Clinical Case Report

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Successful treatment of drug-induced esophageal ulcer in a patient with chronic heart failure

A case report

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Abstract

Rationale: Although esophageal compression due to cardiomegaly may be a risk factor of drug-induced esophageal injuries (DIEIs), the causal relationship between the two conditions has not been fully demonstrated.

Patient concerns: We present a case of a drug-induced esophageal ulcer caused by left atrial enlargement in a 44-year-old woman with end-stage hypertrophic cardiomyopathy. Upper gastrointestinal endoscopy showed a deep, circumferential ulcer in the middle thoracic esophagus. CT revealed that the esophagus was compressed between the enlarged left atrium (LA) and the vertebral body. In the upper gastrointestinal series, retention of contrast media was observed in the esophagus near the LA.

Diagnosis: The ulcer was a result of potassium chloride retention in the esophagus, which was compressed by the enlarged LA.

Intervention: After cessation of potassium chloride administration for 2 months, the ulcer healed and a stricture developed. Two years after the ulcer development, the patient underwent heart transplantation, and subsequent endoscopic balloon dilation was performed for the esophageal stricture.

Outcomes: The patient's oral intake recovered completely without any ulcer recurrence.

Lessons: The case demonstrated that esophageal compression by the enlarged LA caused a drug-induced esophageal ulcer. Preventive care and treatment measures for DIEIs, including an anatomical approach, should be considered for patients with LA enlargement.

Abbreviations: Ao = aorta, DIEIs = drug-induced esophageal injuries, LA = left atrium.

Keywords: cardiomegaly, drug-induced esophageal injuries, endoscopic dilation, esophageal ulcer, heart transplantation, left atrial enlargement

1. Introduction

Over 100 different drugs have thus far been reported to cause drug-induced esophageal injuries (DIEIs).[1] DIEIs occur when caustic drugs dissolve in the esophagus and release their noxious contents.[1,2] The most-important patient-related risk factors for DIEIs are insufficient water consumption and recumbent position while taking medicines, which extend the drug-exposure time in the esophagus.[3] The lesions are frequently located in the middle thoracic esophagus, where the aortic arch and left atrium (LA) physiologically constrict the esophageal lumen and probably delay the transit of medicines.[2,4] In addition, altered esophageal anatomies may be risk factors of DIEIs. Patients with cardiomegaly are particularly susceptible to injury at the site of the esophagus compressed by the LA.[2,4] However, a few studies demonstrated that LA enlargement causes DIEIs and anatomical approaches healed and prevented DIEIs. In this report, we present a case of a potassium chloride-induced esophageal ulcer caused by LA enlargement, which was successfully treated using endoscopic balloon dilation for the stricture after improvement of esophageal compression by heart transplantation.

2. Case report

A 44-year-old woman with pulmonic valve stenosis and atrial septal defect underwent curative surgery at 4 years of age. At the age of 38 years, she noticed exertional dyspnea and was diagnosed with end-stage hypertrophic cardiomyopathy. At the age of 40 years, she was hospitalized for heart failure due to frequent atrial fibrillation attacks and implanted with a cardiac

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Patient consent: We obtained written consent from the patient for publication of this case.

Ethics committee approval is not included, as it is accepted in our hospital that case reports do not require such approval.

The authors have no conflicts of interest to disclose.

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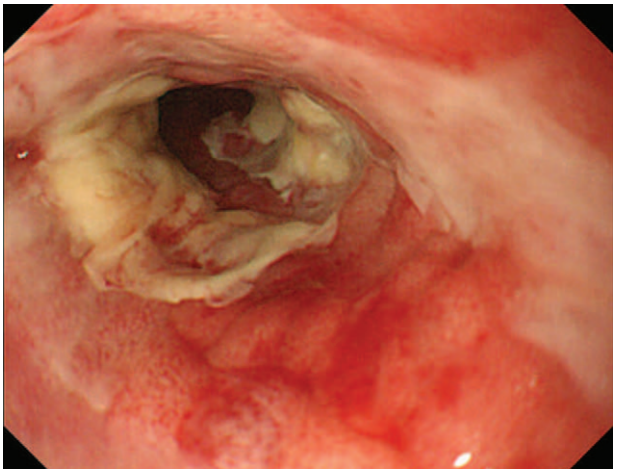

Figure 1. Upper gastrointestinal endoscopy on admission shows a deep circumferential ulcer with white exudates in the esophagus, 28 to 36 cm from the incisors.

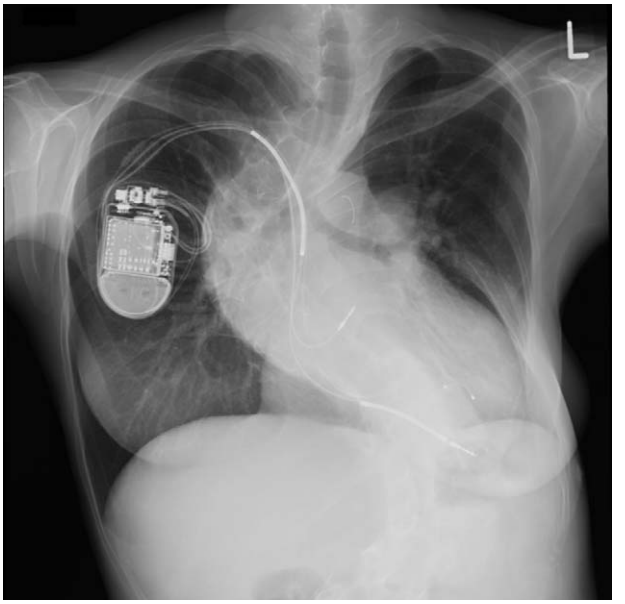

Figure 2. Chest radiography shows cardiomegaly with the cardiothoracic ratio of 56% and scoliosis.

resynchronization therapy with defibrillator. Nonetheless, she had frequent hospital admissions, and in the current instance, she was hospitalized for heart failure exacerbated by atrial fibrillation attacks. She was administered medication for 1 month of hospitalization, which improved the circulation dynamics, but 3 days after discharge, she was readmitted and referred to our department with complaints of epigastric pain and loss of appetite.

She underwent upper gastrointestinal endoscopy for odynophagia and dysphagia, which showed a deep circumferential ulcer with white exudates in the esophagus, 28 to 36 cm from the incisors (Fig. 1). Histopathological findings of the biopsy specimens taken from the ulcer showed only infiltration of inflammatory cells, indicating neither infection nor malignancy. There was no retention of food residues in the esophagus, which could cause physical obstacles, nor any history of ingestion of corrosive substances by mistake. Various drugs were administered to control her chronic heart failure, but only potassium chloride was previously reported to cause DIEIs. The potassium chloride dose was increased during the patient's previous hospitalization to prevent atrial fibrillation attacks and most likely induced ulceration. Chest radiography showed cardiomegaly with a cardiothoracic ratio of 56% and scoliosis (Fig. 2). A transthoracic echocardiogram revealed the presence of mild mitral regurgitation and LA enlargement, with a LA dimension of 55 mm. CT showed that the enlarged LA and vertebral body compressed the esophagus, where a high-density area was noted and suspected to retain drugs (Fig. 3). This high-density area likely contained potassium chloride because the drug was orally administered before CT and was radiopaque for several hours after administration. Collectively, these findings indicated that the ulcer was induced by potassium chloride lodged in the esophagus owing to the LA enlargement. In the upper gastrointestinal series, retention of contrast media was observed at the narrowing site of the esophagus, which is close to the LA, suggesting esophageal obstruction due to LA enlargement (Fig. 4).

Treatment with a proton-pump inhibitor was initiated, and potassium chloride administration was discontinued. Follow-up endoscopy 2 weeks later showed that the ulcer was healing (Fig. 5), and epigastric distress and odynophagia were alleviated. However, conservative treatment with cardiovascular drugs did not effectively control the patient's heart failure, and therefore, she underwent left ventricular assist device implantation and waited for a heart transplantation. Follow-up endoscopy 2 months later showed that the ulcer had scarred, and an esophageal stricture had developed (Fig. 6). The patient complained of dysphagia and vomiting after ingestion of solid meals, but she managed to maintain nutrition on a soft diet without intravenous nutrition and was observed without endoscopic therapy due to severe cardiac dysfunction.

Two years after the development of the esophageal ulcer, the patient underwent heart transplantation. Surgery was completed without any serious complications. Her general condition improved, but her dysphagia worsened as her medications such as immunosuppressive agents increased. Four months after the heart transplantation, endoscopic balloon dilation was performed for the esophageal stricture. Thereafter, her dysphagia improved during meals and while taking medicines. The patient was discharged 5 months after the heart transplantation. No ulcer recurrence has been observed for 10 months since her discharge.

We obtained written consent from the patient for publication of this case. Ethics committee approval is not included, as it is accepted in our hospital that case reports do not require such approval. In this work, we did not use patient data that would allow identifying her.

3. Discussion

In this report, we present a case of a potassium chloride-induced esophageal ulcer. This case is clinically important because the ulcer was clearly caused by esophageal compression due to LA enlargement. An esophageal stricture developed after the ulcer healed following discontinuation of the drug, but was successfully treated with endoscopic balloon dilation after heart transplantation.

DIEIs are caused by various factors related to drug properties, anatomy, and patient lifestyle.[3] Among them, the chemical structure and pharmaceutical forms of drugs are the most

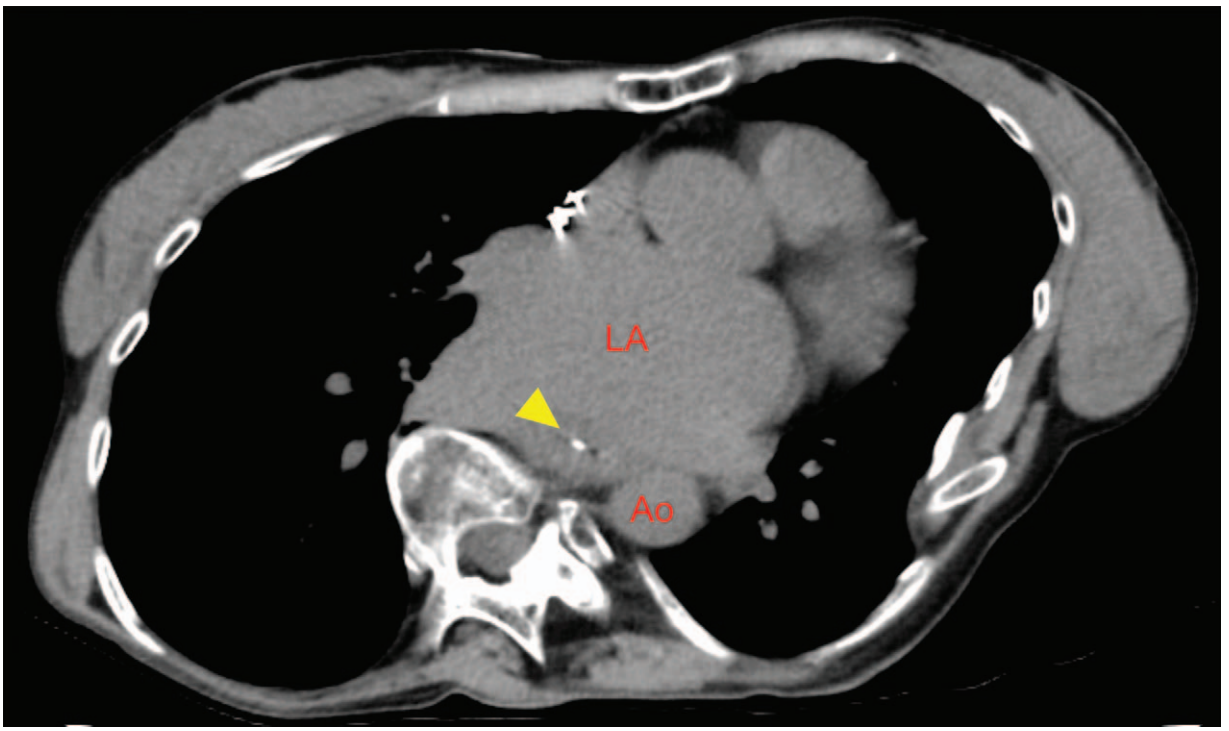

Figure 3. Computed tomography shows that the enlarged left atrium and vertebral body are compressing the esophagus, where a high-density area is seen and suspected to retain drugs (arrowhead). Ao = aorta, LA = left atrium.

significant factors.[3] Oral administration of tablets or capsules have great advantages in ingestion and transportability compared with liquid preparations. However, these forms have disadvantages of increased local concentration of active pharmaceutical ingredients that injure susceptible tissues, particularly the esophagus, compared with liquid preparations.[1] Capsule forms of medicines such as doxycycline, tetracycline, and clindamycin can adhere to the esophagus and cause more serious injuries than the tablet forms.[3] Large pills such as those for clarithromycin, alendronate, and ibuprofen and sustained-release formulations of drugs such as ferrous sulfate and potassium chloride may be more commonly retained in the esophagus and more injurious than the standard preparations of the same medicines.[1,2]

Although LA enlargement may be a risk factor for DIEIs, it has rarely been demonstrated to cause DIEIs thus far. To our knowledge, there was only one report in 1979 about esophageal ulceration due to slow-release potassium in the presence of LA enlargement.[5] In another report, patients with mitral valve disease were found to have delayed esophageal transit of capsules because of the anatomical deformity caused by LA enlargement[6]; in the study, the LA dimensions of the study patients were 22 to 79 mm (mean, 45 mm), while those of the control patients were 21 to 35 mm (mean, 28 mm). In our current case, the LA dimension of the patient was 55 mm, which was large enough to compress the esophagus. However, these previous reports lacked sufficient evidence to demonstrate that the LA enlargement caused the DIEIs. As such, our case is important, because the clinical course verified the causal relationship between the drug-induced esophageal ulcer and anatomical deformities using multiple imaging modalities.

The efficacy of the anatomical approach to prevent DIEIs has rarely been reported and discussed in detail. Treatments for esophageal stricture without releasing the compression from the dilated heart might be ineffective and result in ulcer recurrence. Partial resection of the inferior and/or superior LA wall at the time of surgery for the mitral valve is a common method for treatment of the giant LA.[7,8] This surgery achieved significant reduction in the LA volume, but is not strongly recommended for patients with poor cardiac function, like our patient, because of the high operative mortality of 8% to 23% caused by low-cardiac-output syndrome and respiratory failure.[8] Furthermore, it was difficult to control end-stage chronic heart failure with partial resection and medication. However, over the last decade, heart transplantation has been increasingly performed worldwide.[9] A previous case of a patient with a giant LA who received heart transplantation was reported in 2014,[10] but the efficacy of the transplantation against esophageal compression after the operation was not assessed. In our case, heart transplantation resolved the cardiomegaly as a fundamental cause of anatomical deformities. Considering that no ulcer recurrence was reported during follow-up, the heart transplantation was also beneficial for preventing DIEIs.

The important patient-related risk factors of DIEIs are the amount of fluid ingested with medicines and disability of the patient.[3] Pills are more likely to stick to the esophageal walls if swallowed with insufficient water and in the supine position.[2,3] Patients suffering from chronic heart failure are often restricted in terms of water consumption and their activities. Insufficient water consumption, taking drugs in a recumbent position, and bed rest further cause DIEIs. Additionally, patients with ischemic heart disease often take aspirin, which can cause severe esophageal ulceration and is associated with bleeding.[1,2] Therefore, clinicians should pay attention to not only anatomical changes in the esophagus but also other risk factors of DIEIs associated with cardiac disease in order to prevent DIEIs, especially in patients with LA enlargement. As most patients are

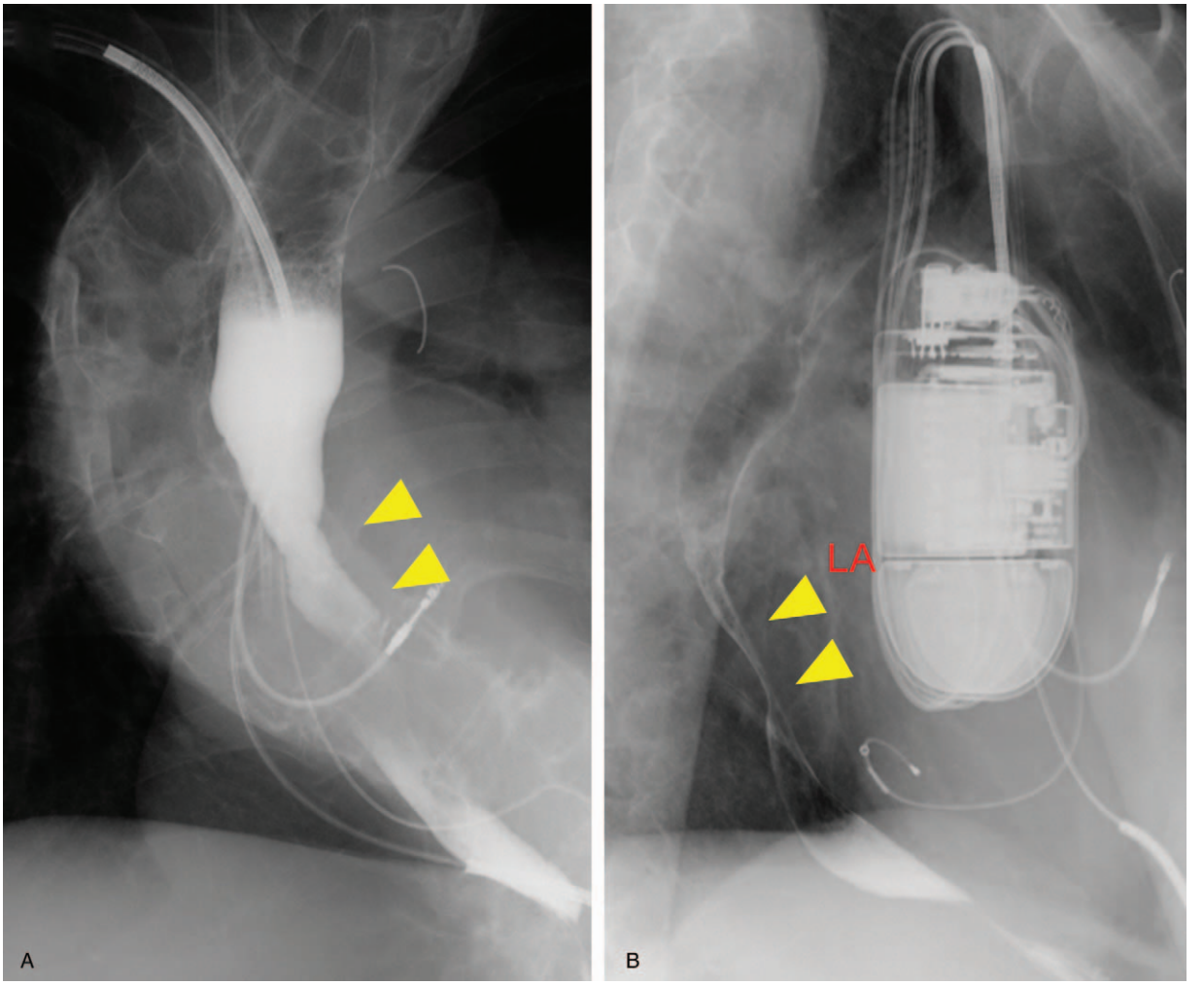

Figure 4. Upper gastrointestinal series. (A) Frontal view and (B) lateral view. Retention of contrast media at the narrowing site of the esophagus is observed at the same height as the left atrium (arrowheads). LA = left atrium.

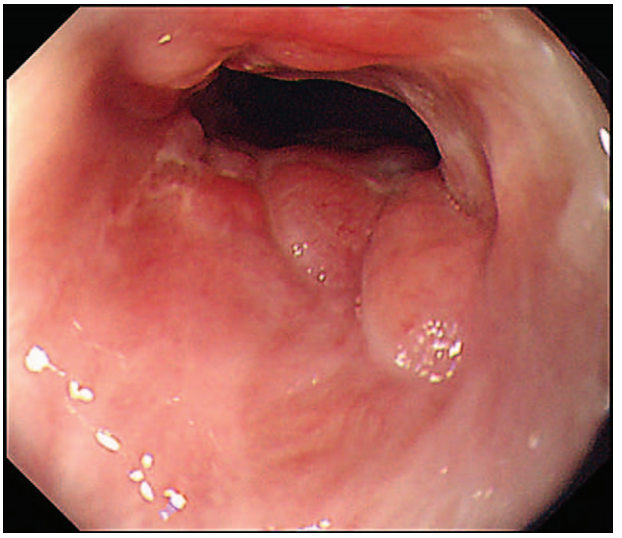

Figure 5. Follow-up endoscopy 2 weeks after treatment with a proton-pump inhibitor shows the ulcer healing in the esophagus.

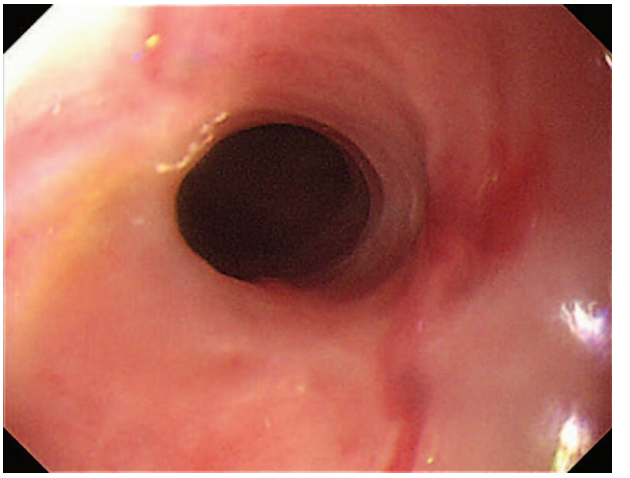

Figure 6. Follow-up endoscopy after 2 months from cessation of potassium chloride administration shows the ulcer scar with a stricture formation.

orally administered medicines without the knowledge of the risk of DIEIs, clinicians should instruct them how to take the medicines, if necessary; restrict their drug dosages; and exchange pharmaceutical forms for safer ones.

There are some limitations to this case report. First, retained potassium chloride was thought to be responsible for the ulcer formation from upper gastrointestinal series and CT findings, but the component was not actually identified by endoscopy. Next, our diagnosis was based on the improvement of the ulcer by withdrawal of potassium chloride. DIEI is basically a diagnosis of exclusion, and the causality was difficult to prove.

In summary, we presented a case of a drug-induced esophageal ulcer caused by esophageal compression due to LA enlargement. For patients with LA enlargement, preventive care and treatment measures for DIEIs, including the anatomical approach, should be considered.

Author contributions

Data curation: Kazuki Maesaka, Shunsuke Yoshii, Kei Nakamoto.
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Validation: Yoshiki Tsujii.
Writing – original draft: Kazuki Maesaka, Yoshiki Tsujii.
Writing – review & editing: Shinichiro Shinzaki, Yoshito Hayashi, Hideki Iijima, Tomohito Ohtani, Yasushi Sakata, Tetsuo Takehara.

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