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ABOUT COVER

Editorial Board Member of World Journal of Gastrointestinal Surgery, Michele Ammendola, MD, Research Associate, Surgical Oncologist, Science of Health Department, Digestive Surgery Unit, University of "Magna Graecia" Medical School, Catanzaro 88100, Italy. michele.ammendola@unicz.it

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The primary aim of World Journal of Gastrointestinal Surgery (WJGS, World J Gastrointest Surg) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, etc.

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CASE REPORT

Lung cancer metastasis-induced distal esophageal segmental spasm confirmed by individualized peroral endoscopic myotomy: A case report

Hong Shi, Su-Yu Chen, Zhao-Fei Xie, Li-Lin Lin, Yan Jiang

Hong Shi, Su-Yu Chen, Zhao-Fei Xie, Li-Lin Lin, Yan Jiang, Department of Endoscopy Center, Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fujian Branch of Fudan University Shanghai Cancer Center, Fuzhou 350014, Fujian Province, China
Co-first authors: Hong Shi and Su-Yu Chen. Co-corresponding authors: Su-Yu Chen and Zhao-Fei Xie.
Corresponding author: Su-Yu Chen, MD, Associate Chief Physician, Department of Endoscopy Center, Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fujian Branch of Fudan University Shanghai Cancer Center, No. 420 FuMa Road, Fuzhou 350014, Fujian Province, China. endosuyuchen@163.com
Abstract BACKGROUND Peroral endoscopic myotomy (POEM) has been widely performed as a standard treatment for achalasia; however, its efficacy and safety for treating distal esopha- geal segmental spasms induced by cancer metastasis remain unknown.
CASE SUMMARY A 72-year-old male was referred to our hospital and complained of progressive dysphagia for two years. Endoscopy revealed a 2 cm long segment esophageal stenosis with intact mucosa and normal cardia. Computed tomography showed a right upper lung mass, and pathology of the right pleural effusion confirmed the diagnosis of right upper lung adenocarcinoma with multiple rib and mediastinal lymph node metastases and right malignant pleural effusion. Individualized POEM was performed first to alleviate dysphagia, and the final diagnosis was changed to esophageal muscle metastasis arising from lung adenocarcinoma. After treatment, the patient could eat soft solid food and received multiple rounds

of pembrolizumab-combination chemotherapy. The patient's progression-free survival was approximately 16 months. Long stable disease was obtained during the 24-month follow-up.

CONCLUSION

The incidence of distal esophageal segmental spasms induced by muscular metastasis arising from lung adenocarcinoma is extremely low. Individualized POEM can effectively improve a patient's nutritional status before subsequent



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Shi H et al. Esophageal malignant spasm treated by POEM

chemotherapy can be combined with immune checkpoint inhibitors.

Key Words: Peroral endoscopic myotomy; Distal esophageal segmental spasm; Lung cancer; Esophageal metastasis; Case report

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Core Tip: The incidence of esophageal metastasis-induced segmental spasm is extremely low. Here, we report for the first time an individualized peroral endoscopic myotomy procedure for treating distal esophageal segmental spasm caused by muscular metastasis arising from lung adenocarcinoma, and this new technique can effectively improve a patient's nutritional status before subsequent chemotherapy combined with immune checkpoint inhibitors.

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INTRODUCTION

Peroral endoscopic myotomy (POEM) has been widely performed as a standard treatment for achalasia; however, its efficacy and safety for treating distal esophageal segmental spasms due to cancer metastasis remain unknown[1]. POEM, also known as one of the key branches of submucosal endoscopy, allows for a wide range of diagnostic or therapeutic interventions within the muscular layer of the gastrointestinal lumen. Here, we present a successful treatment for a patient with lung adenocarcinoma with esophageal muscle metastasis via individualized POEM followed by the addition of pembrolizumab[2,3] to standard chemotherapy consisting of pemetrexed under the guidance of a multidisciplinary team (MDT), which led to long-term progression-free survival.

CASE PRESENTATION

Chief complaints

A 72-year-old male was referred to our hospital because he had symptoms of progressive dysphagia, retrosternal pain and intermittent cough, with significant loss of body weight for two years that had worsened for one month.

History of present illness

On July 4, 2022, the patient was admitted to our hospital for chest computed tomography (CT), which revealed a right upper lung mass and right pleural effusion. A right pleural puncture was performed, which confirmed lung adenocarcinoma by pathology, with immunohistochemical staining showing positive expression of cytokeratin (CK) 7, carcinoembryonic antigen, and thyroid transcription factor-1 (TTF-1). PIK3CA mutations were detected via next-generation sequencing. An endoscopy report at a local hospital led to a suspected diagnosis of jackhammer esophagus, based on an esophageal high-resolution manometry report, low resting pressure of the upper esophagus sphincter, normal pressure of the lower esophagus sphincter, and locally increased pressure in the middle and lower esophagus without normal peristalsis (Chicago classification II and III) (Figure 1).

History of past illness

The patient had been suffering from hypertension for several years.

Personal and family history

No family history was identified.

Physical examination

The Karnofsky Performance Status^[4] score remained above 90 throughout the treatment. Mild tenderness in the right chest was identified by palpation.

Laboratory examinations

Routine blood and biochemical examinations revealed no obvious abnormalities. The tumor biomarkers were generally normal or slightly elevated: Carcinoembryonic antigen = 5.42 ng/mL and neuron-specific enolase = 19.22 ng/mL. The serum albumin level changed from below 40 g/L pre-POEM to above 40 g/L post-POEM.





Figure 1 Esophageal high-resolution manometry report. A: Low resting pressure of the upper esophagus sphincter; B: Normal pressure of the lower esophagus sphincter; C: Locally increased pressure in the middle and lower esophagus without normal peristalsis (Chicago classification II and III).

Imaging examinations

After admission to our hospital, the patient received an esophagogram revealing grade I dilation of the esophageal lumen, segmental stenosis of the distal esophagus, and delayed emptying of barium contrast agent from the esophagus (Figure 2A). Endoscopy revealed a 2 cm long segment of concentric esophageal stenosis 35–37 cm away from the incisors, with apparently normal overlying mucosa (Figure 2B). The cardia had normal contraction and relaxation (Figure 2C). CT revealed a right upper lung mass (Figure 2D), abnormality of the right 9th and 10th ribs, enlargement of mediastinal lymph nodes, right pleural effusion, and thickening of the wall in the lower esophagus far from the lung space-occupying lesion.

FINAL DIAGNOSIS

The pretreatment diagnosis: (1) Right upper lung adenocarcinoma with multiple rib and mediastinal lymph node metastases and right malignant pleural effusion. The tumor was clinically staged as cT1bN0M1c, IVB; and (2) Distal esophageal segmental stenosis of unknown cause. The post-POEM diagnosis was confirmed as esophageal muscle metastasis arising from lung adenocarcinoma.

TREATMENT

After the first MDT discussion, an individualized POEM procedure (Video) was performed first to alleviate the patient's dysphagia before chemotherapy. On July 14, 2022, under general anesthesia, a submucosal injection was performed first at the level of the middle esophagus, 5 cm proximal to the level of stenosis, rather than 13 cm proximal to the gastroesophageal junction (GEJ), as usual. After the submucosal space was entered, a longitudinal tunnel was created until the level of the stenosis was reached. Because it was difficult to dissect the submucosal space at the stenotic segment due to the inability to identify the right posterior wall of the muscular layer (Figure 2E), we had to perform inner circular myotomy of the esophagus to expand the tunnel space, beginning 3 cm distal to the mucosal entry. The circular muscle was thickened. Then, muscle biopsies were taken. Subsequently, myotomy at the narrow segment was performed, extending 2 cm distal to the stenosis segment (Figure 2F). The length of the entire myotomy was approximately 6 cm (33-39 cm away from the incisors) (Figure 2G). After myotomy, the endoscope could be passed smoothly through the distal segment stenosis with minimal resistance. No perioperative adverse events occurred. Esophageal muscle biopsy pathology revealed poorly differentiated adenocarcinoma metastasis from lung adenocarcinoma, with immunohistochemical staining showing positive expression of CK, CK7, CK8/18, NapsinA, and TTF-1 (Figure 2H).

After treatment, the patient's Eckardt score^[5] changed from 9 before POEM to 3 after POEM. Repeated esophagography indicated that the segmental stenosis had vanished and that barium flowed smoothly into the stomach on postoperative days 18 and 54 (Figure 2I), 203 and 745, respectively. Additionally, the esophageal mucosal folds were not interrupted or destroyed even on postoperative day 745 (Figure 3). The patient could eat soft solid food and received multiple rounds of pembrolizumab-combination chemotherapy. Pembrolizumab plus pemetrexed[6] was selected as the chemotherapy regimen for 4 cycles, followed by metronomic oral vinorelbine^[7] for up to 14 cycles, resulting in a progression-free survival (PFS) of sixteen months. After the progression of pleural metastasis, docetaxel[8] was given as an intravenous infusion for 4 cycles.

OUTCOME AND FOLLOW-UP

The patient's progression-free survival was approximately 16 months. Long stable disease was obtained during the 24month follow-up. The patient has been monitored regularly in the outpatient department, and no dysphagia recurrence



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Figure 2 Diagnosis and treatment of the patient. A: Esophagogram revealed grade I dilation of the esophageal lumen, segmental stenosis of the distal esophagus, and delayed emptying of barium contrast agent from the esophagus; B: Endoscopy revealed a 2-cm long segment of concentric esophageal stenosis with apparently normal overlying mucosa; C: The cardia had normal contraction and relaxation; D: Computed tomography revealed a right upper lung mass; E: Unclear hierarchy of the esophageal wall at the narrow segment; F: Myotomy at the narrow segment; G: The length of the entire myotomy was approximately 6 cm; H: Esophageal muscle biopsy result; I: Repeated esophagography on postoperative day 54.

has been noted thus far.

DISCUSSION

To the best of our knowledge, this is the first and only case of lung adenocarcinoma with esophageal muscle metastases that presented with progressive dysphagia as the initial sign. Although poorly differentiated adenocarcinoma of the right upper lung was confirmed by pathology of the right pleural effusion, an accurate diagnosis of segmental concentric stenosis of the distal esophagus with intact mucosa and cardia could not be made via CT or endoscopy. To alleviate the patient's dysphagia, an individualized POEM[9] procedure was performed first formulated by the MDT team. During the process of establishing the esophageal submucosal tunnel, a muscle biopsy was taken from the right posterior wall of the muscular layer at the stenotic segment, revealing esophageal muscle metastasis from lung adenocarcinoma via pathology combined with immunohistochemical staining. The final diagnosis was adjusted accordingly. Metastatic esophageal tumors are relatively rare[10], and most metastatic esophageal tumors take the form of submucosal solid tumors in appearance under endoscopic ultrasound.

The POEM[11-14] procedure, as first described in 2008, is a submucosal tunneling endoscopy technique that allows access to the muscle layers throughout the gastrointestinal tract. By cutting pathological muscle fibers, POEM can be treated not only for motility disorders of unknown cause but also for structural pathologies, such as esophageal diverticula. Regardless of the location, there are four steps to the procedure: Mucosal incision, submucosal tunneling,



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Figure 3 Post-peroral endoscopic myotomy esophagography. A: Continuous mucosal folds on postoperative day (POD) 203; B: Continuous mucosal folds on POD 745

myotomy, and entry closure. It is flexible in terms of the tunnel entry position, the length and depth of the myotomy. In our case, dissection of the inner circular muscle began at the narrow segment of the esophagus, extending 2 cm distal to the stenosis segment. The GEJ remained unchanged due to normal contraction and relaxation of the cardia. Overall, the location of the mucosal incision and the length and depth of the myotomy differed from those of traditional POEM prescribed by Inoue *et al*[11]. No procedure-related complications occurred. Both the short-term and long-term outcomes of individualized POEM were excellent.

As reported, needle tract seeding following endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a rare but serious complication that may lead to poor prognosis[15]. To reduce the risk of tumor dissemination, EUS-FNA should be performed only when the results obtained via this procedure are useful for therapeutic decision-making. From a technical perspective, the procedure of our individualized POEM is more like an endoscopic unroofing technique for gastric gastrointestinal subepithelial tumors[16] rather than EUS-FNA. Although tumor translocation caused by endoscopic unroofing gastric muscle biopsy has not yet been reported, the risk of tumor dissemination to the mucosal incision must be estimated. Fortunately, all post-POEM esophagography examinations revealed continuous mucosal folds.

Obviously, for the palliative treatment of benign or malignant esophageal strictures, flexible self-expanding metal (SEMS)[17,18] can effectively provide rapid relief of dysphagia. However, despite the specific characteristics of recently developed stents, recurrent dysphagia due to food impaction, tumoral and granulation tissue overgrowth, or stent migration remains a major challenge. In our case, the smooth mucosa at the stenotic segment was more likely to lead to stent migration in a short period because of insufficient friction between the SEMS and the esophageal wall.

As reported previously [2,19], in patients with previously untreated metastatic non-squamous non-small cell lung cancer (NSCLC) without epidermal growth factor receptor or alkaline mutations, the addition of pembrolizumab to standard chemotherapy consisting of pemetrexed-platinum resulted in significantly longer overall survival and progression-free survival than did chemotherapy alone. Pembrolizumab plus pemetrexed-platinum improved ovarian stimulation cycles and PFS, regardless of programmed cell death ligand-1 expression. Moreover, the metronomic formulation and safety of vinorelbine^[7,20] reduces the length of hospitalization. In our case, pembrolizumab plus pemetrexed was selected as the first-line regimen, followed by pembrolizumab plus oral vinorelbine. Arrieta et al[21] described that the combination of pembrolizumab plus docetaxel was well tolerated and improved the objective response rate and PFS in patients with previously treated advanced NSCLC. Our patient received intravenous docetaxel to control tumor progression.

CONCLUSION

Here, we are the only one to report an individualized POEM procedure for treating distal esophageal segmental spasm



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induced by muscular metastasis arising from lung adenocarcinoma, and this new technique can effectively improve a patient's nutritional status before subsequent chemotherapy combined with immune checkpoint inhibitors.

FOOTNOTES

Author contributions: Shi H, Chen SY and Xie ZF were responsible for the study concept and design, including endoscopic procedures; Chen SY drafted the manuscript; Chen SY and Shi H revised and finalized the manuscript; all authors conducted the endoscopic operations together, read and approved the final manuscript.

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