’s esophagus, only a few cases have documented treatment with radiofrequency ablation for squamous neoplasia of the esophagus.6-8 The follow-up plan for our patient will likely consist of close surveillance endoscopy every 6 months for the first year after clearance, followed by annual surveillance endoscopy thereafter to assess for complete eradication, although data to support this course of follow-up is currently lacking.

Disclosures

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