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Case Report

Achalasia and Esophageal Cancer: A Case Report and Literature Review

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Abstract

Achalasia is a rare esophageal motility disorder characterized by the inability of the lower esophageal sphincter to relax and the absence of normal esophageal peristalsis. This condition leads to difficulties in swallowing (dysphagia), regurgitation of food, and chest pain. Clinical observations suggest an association between achalasia and esophageal tumors, as achalasia can increase the risk of developing esophageal cancer. We explore the pathophysiology of achalasia, its clinical manifestations, and the associated risk of esophageal malignancies, supported by recent research and clinical evidence, including specific case studies.

Introduction

Achalasia is primarily caused by the degeneration of the myenteric plexus in the esophageal wall, leading to impaired relaxation of the lower esophageal sphincter (LES) and loss of esophageal peristalsis.[1] Although the exact etiology is not fully understood, it is believed to involve autoimmune mechanisms and viral infections. Key pathological features include the absence of peristalsis, LES hypertonicity, and symptoms such as dysphagia and regurgitation. In this condition, the esophagus fails to contract and move food toward the stomach, while the LES remains tightly closed, preventing the passage of food into the stomach. Consequently, food stasis in the esophagus leads to common symptoms like difficulty swallowing and regurgitation.

Patients with achalasia typically present with progressive dysphagia to both solids and liquids, regurgitation of undigested food, chest pain, and weight loss. The diagnosis is often confirmed through esophageal manometry, which shows absent peristalsis and elevated LES pressure, and barium swallow studies, which reveal a dilated esophagus with a narrowed gastroesophageal junction (bird-beak appearance).[2]

Case presentation

Achalasia is associated with an increased risk of esophageal squamous cell carcinoma (SCC) and, less commonly, esophageal adenocarcinoma. Several studies have highlighted this elevated risk, noting that chronic inflammation and food stasis in the esophagus lead to prolonged irritation and inflammation, which predispose the esophageal mucosa to malignant transformation.[3] Additionally, the altered esophageal environment caused by food stasis can result in changes to the microbiota, further contributing to carcinogenesis. Furthermore, the risk of esophageal cancer increases with the duration of achalasia, with patients who have had the condition for over 10 years being at particularly higher risk.

Case 1

A 53-year-old male with a history of achalasia presented in January 2022 for treatment of progressive dysphagia to both solids and liquids, which had been ongoing for approximately two years. His symptoms included regurgitation of undigested food, occasional chest discomfort, and unintentional weight loss of 4 kg over the previous six months. Diagnostic esophagogram and high-resolution manometry confirmed the diagnosis of type II achalasia, with absent esophageal peristalsis and incomplete relaxation of the lower esophageal sphincter. He underwent peroral endoscopic myotomy (POEM) for symptom relief.

Initially, the patient reported improvement in dysphagia symptoms, with an ability to tolerate both solid and liquid food without difficulty. However, by April 2022, he developed significant gastroesophageal reflux disease symptoms, characterized by frequent heartburn, acid regurgitation, and occasional epigastric pain. A proton pump inhibitor was prescribed, and lifestyle modifications were advised, but his reflux symptoms persisted, although somewhat controlled with medication.

In May 2024, during a routine follow-up, the patient reported worsening reflux and the new onset of retrosternal discomfort, along with a recurrence of mild dysphagia. Physical examination was unre-

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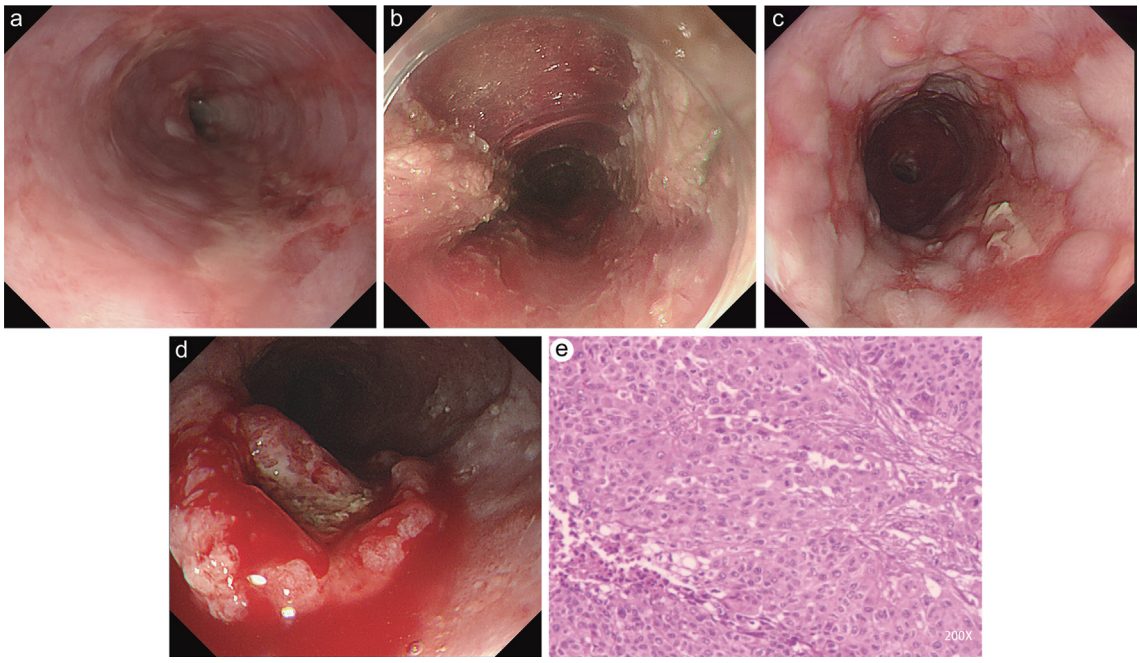

Fig. 1. Male, 53 years old. (a) Diagnosed with achalasia; (b) Underwent peroral endoscopic myotomy (POEM) surgery for achalasia; (c) Severe reflux symptoms 23 months later; (d) Esophageal squamous cell carcinoma located 25 cm from the incisors; (e) Moderately to poorly differentiated squamous cell carcinoma, hematoxylin, and eosin stained at 200× magnification.

markable, but given the recurrence of symptoms, an upper gastrointestinal endoscopy was performed. The endoscopy revealed a friable, ulcerated lesion located 25 cm from the incisors, which was suspected to be malignant. Biopsy specimens were obtained from the lesion.

Histopathological analysis confirmed the presence of esophageal squamous cell carcinoma (Fig. 1). The lesion was staged using endoscopic ultrasound and computed tomography scans, which revealed local infiltration but no distant metastases. Additional laboratory findings, including a complete blood count, liver function tests, and tumor markers (e.g., carcinoembryonic antigen, SCC), were within normal limits, except for a slightly elevated SCC antigen level. Positron emission tomography was planned for further evaluation.

This case highlights the potential long-term risk of esophageal cancer following POEM in patients with achalasia, especially in the context of chronic reflux. Early recognition and surveillance in high-risk patients may be crucial for timely intervention. Further therapeutic options, including surgical resection, chemotherapy, and radiation therapy, are under consideration for this patient, depending on the staging results.

Case 2

A 51-year-old female with a known history of achalasia presented with progressive dysphagia and intermittent retrosternal pain, particularly when consuming solid foods, over the past year. She had previously experienced episodes of regurgitation and occasional heartburn, but these symptoms had become more pronounced in recent months. Her medical history was otherwise unremarkable, with no prior history of gastroesophageal reflux disease or family history of malignancy.

On physical examination, the patient was in good general condition, with no significant weight loss or other systemic symptoms. Laboratory investigations, including a complete blood count, basic metabolic panel, and liver function tests, were within normal limits. Due to the progressive nature of her symptoms, an upper gastrointestinal endoscopy was performed.

Endoscopy revealed an esophageal lesion located approximately 25 cm from the incisors, appearing as a raised, irregular mucosal area with mild friability. Biopsies were taken from the lesion for further pathological evaluation.

Histopathological examination of the biopsy specimens revealed high-grade intraepithelial neoplasia. Immunohistochemical staining was performed to further characterize the lesion, and strong nuclear positivity for P53 was observed in approximately 85% of the cells, indicating a high likelihood of tumor suppressor gene mutation. The Ki-67 index showed high expression, with a labeling index of 95%, suggesting rapid cell turnover and aggressive cellular proliferation (Fig. 2). No evidence of invasive carcinoma was identified at this stage, and the lesion was confined to the mucosal layers, consistent with high-grade dysplasia.

Given the high-risk pathological features, the endoscopic ultrasound was performed to assess the depth of invasion. No submucosal invasion was detected, and there was no involvement of regional lymph nodes. A computed tomography scan of the chest and abdomen showed no signs of distant metastasis.

This case illustrates the potential progression of achalasia to premalignant lesions, as demonstrated by the presence of high-grade intraepithelial neoplasia. The strong P53 positivity and elevated Ki-67 index further underscore the aggressive nature of this dysplastic lesion. Close surveillance and timely intervention, including endoscopic or surgical resection, are being considered to prevent progression to invasive esophageal carcinoma.

Discussion

A systematic review and meta-analysis have shown that the incidence of esophageal cancer in patients with achalasia is sig-

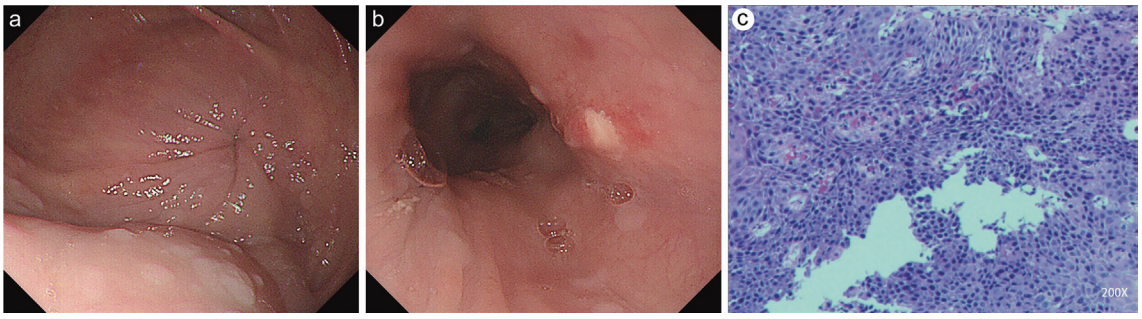

Fig. 2. Female, 51 years old. (a) Achalasia with esophageal dilation; (b) Elevated lesion located 25 cm from the incisors; (c) Pathology indicates high-grade intraepithelial neoplasia.

nificantly higher than in the general population. For instance, one study found that among 241 achalasia patients observed over 25 years, nine developed cancer, resulting in a cancer incidence rate of 88 per 100,000 patient-years, which is 14.5 times higher than the age- and sex-adjusted population.[4] Further supporting this, a cohort study involving 2,896 patients discharged with achalasia used standardized incidence ratios (SIR) to estimate the relative risk of esophageal cancer compared to the general population. The findings indicated that achalasia patients had a significantly higher risk of both esophageal squamous cell carcinoma (SIR 11.0, 95% confidence interval (CI) 6.0–18.4) and adenocarcinoma (SIR 10.4, 95% CI 3.8–22.6). Interestingly, despite a similar number of males and females in the achalasia cohort, 20 out of the 22 cases of esophageal cancer occurred in male patients.[5] A broader analysis that included 16 studies estimated the incidence of esophageal cancer in achalasia patients to be 1.36 cases per 1,000 person-years (95% CI: 0.56, 2.51). This rate is more than 10 times higher than that reported by the International Agency for Research on Cancer for the general population, underscoring achalasia as a major risk factor for the development of esophageal cancer.[6]

Another study involving 583 patients identified several risk factors for cancer development in achalasia patients. Key risk factors included having a sigmoid-shaped esophagus (risk ratio (RR) = 17.64, 95% CI 4.13–75.43), a symptom duration of more than 280 months (RR = 19.62, 95% CI 4.59–83.80), and an esophageal diameter greater than 71 mm at diagnosis (RR = 21.07, 95% CI 9.29–47.82).[7] A study involving 7,487 patients who underwent intervention for achalasia found that 101 patients (1.3%) developed esophageal cancer. Multivariate analysis indicated that the risk of esophageal cancer increased with the need for re-intervention after surgical myotomy (hazard ratio (HR) = 5.1; 95% CI 1.12–23.16) and balloon dilation (HR = 1.48; 95% CI 0.95–2.29).[8] Moreover, a study involving 2,714 patients with achalasia and related esophageal motility disorders reported that 24 patients (21 men and three women) developed esophageal cancer. The incidence from disease onset to diagnosis was estimated at 0.078 cases per 100 person-years. Kaplan-Meier estimates highlighted that long-term achalasia, older age, male gender, and frequent alcohol consumption are statistically significant risk factors for esophageal cancer development.[9]

Given these findings, early detection and management of achalasia are crucial to mitigating the risk of esophageal cancer. Effective treatments, such as pneumatic dilation, Heller myotomy, and POEM, can alleviate symptoms, but regular monitoring for malignancy remains essential. Surveillance strategies may include periodic endoscopic examinations and biopsies of any suspicious lesions. For instance, a meta-analysis of 40 studies involving 11,978 achalasia patients reported an SCC incidence of 312.4 per 100,000 patient-years and an adenocarcinoma incidence of 21.23 per 100,000 patient-years, emphasizing the need for ongoing vigilance.[10]

Conclusions

Achalasia significantly increases the risk of esophageal cancer, particularly squamous cell carcinoma. The chronic inflammation and food stasis associated with achalasia are major contributing factors to this heightened risk. Effective management of achalasia, combined with vigilant surveillance for early signs of cancer, is essential in reducing the morbidity and mortality associated with this condition. Future research should focus on identifying the molecular mechanisms linking achalasia to esophageal cancer and developing targeted therapies to prevent malignant transformation.

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Conflict of interest

One of the authors, Prof. Fachao Zhi has been an associate editor of *Cancer Screening and Prevention* since March 2022. All authors have no other conflicts of interest or financial ties to disclose.

Author contributions

Conceptualization (FZ, WQ), writing—original draft preparation (WQ, QL). All the authors have read and agreed to the published version of the manuscript.

Ethical statement

This study complies with ethical standards and has been conducted in accordance with the Declaration of Helsinki (as revised in 2013). Ethical approval was obtained from Nanfang Hospital. The patient provided written informed consent for the publication of this case report and accompanying images.

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