Early diagnosis and management of esophageal leakage after peroral endoscopic myotomy for achalasia

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ABSTRACT

Background/Aims: To improve the understanding of esophageal leakage after peroral endoscopic myotomy (POEM).

Materials and Methods: From August 2010 to April 2013, patients with postoperative esophageal leakage were identified from the database of cases with achalasia who had undergone POEM and their medical records were reviewed.

Results: Three patients (0.4%, 3/679) developed esophageal leakage after POEM. All three patients had non-severe chest or upper abdominal pain within 3 days after the procedure. Infections were observed, and computed tomography scans showed pleural effusion in all three patients. Pneumonia occurred in two of the three patients. Esophageal leakage was confirmed by gastroscopy. Incision rupture due to an early breaking-off of the clips at the tunnel entry was revealed in two cases. When detected, the entry was immediately closed using metal clips. A thoracic drain was placed in all cases. An enteric feeding tube was also placed to help correct nutrition deficiencies. Successful leakage closure was achieved in all three cases and no surgical intervention was needed.

Conclusion: Early diagnosis and treatment can improve the status of patients with esophageal leakage after POEM and can shorten the recovery time.

Keywords: Peroral endoscopic myotomy, esophageal leakage, achalasia

INTRODUCTION

Achalasia is a major primary esophageal dysmotility disorder, with dysphagia as the chief complaint. Mainly because the mechanisms underlying the loss of neurons in achalasia are not yet understood, treatment remains confined to disrupting the lower esophageal sphincter (LES) (1,2). Peroral endoscopic myotomy (POEM) has been developed as a minimally invasive endoscopic treatment and provides a curative method for esophageal achalasia. It has become widely accepted because of its general perioperative safety and excellent short-term outcomes in terms of symptom resolution and improvement in esophagogastric junction (EGJ) physiology (3-13).

Nevertheless, as with any surgical procedure, the possibility of complications occurring during and after the POEM procedure still exists. POEM-related complications include subcutaneous/mediastinal emphysema, pneumothorax, pneumoperitoneum, pleural effusion, hemorrhage, and infection (14,15). It is well known that esophageal leakage is a severe postoperative complication of esophageal surgery, with a high mortality rate. However, heretofore, it has not been reported as a complication of POEM. Although esophageal leakage has a low incidence, it can have serious conditions. Furthermore, delayed diagnosis and therapy could result in risks in morbidity and mortality. In this study, the medical records of three patients with esophageal leakage after POEM were reviewed in order to provide information regarding the mechanism, early diagnosis, and optimal management of this severe complication.
MATERIALS AND METHODS

Study design
From August 2010 to April 2013, 679 patients underwent successful POEM in our center. Patients who had esophageal leakage after the procedure were identified and their medical data were reviewed. Patients were followed up for 11–18 months, and the score of Eckardt symptoms was employed to objectively assess their symptom relief. In this study, written forms of consent to undergo POEM from the patients included were collected. The study was approved by the Institutional Research Ethics Committee.

POEM procedure
A single-channel gastroscope with a transparent cap attached to the gastroscope tip was employed (16). Other equipment and the POEM procedure have been reported in detail in previous papers (3-13). After careful hemostasis, a copious amount of saline is sprayed into the submucosal tunnel. The mucosal entry is closed by using four to six clips.

Post-procedure management
Proton pump inhibitor (PPI), antibiotic, and hemocoagulase could be used postoperatively. Symptoms, including chest/abdominal pain, hematemesis/melena, dyspnea, and abdominal distention, should be carefully observed. A chest computed tomography (CT) scan was performed on the first day after POEM in 476 of the 679 included patients (70.1%), and postoperative esophageal leakage was detected in three patients. Patients fasted in the first day after POEM, and a full liquid diet was then permitted on the second day if there were no abnormal symptoms or CT scan findings. Patients were discharged on the third day with instructions to continue the PPI and a liquid diet for 1 week, followed by a semiliquid diet for another week, before resuming a normal diet. Patients were asked to discontinue the PPI medication at 4 to 8 weeks after the POEM.

Diagnosis of esophageal leakage
The diagnosis of esophageal leakage depends on recognizing its clinical features and confirming its presence by endoscopy. Esophageal leakage is suspected if chest pain, a continuous high fever, or dyspnea occurred. However, the early signs of esophageal leakage might be nonspecific until the start of oral intake. A chest CT scan may help detect this complication if it shows a large pleural effusion, pneumonia, or segmental atelectasis of the lungs, all of which can be early signs of esophageal leakage. Emergency endoscopy was performed for confirmation in all patients suspected of esophageal leakage.

Data collection and analysis
Data on esophageal leakage after POEM were collected and analyzed. Commercial software (IBM SPSS Statistics 18; SPSS, Chicago, IL, USA) was used for the statistical analysis, and p<0.05 was accepted to be statistically significant.

RESULTS
Three patients developed leakage after POEM (Table 1). There were no special technical difficulties in cases 1 or 3, but difficulty creating the submucosal tunnel was noted in case 2 because of severe fibrosis in the submucosal layer from a previous laparoscopic Heller myotomy (LHM). Full-thickness myotomies of internal circular and longitudinal muscular layers were done in all three patients.

All patients with leakage reported chest or upper abdominal pain within 3 days after POEM, but it was not severe in any of these patients. Manifestations of infection, including fever and increased white blood cell counts, were observed in all three patients. CT scans on postoperative day 1 showed a pleural effusion in all three patients and pneumonia in two of the patients.

All the patients with leakage were fasted and treated with antibiotics. No other special treatment was initiated for case 1 because only a low fever and small pleural effusion were present. This patient was discharged from the hospital after tolerating a liquid oral intake for 3 days, but subsequently developed a cough, chest pain, and high fever 1 week after discharge. A chest CT at that time revealed a pulmonary abscess on the left. The patient was treated with antibiotics and nutritional support for approximately 2 months, which relieved the cough and chest pain but not the fever. Gastroscopic exploration was thus performed, which revealed a leak orifice at the tunnel entrance. An enteric feeding tube was placed into the descend-
ing duodenum. Meanwhile, a thoracic drain was placed under ultrasound guidance. The patient’s temperature decreased to normal after a week, and the leak orifice was confirmed to be healing 1 month later.

In cases 2 and 3, a thoracic drain was placed immediately after the CT scans on postoperative day 1 identified the presence of possible esophageal leakage. The temperature of both patients fell after sufficient drainage, and a liquid diet was subsequently allowed. However, after oral intake resumed, the drainage changed to purulent, and a moderate fever recurred. Esophageal leakage was thus highly suspected. An esophageal X-ray with diatrizoate and oral methylene blue was performed, but no obvious esophageal leakage was detected. Both patients immediately underwent emergency gastroscopy. The clips (HX-600-135, Olympus) used to close the incision at the tunnel entry site were noted to be loose or broken off, and an orifice of leakage was detected at the tunnel entrance in both patients. When we thoroughly investigated the operation records, folding of the mucosa over the incision line after clipping was observed, indicating that the closure of the tunnel entry had been unsatisfactory. This had presumably led to dehiscence because of the relatively high tension in the area. The leakage was washed with abundant sterile saline and then closed with metal clips (ResolutionTM; Boston, MA, USA). A gastrointestinal decompression tube was placed near the orifice, and an enteric feeding tube was placed into the descending duodenum. The patients were restricted from oral intake and fed with a nutrient solution through the feeding tube. The body temperature, routine blood test results, and amount and character of the gastric and thoracic drainage were monitored. A PPI and antibiotics were administered to both patients, and closure of the leakage was subsequently confirmed by gastroscopy. Figure 1 shows the views during emergency endoscopy for these two patients, illustrating the diagnosis and closure of the leakage.

Complete healing of the esophageal leakage was successfully achieved in all three patients without surgical intervention. A follow-up of 11 to 18 months was taken with all three patients. The follow-up results are shown in Table 2. All the patients had continued relief of their dysphagia, and none reported gastro-esophageal reflux symptoms, such as acid reflux or heartburn. The Eckardt scores decreased from pre-treatment (6, 9, and 8) to post-treatment (0, 1, and 0, respectively). At follow-up endoscopy, the endoscope passed smoothly through the esophagus to the gastric cardia in all three patients. No objective evidence of reflux was seen during endoscopy. The follow-up esophageal barium swallow and manometry showed relaxation and a normal pressure at the LES (Figure 2).

DISCUSSION

Esophageal leakage, with an incidence of 4%–30%, is one of the most serious complications of esophageal surgery (17). The rate of clinically significant esophageal perforation reported in the literature for LHM ranges from 0 to 4.6% (18). The 0.4% incidence (3/679) of esophageal leakage after POEM reported in

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Eckardt score</th>
<th>Endoscopy</th>
<th>Esophageal barium swallow</th>
<th>Esophageal manometry 4-s IRP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>Open</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Open</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
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IRP: integrated relaxation pressure
In this study, all three patients who developed leakage had a long history of achalasia with severe dysphagia; this was particularly notable for case 2. Recurrent inflammation of the esophageal wall caused by frequent retention of food resulted in thickening of the mucosa and fibrosis formation in the submucosa. LHM, pneumatic dilation, or botulinum toxin injection can make this situation worse. It is difficult to create a tunnel in the submucosa in the presence of severe fibrosis. The submucosal fibrosis and mucosa thickening may increase the risk of a mucosal defect and subsequent leakage. Establishing the submucosal tunnel close to the muscle is important not only to avoid injuring the mucosal flap but also because of the lower vascularity in this area. Repeated injection of saline can be performed when the submucosal dissection plane becomes unclear; this will clear the demarcation between the mucosal layer and muscularis propria. Furthermore, the mucosal entry site should be tightly closed by metal clips after carefully washing the submucosal tunnel. However, a thick mucosa will be difficult to sew up tightly. Furthermore, endoscopic exploration in cases 2 and 3 showed that the clips used to close the tunnel entry broke off early, which was likely an important contributor to the esophageal leakage. This suggests that common clips are not powerful enough to tightly close the thick mucosal incision. Closing the tunnel entry by using Boston clips may be more effective for these types of patients and is recommended. Over-the-scope clips (OTSC) have been described as a good option for closing the mucosal incision during POEM. The use of OTSC may simplify the procedure and result in a more durable (i.e., full-thickness) closure (19). For patients with complicated situations, we also recommend extending the fasting time and placing a gastrointestinal decompression tube immediately after POEM to keep the wound surface clean to facilitate healing of the mucosal incision.

Although all three patients with leakage in our study underwent full-thickness myotomy, this is unlikely to be the cause of leakage after POEM. In our previous study (9), full-thickness myotomy was not associated with any infectious complications. These results supported the hypothesis that endoscopically performing two-level perforation of the gastrointestinal wall using the submucosal technique, even into the mediastinum, is feasible as long as the mucosal opening is sufficiently closed and ongoing spillage is avoided (20,21).

Early signs of an esophageal leak might be nonspecific and include such signs as chest pain, fever, and increased white blood cell; these occurred in all three patients in the current study. However, these nonspecific symptoms may be controlled by antibiotics if patients are fasted. Indeed, about 20% of leakages are not found and some became symptomatic only after resuming diet (22). In our experience, a change in the volume and/or characteristics of thoracic tube drainage and a slow course of recovery after oral intake might be useful hints suggesting that leakage is present.

The diagnosis of esophageal leakage is difficult, especially in the early stages of a small leak. Chest CT scans will help detect an esophageal leak, but they are less sensitive than esophageal X-ray in identifying leakage. Radiology remains the cornerstone of leakage evaluation, but they are also not completely reliable in detecting small leaks. In the current study, all leakages were detected by endoscopic exploration. Endoscopy, by providing direct vision, may be more sensitive than radiological imaging in detecting a small leakage. In the future, endoscopy may be even more useful in diagnosing a leak if it is combined with fistulography, allowing fluoroscopic imaging of the leak (23). Furthermore, endoscopy may be the most important and effective treatment for esophageal leakage. Closure of the leakage orifice by metal clips will substantially shorten its course. The duration of healing for cases 2 and 3 was shorter than for case 1 using the same basic conservative treatment. No increase in complications was observed in cases 2 and 3 by performing an endoscopic examination in the first few postoperative days. Moreover, a gastrointestinal decompression tube and enteric feeding tube could be placed at the same time under direct vision by the endoscope, contributing to the closure of the leakage. The use of a fibrin sealant during endoscopic treatment to seal a leak or fistula has been described. Two sealant components, fibrinogen and thrombin, stimulate the coagulation cascade when sealant is placed into the fistulous tract, and the fibrin will subsequently be slowly replaced by collagen (24). Sometimes, endoscopic sealing by clips alone may not be sufficient for a large leak, so combining clipping and fibrin sealing is probably more effective in these situations. Endoscopic suturing systems have been in use for the treatment of gastroesophageal reflux disease. The same technical principle should also be suitable for closing a mucosal defect; suturing may be an interesting new method for leakage treatment by endos-
Esophageal leakage is often accompanied by malnutrition, lack of food intake, and hypercatabolism (28). Malnutrition leads to hypoproteinemia, which increases the risk of leakage by enhancing the difficulty of performing POEM. Early diagnosis is difficult because typical symptoms of esophageal leakage are often lacking before oral intake is begun. Leakage should be considered if recovery is unusual or proceeding slowly. Endoscopy is recommended as an effective and safe method to detect a small leakage and as an effective treatment for closing the leak in its early stages. Adequate nutritional support through an enteral feeding tube is another important strategy to reduce morbidity and recovery time. Patients with esophageal leakage after POEM can achieve complete recovery in a short time without surgical intervention by endoscopic closure of the leak, sufficient drainage, and optimal conservative management. The long-term effectiveness of POEM is not diminished by esophageal leakage when endoscopy is used for early detection and therapy.

Ethics Committee Approval: The study was reviewed and approved by the Institutional Review Board of Zhongshan Hospital, Fudan University.

Informed Consent: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

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