

Massive esophageal bleeding in long-standing achalasia complicated by esophageal carcinoma and aspirin-induced stasis ulcer

Case report

Joon Hyun Cho, MD, PhD*

Abstract

Rationale: Esophageal hemorrhage may occasionally develop subsequent to esophagitis and stasis ulcer, but potentially fatal esophageal bleeding is very uncommon in primary achalasia.

Patient concerns: We describe a case of a 64-year-old man with long-standing achalasia and megaesophagus who presented acute episodes of life-threatening upper gastrointestinal bleeding.

Diagnoses and interventions: Five esophagogastroduodenoscopies (EGD) were conducted and during each large amount of static food, bloody material, and clots should be removed from the esophagus because of impaired esophageal transit. Eventually, diffuse multiple irregular ulcers were observed in the middle and lower portions of the esophagus that were presumed to have been caused by aspirin stasis based on considerations of previous drug use. EGD also revealed a 2.0 × 2.5 cm flat nodular lesion with central ulceration at the mid-to-lower esophagus and adherent blood clots suggestive of bleeding stigma. The biopsy specimen demonstrated esophageal cancer. Accordingly, a diagnosis of massive esophageal hemorrhage in long-standing achalasia complicated by squamous cell carcinoma, possibly triggered by acute mucosal irritation and ulcer caused by aspirin stasis, was made. The patient then successfully underwent the Ivor-Lewis operation. Resultantly, the tumor was diagnosed as moderately differentiated squamous cell carcinoma stage IIA (T2N0M0).

Outcomes: The patient's postoperative course was uneventful, and no evidence of tumor recurrence or metastasis has been found during the 6 months of follow-up examination. He was tolerating normal food with only minimal reflux symptoms.

Lessons: Although, fortunately in the described case, esophageal cancer was diagnosed at a relatively early stage because it is the acute presentation of life-threatening upper gastrointestinal bleeding, this report cautions that when symptoms of dysphagia are aggravated, taking drugs capable of acting as local irritants, such as aspirin, could cause fatal esophageal hemorrhage in achalasia.

Abbreviation: EGD = esophagogastroduodenoscopy.

Keywords: achalasia, esophageal cancer, esophageal hemorrhage, stasis ulcer, upper gastrointestinal bleeding

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Division of Gastroenterology and Hepatology, Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Republic of Korea.

* Correspondence: Joon Hyun Cho, Division of Gastroenterology and Hepatology, Department of Internal Medicine, Yeungnam University College of Medicine, 170 Hyeonchung-ro, Nam-gu, Daegu 42415, South Korea (e-mail: ygwgo96@yu.ac.kr).

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1. Introduction

Achalasia is an idiopathic primary esophageal motor disorder with an estimated incidence of 1 in 100,000 and a prevalence of 1 in 10,000.^[1] It is characterized by the absence of esophageal peristalsis and failure of the lower esophageal sphincter (LES) to relax on swallowing, which leads to an accumulation of food debris and fluid in a dilated esophagus. The etiology of achalasia has not been elucidated, and by nature the disease is progressive. Therefore, its treatment is substantially palliative and aims to relieve symptoms by lowering LES pressure, principally via pneumatic dilation or Heller myotomy, and thus, improving passive esophageal transit.^[2]

If left untreated or treated improperly, achalasia causes progressive esophageal dilation, elongation, tortuosity, and loss of functionality and eventually leads to characteristic “sigmoidochealomegaesophagus.”^[3] Important morbidities afflict patients with end-stage disease, such as pulmonary complications, malnutrition, disabling dysphagia, infections, esophagitis, esophageal-tracheal fistula, esophageal diverticula, and rarely, esophageal squamous cell carcinoma.^[4] Furthermore, although it is

infrequent, the development of esophageal hemorrhage subsequent to stasis and chronic mucosal irritation is possible.^[5] However, fatal esophageal bleeding is extremely rare in primary achalasia. Here, we describe a case of life-threatening bleeding in a patient with “megaesophagus” in long-standing achalasia complicated by esophageal carcinoma and aspirin-induced stasis ulcer.

2. Case presentation

A 64-year-old man was admitted to our institution with an acute episode of hematemesis and melena. He had been diagnosed with achalasia 20 years previously at our institution, but had declined any treatment except intermittent irregular endoscopic follow-up. Although he experienced intermittent discomfort due to dysphagia for solids and liquids and regurgitation of retained food, he had tolerated these symptoms and had been able to live a relatively normal life. However, his dysphagia worsened recently, and for several days before visiting our emergency room, he had taken a 100 mg aspirin tablet daily in the belief that it might be good for his health. He had no notable medical history, other than achalasia, was a nonsmoker and nonalcohol drinker, and had no history of gastrointestinal bleeding.

On arrival at our emergency room, the patient was hypotensive and appeared acutely sick. His initial vital signs were temperature 37.1°C, blood pressure 90/60 mm Hg, heart rate 117 beats/min, respiratory rate 19/min, and oxygen saturation in room air 97%. A physical examination showed pale conjunctiva and nail beds due to anemia. An initial routine laboratory study showed anemia (red blood cell count 2.80 M/ μ L, hemoglobin 8.5 g/dL), acute renal impairment (creatinine 1.98 mg/dl, ureic nitrogen 38 mg/dl), hypoalbuminemia (serum albumin 3.1 g/dL), and neutrophilic leukocytosis (white blood cells 14.2 k/mL, neutrophils 84.1%). Other laboratory findings included platelets 336 k/mL and normal coagulation screening results. Chest X-ray showed an extremely enlarged esophagus occupying almost the entire right hemithorax with a proximal isolated air-fluid level and a food content like density. Thoracoabdominal computerized tomography confirmed the presence of marked esophageal dilatation with distal narrowing compatible with achalasia and also demonstrated a large amount of clotted blood in esophageal lumen and active extravasation at the mid-to-lower esophagus (Fig. 1). After immediate large volume resuscitation with vigorous intravenous fluids and packed red blood cells (RBCs), and nasogastric aspiration, the patient underwent emergent esophagogastroduodenoscopy (EGD). EGD revealed a large, twisted megaesophagus, and active oozing bleeding, large amounts of fresh blood clots, and food in the esophagus, which prevented visualization of the bleeding focus (Fig. 2A). Accordingly, an emergent surgical opinion was sought. However, the patient subsequently vomited large amounts of fresh blood and clots repeatedly and complained of dyspnea, and soon after that, cardiac arrest occurred about 11 hours after admission, despite intensive care in our emergency room. Endotracheal intubation, ventilation by Ambu bagging, and cardiac massage with intravenous vasopressors and inotropes were performed immediately and continued for 10 minutes, after which he was successfully resuscitated.

On hospital day 2, the patient presented ongoing melena and repeat EGD was performed. However, we failed to locate the bleeding focus and perform endoscopic hemostasis due to large amounts of blood, blood clots, and food material. On hospital

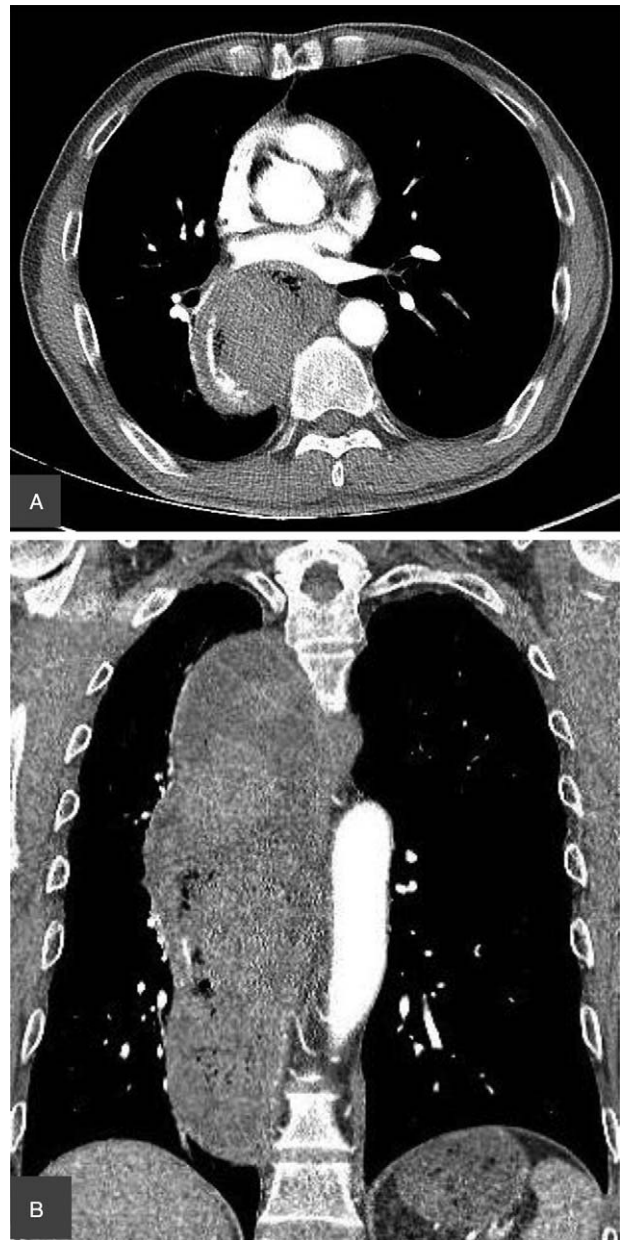


Figure 1. Thoracic CT images. Initial axial (A) and coronal (B) CT images obtained at presentation showing marked esophageal dilatation compatible with achalasia, a large amount blood clots in esophageal lumen, and active extravasation at the mid-to-lower esophagus. CT = computed tomography.

day 3, repeat EGD still showed large amounts of fresh blood and clots, but after removing them as much as possible by endoscopic suction and using a snare, we were able to identify diffuse multiple irregular ulcers in the middle and lower portions of the esophagus (Fig. 2B). However, it was difficult to define the bleeding focus because the endoscopic visual field was limited by the large amount of blood and blood clots present. Intensive supportive care involving vigorous intravenous fluid resuscitation, packed RBC transfusion, intravenous high-dose proton-pump inhibitors, nil-per-os, and total parenteral nutrition was continued. Thereafter, the amount of melena reduced and vital signs stabilized.

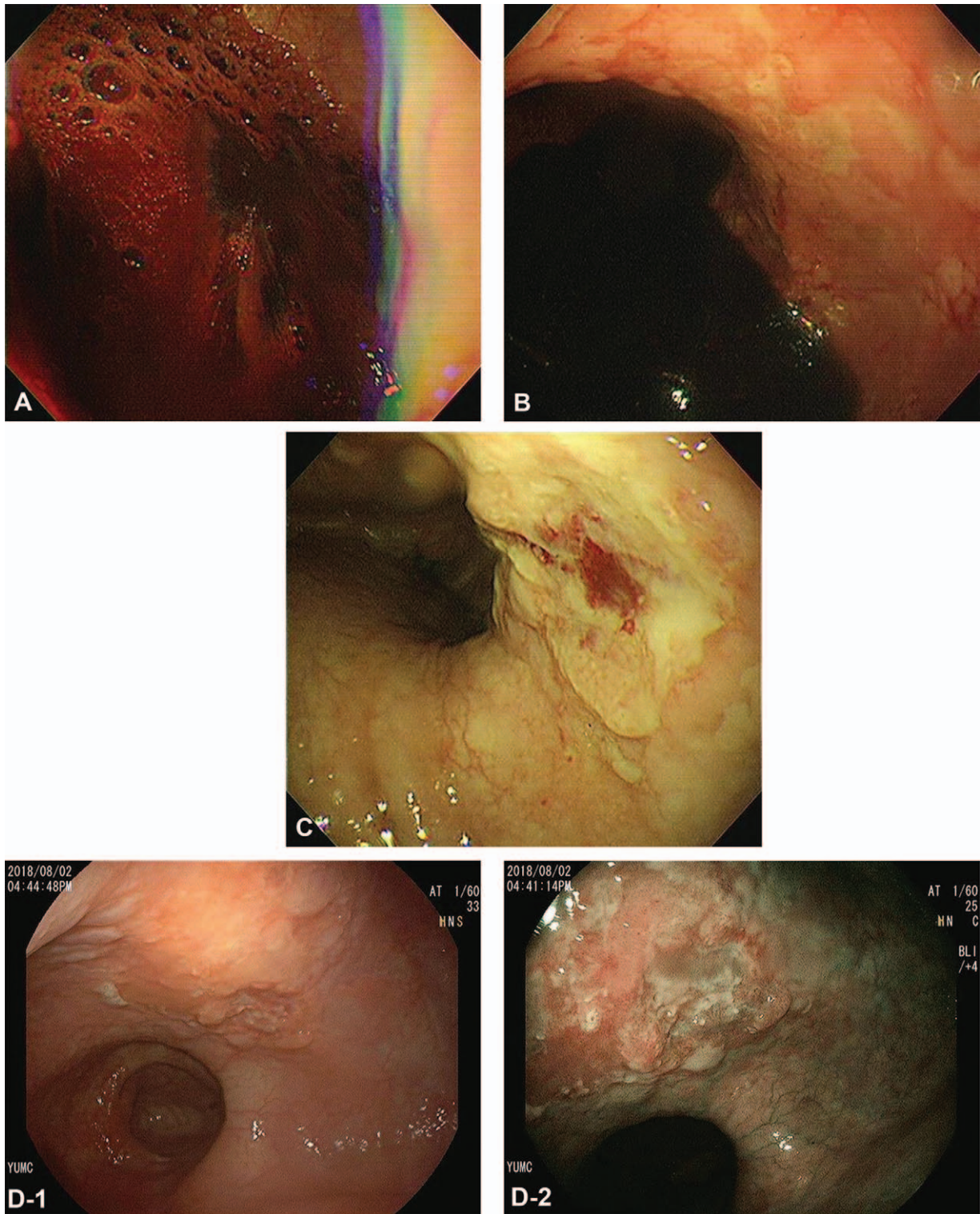


Figure 2. Endoscopy images. (A) Initial endoscopy image obtained at presentation showing active bleeding with large amounts of fresh blood and blood clots in a markedly dilated esophagus; (B) Endoscopy image obtained on hospital day 3 showing diffuse multiple irregular ulcers in the middle and lower portions of the esophagus; (C) Endoscopy image obtained on hospital day 5 showing a flat nodular lesion with central ulceration and adherent blood clots at the mid-to-lower esophagus; (D) Endoscopy image obtained on hospital day 13 showing a 2.0×2.5cm sized, poorly demarcated, flat nodular lesion with central ulceration accompanied by surrounding reddish mucosal irregularity at the mid-to-lower esophagus (30–33 cm from upper incisors) on white light images (D-1) and narrow band images (D-2).

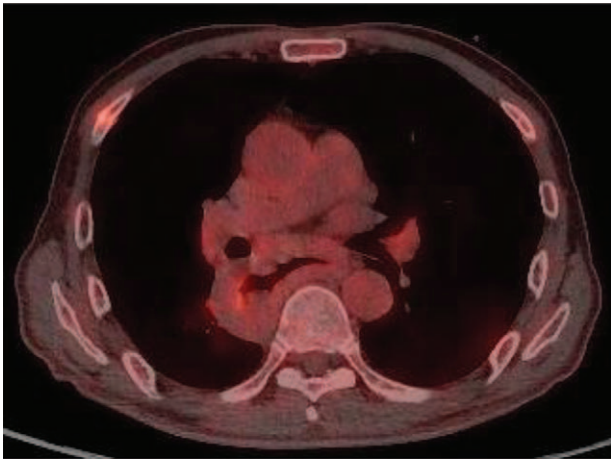


Figure 3. Position emission tomography/computed axial tomography image. The image shows mild FDG uptake at the mid-to-lower esophagus.

On hospital day 5, after removing as much stagnant material and blood as possible, follow-up EGD revealed diffuse, multiple, shallow healing stage ulcers with exudate in the middle and lower portions of the esophagus and a flat nodular lesion with central ulceration at mid-to-lower esophagus (30–33 cm from upper incisor teeth) (Fig. 2C). Adherent red blood clots on a flat nodular lesion suggested bleeding stigma, but no active bleeding was observed. Endoscopic biopsy was deferred due to bleeding concerns. The next day, he was successfully weaned off mechanical ventilation and the endotracheal tube was removed. Thereafter, he presented intermittent small amounts of melena and laboratory studies showed only a slight fall in serum hemoglobin.

On hospital day 13, after blood clot removal, follow-up EGD revealed an approximately 2.0 × 2.5 cm sized, poorly demarcated, flat nodular lesion with central ulceration accompanied by surrounding reddish mucosal irregularity at the mid-to-lower esophagus (Fig. 2D). No specific abnormalities except chronic superficial gastritis in stomach (including cardia) were observed. Endoscopic biopsy specimens showed moderately differentiated squamous cell carcinoma. Subsequent positron emission tomography/computed axial tomography demonstrated mild FDG uptake in the mid-to-lower esophagus and no other hypermetabolic lesion (Fig. 3).

Radical esophagectomy was planned to treat the esophageal malignancy, and the patient underwent an Ivor–Lewis operation successfully. Histopathologic examination of the resected esophagus revealed moderately differentiated squamous cell carcinoma with keratin pearl formation that invaded the proper muscle layer (Fig. 4). The tumor was diagnosed as stage IIA (T2, N0, M0) according to the tumor node metastasis classification for esophageal cancer,^[6] and was of histopathological grade G2 (moderately differentiated). The patient's postoperative course was uneventful, and he was discharged 10 days after surgery. He has since been followed up for 6 months at our outpatient department without any evidence of tumor recurrence or metastasis. He was tolerating normal food with only minimal reflux symptoms.

3. Discussion

Achalasia is a relatively rare disorder of unknown etiology characterized by failure of LES relaxation and loss of peristalsis

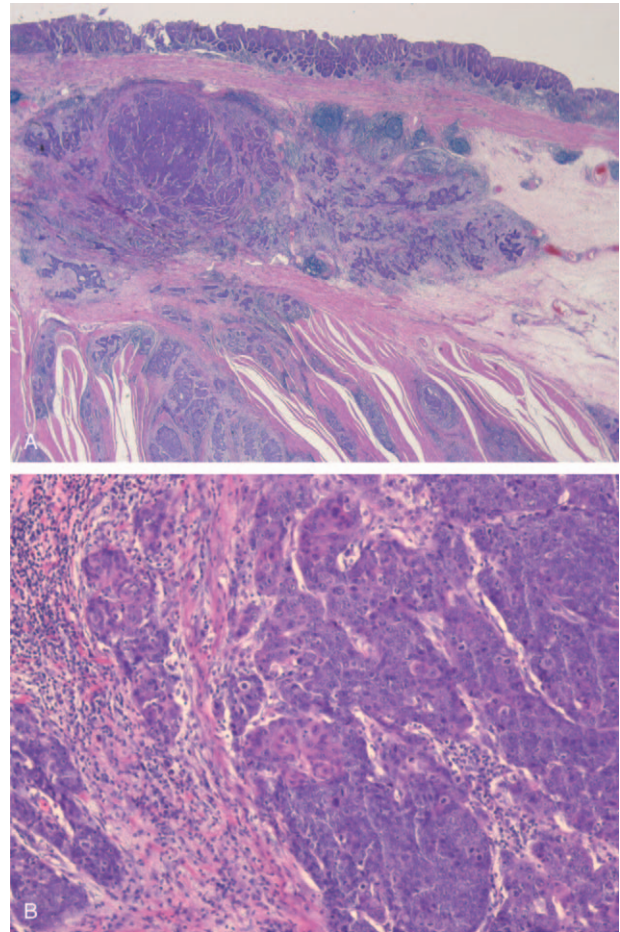


Figure 4. Histology of the surgically-resected esophagus. (A) H&E staining showed the tumor invaded proper muscle layer (original magnification ×10), and (B) moderately differentiated squamous cell carcinoma with keratin pearl formation (original magnification ×200).

along the esophageal body.^[7] Its predominant symptoms include dysphagia for solids and liquids, alimentary regurgitation, and bad breath. Even adequate treatment with sufficient symptom control may not prevent persistent esophageal distension with food and fluid retention, bacterial overgrowth, and impaired clearance of regurgitated acidic gastric contents. Furthermore, these phenomena can lead to chronic inflammation of esophageal mucosa, which potentially increases epithelial susceptibility to carcinogens produced by bacteria^[8–10] and the risks of hyperplasia, dysplasia, and squamous cell carcinoma.^[11] In addition, treatment modalities that lower LES pressure on aperistaltic esophagi with poor acid clearance can aggravate gastroesophageal acid reflux and lead to Barrett's metaplasia^[12] and adenocarcinoma.^[13,14] However, despite these proposed mechanisms, the precise risk of esophageal cancer development in patients with achalasia remain unclear. Several recent well-designed studies have shown the risk of cancer appears to be 10 to 50 times higher than in the general population.^[15,16] The co-occurrence of achalasia and esophageal cancer was first noted by Fagge in 1872.^[17] Achalasia has frequently been reported to predispose the development of esophageal squamous cell carcinoma, to the extent that the relation between achalasia and esophageal squamous cell carcinoma appears to be well-established.^[7,18–20]

The problem of detecting esophageal cancer in patients with achalasia may be that the dilated esophagus readily compensates for partial obstruction of the lumen by a tumor. Furthermore, patients usually adapt to dysphagia to some extent, and consequently, if endoscopic surveillance is not properly performed, esophageal cancer is often diagnosed at an advanced stage. Thus, the prognosis of “achalasia-carcinoma” is considered poor.^[9] However, fortunately in the described case, esophageal cancer was diagnosed at a relatively early stage in end-stage achalasia because it is unexpected acute presentation of life-threatening upper gastrointestinal bleeding.

Although the development of esophageal bleeding subsequent to stasis and chronic mucosal irritation is possible,^[5] the presentation of life-threatening hemorrhage in primary achalasia is very uncommon. Few cases of massive bleeding have been reported in patients with esophageal involvement by an underlying disease, such as esophagitis due to cytomegalovirus colonization^[21] or esophageal varix.^[22] Other reports of massive bleeding in achalasia have involved bleeding from an esophagopulmonary fistula as a complication of stasis ulcer^[23] and bleeding in non-Hodgkin’s esophageal lymphoma.^[24] Thus, the described case of massive bleeding associated with esophageal cancer and acute mucosal irritation and ulcer caused by drug stasis in achalasia is very rare.

Causes of ulceration in achalasia include stasis ulcer, pill esophagitis, and malignancies.^[25] In the described case, the patient had adapted to intermittent discomfort by dysphagia, refused treatment, and was not regularly followed-up. Furthermore, when his symptoms worsened, he had self-administered aspirin for several days before he initially presented with hematemesis. It would appear that retained aspirin and stasis over an atonic esophagus may have caused acute mucosal irritation on already vulnerable, hypertrophic, and hypervascular esophageal mucosa, and that this had led to mucosal ulceration and bleeding. The development of neoplasms may, of course, facilitate bleeding over tumoral mucosa, which is usually more friable and atrophic, but massive bleeding from a tumor as was observed in the described case remains exceptional.

4. Conclusion

This report describes a case of massive esophageal hemorrhage in a patient with long-standing achalasia complicated by squamous cell carcinoma, possibly triggered by acute mucosal irritation and ulcer caused by aspirin stasis. Although achalasia is progressive in nature and even adequate treatment may not prevent persistent esophageal distension, relieving symptoms by improving passive esophageal transit by lowering LES pressure (eg, by pneumatic dilation) might reduce acute mucosal irritation and ulcer development by drug stasis such as aspirin or nonsteroidal anti-inflammatory drugs. Although, fortunately in the described case, esophageal cancer was diagnosed at a relatively early stage because it is the acute presentation of life-threatening upper gastrointestinal bleeding, this case cautions that when symptoms of dysphagia are aggravated in patients with achalasia, taking a drug that could act as a local irritant, such as aspirin, increases the risk of fatal esophageal hemorrhage.

Author contributions

Conceptualization: Joon Hyun Cho.

Data curation: Joon Hyun Cho.

Investigation: Joon Hyun Cho.

Resources: Joon Hyun Cho.

Writing – original draft: Joon Hyun Cho.

Writing – review and editing: Joon Hyun Cho.

Joon Hyun Cho orcid: 0000-0002-3584-6300.

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