

## Single Case

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# Very Delayed Perforation after Esophageal Endoscopic Submucosal Dissection and Intralesional Triamcinolone Injection

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## Keywords

Esophagus · Endoscopic submucosal dissection · Triamcinolone · Ulcer

## Abstract

We report a case of delayed perforation following esophageal endoscopic submucosal dissection (ESD). A patient with Parkinson's disease presented with two superficial carcinomatous lesions in the middle third of the esophagus. ESD was performed, and 4/5 of the esophageal circumference was resected, including the adjacent lesion area. Immediately post-ESD, triamcinolone acetonide was injected into the submucosa underlying the ulcer to prevent scarring and stenosis. Histopathological examination of the resected specimen revealed squamous cell carcinoma limited to the lamina propria with negative margins. Seventeen days post-ESD, the patient experienced sudden-onset chest pain during a meal. Computed tomography showed pneumomediastinum, which indicated a delayed perforation. We immediately performed subtotal esophagectomy. A sharply torn longitudinal perforation was present in the post-ESD ulcer. Delayed perforation after esophageal ESD is extremely rare. In this case, the perforation might have been caused by food impaction and delayed ulcer healing due to triamcinolone injection.

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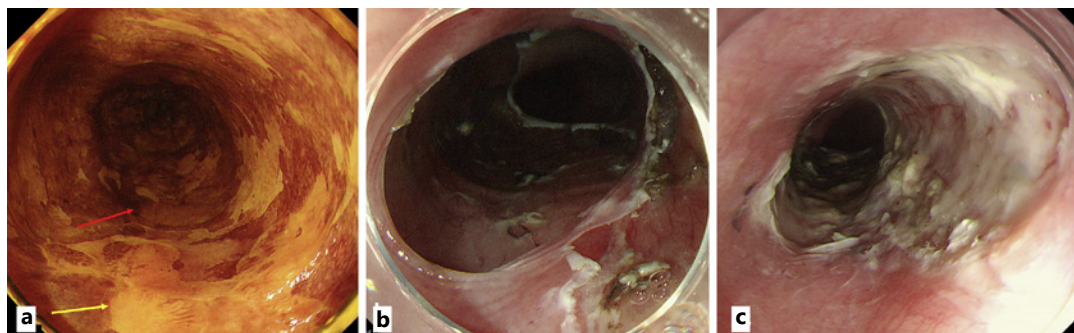
## Introduction

Endoscopic resection has gained widespread popularity as a minimally invasive treatment for superficial esophageal neoplasms. Esophageal endoscopic submucosal dissection (ESD) has the advantage of a higher complete resection rate than esophageal endoscopic mucosal resection [1]. However, complications following esophageal ESD, including bleeding, perforation, and stenosis, can occur and remain problematic. Perforation, in particular, can cause pneumomediastinum and is potentially fatal, thus necessitating surgical treatment.

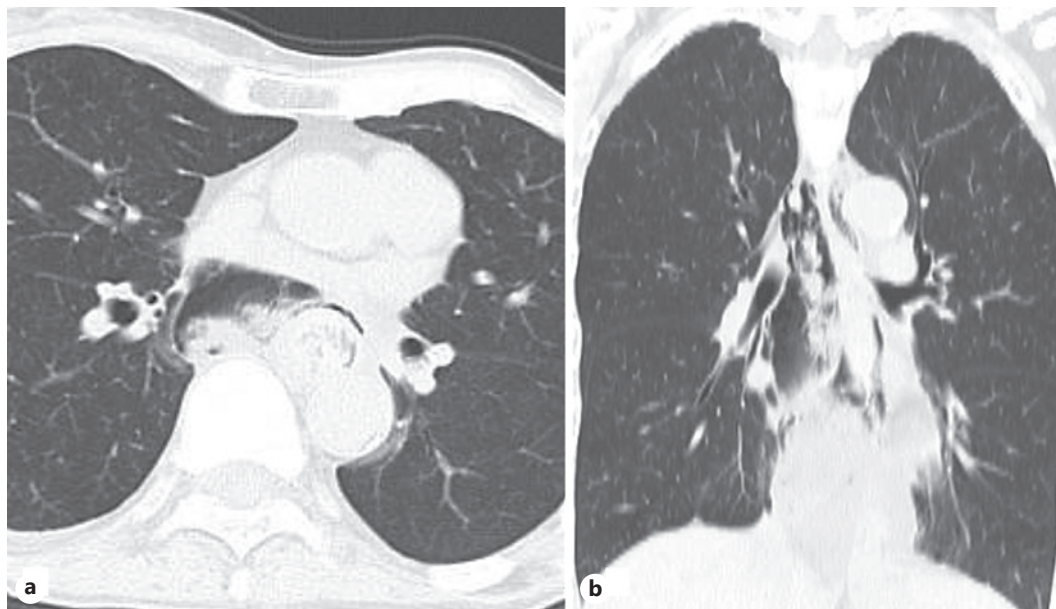
Subcircumferential resection by esophageal ESD can cause strictures and impair quality of life with dysphagia [2, 3]. Various methods have been reported to prevent strictures [4]. Among them, local steroid injection is widely accepted as the standard method for noncircumferential resection because of its simplicity and favorable associated outcomes [5]. However, the possibility of delayed perforation following inadequate steroid injection requires sufficient attention [6, 7]. Herein, we present a case with delayed perforation following esophageal ESD due to triamcinolone injection and food bolus impaction at the location of the ESD-induced ulcer.

## Case Report

A 64-year-old woman with Parkinson's disease presented with two superficial esophageal cancers in the middle thoracic esophagus. One of the lesions was morphologically 0-IIc, 20 mm in size, located 26 cm from the incisor. The other was morphologically 0-IIb, 10 mm in size, located 29 cm from the incisor (Fig. 1a). The biopsy specimens from each lesion histopathologically revealed squamous cell carcinoma, and the preoperative diagnosis was intramucosal cancer. Thus, we performed ESD for both lesions. The following devices were used: a conventional single-channel endoscope (GIF- H290T; Olympus Medical Systems Corporation, Tokyo, Japan) with a transparent hood (Elastic Touch, slit and hole type, M [long]; Top Co., Tokyo Japan); an electrosurgical generator (VIO®3; ERBE Elektromedizin, Tübingen, Germany); a short needle-type endoknife, equipped with a water-jet function (FlushKnife 1.5 mm, DK2618JB-15, Fujifilm Medical, Tokyo, Japan); and carbon dioxide for the inflation system. After the adjacent lesions were resected, respectively, in one piece, an artificial ulcer spanning four-fifths of the esophageal circumference was



**Fig. 1.** Endoscopic images of superficial esophageal cancers and mucosal defects by endoscopic submucosal dissection (ESD). **a** Two adjacent superficial esophageal cancers (yellow and red arrows) in the middle thoracic esophagus shown as iodine-unstained lesions on chromoendoscopy. Adjacent mucosal defects spanned nearly the entire circumference of the esophagus, without muscle damage and perforation, immediately after ESD (**b**) and the day after ESD (**c**).



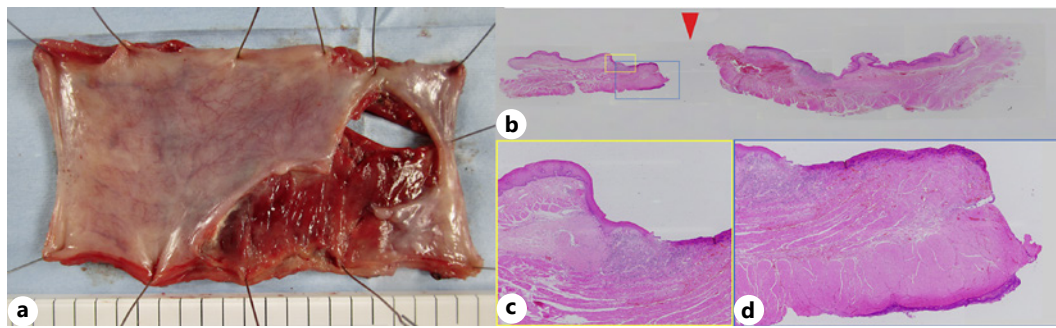
**Fig. 2.** Computed tomography (CT) images. CT showed food residue in the mediastinum and mediastinal emphysema in axial (**a**) and coronal (**b**) sections.

created without any complications or damage to the muscularis propria (Fig. 1b). Immediately after ESD, triamcinolone acetonide (120 mg) was locally injected using a 25-gauge needle into the submucosa underlying the ulcer to prevent scarring and stenosis. Histopathological examination of the resected specimen revealed squamous cell carcinoma limited to the epithelium with negative margins and without lymphovascular invasion, indicating a curative resection.

The patient did not receive proton-pump inhibitor therapy during the follow-up period. Upper endoscopy performed the next day revealed no perforation at the residual ulcer (Fig. 1c). The patient started eating 2 days after ESD and was discharged 1 week later after a good clinical course. However, the patient experienced sudden-onset chest pain during a meal on day 17 after ESD, while hospitalized for the treatment of Parkinson's disease. Computed tomography showed pneumomediastinum, indicating a delayed perforation (Fig. 2). Severe mediastinitis was suspected; therefore, emergency surgery was performed (esophagostomy and enterostomy following subtotal esophagectomy). A bolus of food in the mediastinal space was identified during surgery. A large longitudinal perforation, 17 mm in size, was present at the site of the upper ulcer where ESD was performed (Fig. 3). The perforation was not contused but sharply torn, without histological necrotic tissue in the muscular layer below the artificial ulcer. Early surgical treatment prevented worsening mediastinitis and resulted in the successful management of delayed perforation after esophageal ESD. The patient was discharged under enteral nutrition on day 14 after perforation, and she underwent a gastric tube reconstruction 1 month later.

### Discussion/Conclusion

Perforation during the procedure is a major complication of esophageal ESD, with an incidence of approximately 1.5–5% [8]. Very few cases of delayed perforation following esophageal ESD have been reported, unlike the intraprocedural perforation [9–11]. Generally,



**Fig. 3.** Macroscopic and microscopic findings of resected specimen by subtotal esophagectomy. **a** A large, 17-mm longitudinal perforation was identified at the site of the upper artificial ulcer after the resection of the surgical specimen. **b** Histopathological image of the perforation site (red arrow) stained with hematoxylin and eosin. High-power views (magnification,  $\times 20$ ) of the areas in the yellow box (**c**) and the blue box (**d**) showed no necrotic tissue or neutrophilic infiltration in the ulcer area.

delayed perforation occurs within a few hours or days after ESD [12, 13]. During our extensive literature search, we found only four cases of delayed perforation after esophageal ESD (excluding perforations caused by endoscopic procedures such as balloon dilation after ESD). The clinical characteristics of previously reported cases are summarized in Table 1 [9–11]. In all of the cases, the mucosal defect was more than half of the total circumference, and in one case, local steroid injection was performed.

Local triamcinolone injection is one of the common methods to prevent strictures after esophageal ESD. In the present case, the mucosal defect had remained mostly unchanged from the time of triamcinolone injection until the perforation occurred. Injection of triamcinolone acetonide is not harmful if injected only into the submucosal layer. However, the inadvertent injection of triamcinolone acetonide into the muscularis propria may be a cause of perforation. Triamcinolone acetonide is a corticosteroid known not only to have sustained anti-inflammatory effects but also to cause tissue vulnerability. An experimental animal study using live pigs showed that injection of triamcinolone acetonide into the muscularis propria can cause deep mural damage [7]. In our case, histological analysis of the surgical specimen did not reveal necrotic tissue in the muscularis propria, suggesting that triamcinolone was injected correctly.

Considering that the patient complained of difficulty swallowing, the perforation might have been caused by the obstruction of food passage in the esophagus. A case of esophageal perforation due to food bolus impaction occurring after esophageal ESD has previously been reported [11]. Several reports have also demonstrated that circumferential ESD may cause impairment of esophageal motility, especially subsequent to triamcinolone injection [14, 15]. Esophageal motility and dysphagia after ESD were investigated using high-resolution manometry in these studies. In patients with circumferential ESD, the distal contractile integral was decreased, and the frequency of failed or weak contractions increased. In our case, delayed perforation could have been caused by the combined effect of fragility at the ulcer remnant and the pressure of food impaction due to impaired esophageal motility. The gastrointestinal dysfunction of Parkinson's disease might also have been associated.

In cases of esophageal ESD, surgery is considered for treatment of delayed perforation [8]. Alternatively, self-expandable metallic stents may help patients with delayed perforations after esophageal ESD [10]. In our case, however, there was a concern that stent placement

**Table 1.** Clinicopathological features for delayed perforation treated by esophageal endoscopic submucosal dissection

First author	Age, years	Sex	Tumor size, mm	Tumor location	Degree of mucosal defect	Histological type	Depth of tumor invasion	Steroid use	ESD to perforation, days	Treatment	Perforation to discharge, days	Outcome
Omae 2018 [10]	71	Male	-	Lt and Mt	4/5	HGD in BE	-	None	1	Conservative therapy (temporary stent placement)	13	Alive
Matsuda 2015 [9]	83	Male	45	Mt	3/4	SCC	LPM	Local steroid injection	10	Subtotal esophagectomy	88	Alive
Matsuda 2015 [9]	75	Male	4	Mt	1/2	SCC	EP (incomplete ESD due to fibrosis)	None	6	Subtotal esophagectomy	47	Alive
Sato 2014 [11]	61	Male	11	Mt	-	SCC	EP	Oral steroid	-	Conservative therapy (ventilation and pleural drain insertion)	90	Alive
Our study	64	Female	15	Mt	4/5	SCC	EP	Local steroid injection	17	Subtotal esophagectomy	14	Alive
			12	Mt	(adjacent lesions)	SCC	EP					

BE, Barrett's esophagus; EP, epithelium; ESD, endoscopic submucosal dissection; HGD, high-grade dysplasia; LPM, lamina propria; Lt, lower thoracic esophagus; Mt, middle thoracic esophagus; SCC, squamous cell carcinoma.

would leave food residues in the mediastinum. The effectiveness of an endoluminal vacuum therapy has also been reported, although this product is not available in Japan [16]. Thus, the decision was made to operate immediately after consultation with the surgeon. As the histopathological results of ESD specimens had already shown a curative resection, only a subtotal esophagectomy without lymph node dissection was performed. Early surgery helped to avoid mortality and long-term recumbency and maintained the patient's physical functions.

In conclusion, the impairment of esophageal motility and prolonged ulcer healing may have caused delayed perforation after ESD. These cases must be followed up carefully, and prompt surgical treatment must be provided when delayed perforation after esophageal ESD can lead to severe consequences.

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### Statement of Ethics

Ethics approval is not required in accordance with our national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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### Author Contributions

Conceptualization: Taro Iwatsubo, Toshihisa Takeuchi, Shinpei Kawaguchi, Kazuhiro Ota, Yuichi Kojima, and Kazuhide Higuchi. Data curation: Taro Iwatsubo, Sang-Woong Lee, Shinpei Kawaguchi, Kazuhiro Ota, and Yuichi Kojima. Supervision: Taro Iwatsubo and Toshihisa Takeuchi. Writing – original draft and Writing – review and editing: Taro Iwatsubo.

### Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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