

[CASE REPORT]

Intraperitoneal Abscess as a Postoperative Complication of Gastric Endoscopic Submucosal Dissection

Kazuya Miyaguchi^{1,2}, Tomoaki Tashima¹, Kei Sugimoto¹, Rie Terada¹, Yumi Mashimo¹,
Hiroyuki Imaeda² and Shomei Ryozaawa¹

Abstract:

We herein report a case of intraperitoneal abscess as a postoperative complication of gastric endoscopic submucosal dissection (ESD). A 70-year-old man who underwent ESD for early gastric cancer sought consultation for abdominal pain on postoperative day 28. Abdominal computed tomography revealed intraperitoneal abscess rupture. He underwent image-guided laparoscopic irrigation. His postoperative course was favorable, and he was discharged after 27 days. Intraoperatively, a white plaque adhering to the gastric wall was surrounded by a large pus volume and suspected to be ESD-associated. We present this case with a literature review of the association between intraperitoneal abscess and ESD.

Key words: blood transfusion, early detection of cancer, endoscopic submucosal dissection, gastric cancer, hypertension, intraperitoneal abscess

(Intern Med 60: 2777-2781, 2021)

(DOI: 10.2169/internalmedicine.6936-20)

Introduction

In Japan, endoscopic submucosal dissection (ESD) is a widely established standard treatment of gastrointestinal cancers. ESD has been demonstrated to be safe with favorable short-term results, even in elderly patients and those with underlying conditions (1, 2). Typical complications of gastric ESD are bleeding and perforation. A multicenter prospective study of approximately 10,000 patients reported postoperative bleeding in 4.4% of patients, blood transfusion in 0.7%, intraoperative perforation in 2.3%, delayed perforation in 0.4%, and emergency surgery due to complications in 0.2% (3). Other reported complications that are rare but necessitate caution are stenosis, pneumonitis, and air embolism (4-8). ESD for gastric cancer should always be performed considering risks of complications.

Delayed perforation and associated abscess formation are rare postoperative complications of ESD (9-11). Most cases of delayed perforation occur within several days after ESD. In particular, 1 study reported a median time to the onset after ESD of 11 hours (12). Delayed perforation might be

caused by thermal degeneration due to excessive current applied during dissection.

In the present case, both the intraoperative findings and follow-up endoscopy performed 28 days after ESD revealed an intraperitoneal abscess despite the absence of perforation at the mucosal defect. This is the first report of such a case in Japan. We describe the clinical course of this case and discuss the causes of abscess formation.

Case Report

The patient was a 70-year-old man undergoing treatment for poorly managed type 2 diabetes mellitus (DM). His glycated hemoglobin (HbA1c) level was 10.0%, and he was hypertensive. He had been treated for DM for 10 years and had neuropathy with no evidence of nephropathy. His medications included metformin (2,250 mg/day), voglibose (0.2 mg/day), and vildagliptin (100 mg/day). He had no history of smoking or drinking. The patient underwent screening esophagogastroduodenoscopy at a family clinic that revealed a 30-mm type 0-IIc early gastric cancer in the upper posterior wall (Fig. 1a). He underwent ESD under intravenous

¹Department of Gastroenterology, Saitama Medical University International Medical Center, Japan and ²Department of Gastroenterology, Saitama Medical University, Japan

Received: December 15, 2020; Accepted: February 1, 2021; Advance Publication by J-STAGE: March 22, 2021

Correspondence to Dr. Tomoaki Tashima, t.tashima1981@gmail.com

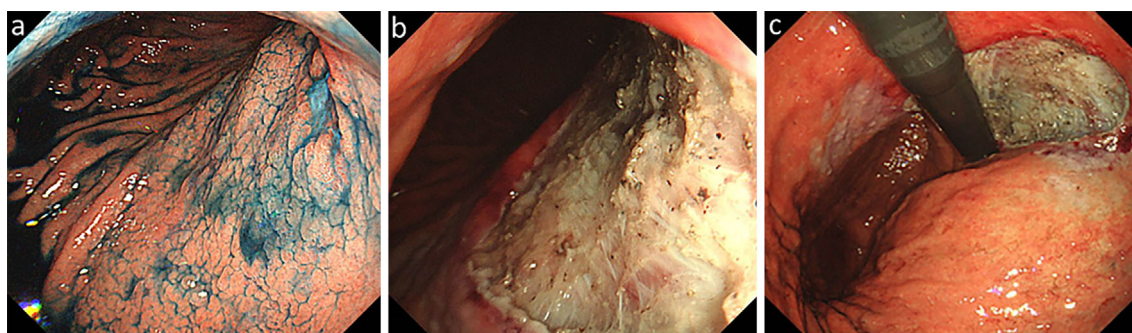


Figure 1. Images of the gastric lesion. (a) A 30-mm type 0-IIc early-stage gastric cancer is detected in the upper posterior wall of the stomach. (b) A mucosal defect after endoscopic submucosal dissection (day 1). (c) Retroflexed view of the mucosal defect (day 1).

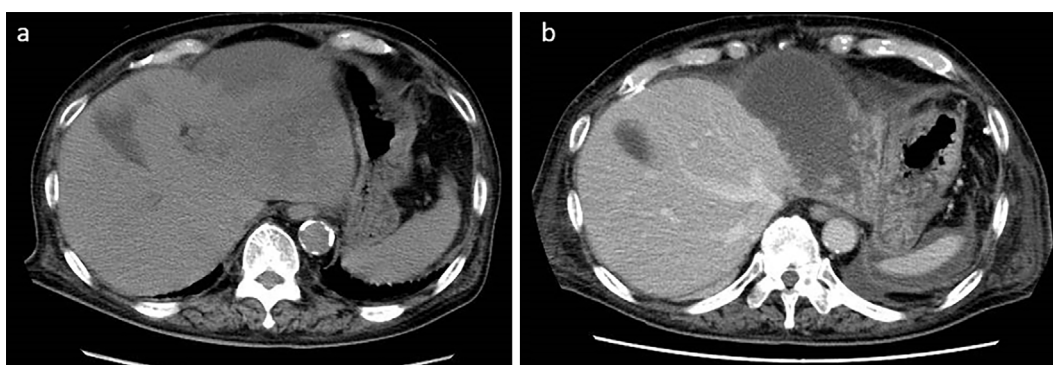


Figure 2. Abdominal computed tomography (CT) images. (a) Intraperitoneal abscess on the day of hospitalization (non-contrast-enhanced CT axial image). (b) Ruptured intraperitoneal abscess at 2 days after hospitalization (contrast-enhanced CT axial image)

anesthesia in an endoscopy room. The ESD procedure was performed using a therapeutic endoscope (GIF-Q260J; Olympus Medical Systems, Tokyo, Japan) with a transparent attachment cap (D-201-11804; Olympus Medical Systems) and high-frequency generator (VIO300D; EndoCut I, effect 2, duration 4, interval 1; Erbe Elektromedizin, Tübingen, Germany) with carbon dioxide insufflation. Subsequently, after local injection of sodium hyaluronate solution, an initial mucosal incision and submucosal dissection were performed using a 2.0-mm DualKnife J (KD655-L; Olympus Medical Systems). Hemostasis for procedural bleeding was attempted using hemostatic forceps (FD-410LR; Olympus Medical Systems) in the soft coagulation mode (effect 4, 70 W).

The procedure took only 30 minutes, and no perforation was observed (Fig. 1b, c). The lesion was fully resected. The final histopathological findings revealed that the lesion was a well-differentiated intramucosal cancer with no lymphovascular invasion and had negative margins (tumor diameter, 28×19 mm). Second-look endoscopy showed no perforation or bleeding, and blood tests and radiography showed no new changes. The patient experienced no symptoms, such as a fever or abdominal pain. He was administered a proton pump inhibitor (omeprazole, 20 mg/day) for 4 weeks starting on the day of the ESD procedure and dis-

charged home on day 5 after ESD.

The patient presented to our hospital in the morning of day 28 after ESD with gradually developing upper abdominal pain and a fever (38.5°C). Blood tests at admission revealed an increased inflammatory response and hepatic dysfunction (white blood cells, 18,000/μL; aspartate aminotransferase, 75 U/L; alanine aminotransferase, 80 U/L; alkaline phosphatase, 483 U/L; lactic acid dehydrogenase, 228 U/L; and C-reactive protein, 28.0 mg/dL). His renal function was normal (creatinine, 0.54 mg/dL; estimated glomerular filtration rate, 69.8 mL/min/1.73 m²). Abdominal computed tomography (CT) showed fluid retention with a capsule-like covering and an abscess directly beneath the left hepatic lobe. However, no gastric wall thickening or free air was observed (Fig. 2a). After blood culture results were found to be negative, the patient was administered antibiotics with meropenem 3.0 g/day.

However, on day 3 (day 31 after ESD), the patient developed signs of peritoneal irritation requiring abdominal CT be performed again, which revealed intraperitoneal rupture of the abscess (Fig. 2b). On the same day, we performed laparoscopic irrigation and inserted a drain. An abscess was observed beneath the left hepatic lobe (Fig. 3a), and a white plaque was found adhering to a wide area on the gastric wall in the laparoscopic view (Fig. 3b). The abscess was

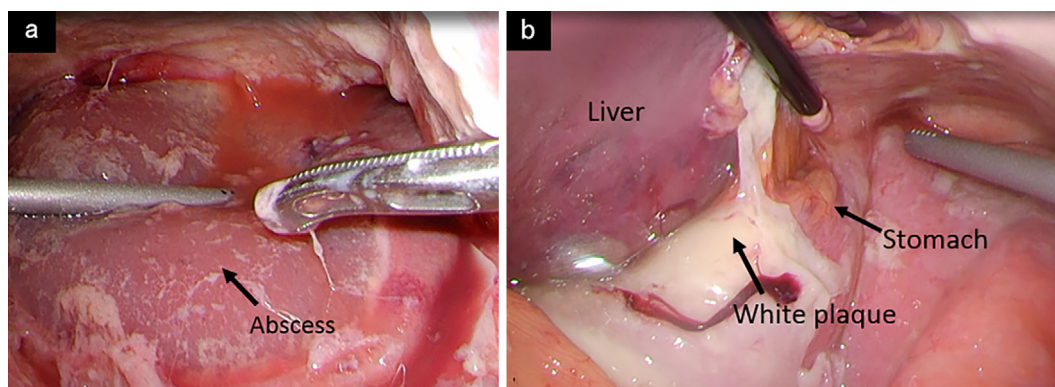


Figure 3. Laparoscopy images. (a) The abscess is surrounded by a large volume of pus beneath the hepatic left lobe. (b) A white plaque adheres to the gastric wall.

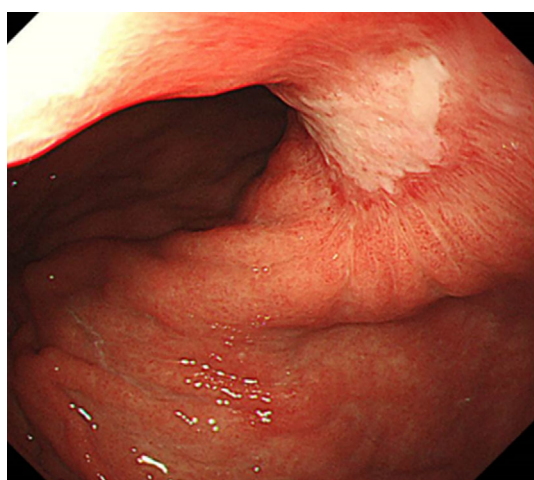


Figure 4. The mucosal defect after endoscopic submucosal dissection without perforation (day 28).

scraped, the abdominal cavity was washed, and drainage was completed. *Klebsiella pneumoniae* was found in the abscess specimens. After laparoscopic surgery, upper gastrointestinal endoscopy was performed to visualize the ESD site. A mucosal defect of the ESD showed inadequate ulcer healing (Fig. 4). It was not necessary to perform endoscopic treatment at this stage of the ulcer because there was no perforation site at the ulcer. We had prescribed proton pump inhibitors to the patient for four weeks. Based on these findings, we suspected that the abscess was a post-ESD complication. The patient subsequently demonstrated a favorable course and was discharged home 27 days after admission.

Discussion

Abscess formation caused by a post-ESD mucosal defect with no perforation has been inadequately described, this is a report of a very rare case. Based on the laparoscopic findings (presence of white plaque on the upper posterior gastric wall accompanied by a large amount of pus surrounding the abscess), we believe that the abscess formation resulted from the ESD procedure.

Previous case reports of intraperitoneal abscess formation revealed the presence of a perforation based on imaging studies, such as abdominal CT (9-11). In such cases, we should consider phlegmonous gastritis as a differential diagnosis. Early diagnosis of phlegmonous gastritis is difficult due to the nonspecific nature of its clinical manifestations, including acute abdominal disease, sudden onset of abdominal pain, high fever, nausea, and vomiting. However, in this case, there were no such findings.

One possible reason for the extremely late formation of the intraperitoneal abscess (28 days after ESD) is that the repair of the mucosal defect was slowed due to poor DM control. DM is known to delay wound healing. The multivariate analysis in one study revealed that DM (odds ratio: 1.743; 95% confidence interval: 1.017-2.989, $p=0.043$) was a risk factor for delayed ulcer healing. Furthermore, iatrogenic ulcers caused by ESD in patients with DM tend to take over three months to heal. Other risk factors for delayed ulcer healing may include coagulation abnormality, a specimen size greater than 4 cm, and electrocoagulation (13). Similarly, nephropathy might cause delayed wound healing. Therefore, causes are reportedly multifactorial, including poor nutrition, inadequate peripheral blood flow, and decreased immunity (14). However, no previous report has described delayed wound healing of a mucosal defect after ESD due to nephropathy.

In this case, the ulcer was obviously not caused by perforation. There may thus have been a pre-existing minor perforation that was not detected by endoscopy or CT, and inflammation spread slowly. As the patient had diabetic neuropathy, he was less likely to feel any pain than he otherwise might have been. Therefore, when exactly the abscess was formed was unclear. This is an extremely rare case of abscess formation without any perforation. Barring the absence of perforation, if we examine reasons for abscess formation in this case, two factors may have contributed to the formation of the intraperitoneal abscess. The first was the ESD technique. Generally, the mechanism underlying delayed perforation supposedly involves repeated coagulation causing ischemic changes in the gastric wall and leading to ne-

crisis (15). In this case, ESD was performed in the upper posterior wall, where the gastric wall was relatively thin. Therefore, we took care to avoid cutting the submucosal layer and injecting the needle into the submucosal layer. Transportal and direct inflammatory spillovers from adjacent organs such as the gallbladder are possible routes of infection in liver abscesses (16). However, in this case, infection via the portal vein could be excluded because the abscess was located outside the liver and adhered to the ESD-treated gastric wall, with no findings of cholecystitis. Therefore, the route of transmission was probably direct invasion (infiltration). This is consistent with the surgical findings. The gastric wall is relatively thin, and the upper part is more prone to perforation than the lower part (17). In our case, the mucosal defect was in the upper part of the gastric body (upper-third of the stomach). A previous study reported that perforation more commonly occurred in the upper-third than in the lower two-thirds of the stomach (15), implying that thinner muscular layers are more susceptible to perforation than thicker ones. Assuming that the ESD procedure contributed to abscess formation, apart from repeated excessive coagulation, injection into the submucosal layer might be a more likely cause, as penetration into the muscular layer of the gastric wall might have led to an extremely small perforation. Puncturing the muscular layer during local injection should be avoided by ensuring that the needle reaches only the submucosal layer.

The second contributory factor might have been that patients who have DM are usually administered proton pump inhibitors after ESD. Despite the administration of multiple hypoglycemic drugs, the patient's condition was poorly controlled, and his HbA1c level was 10.0%, which made him susceptible to infection. The causative bacterium was *Klebsiella*, an enteric bacterium that is not part of the normal intraoral flora. Therefore, the bacteria probably migrated because of the breakdown of the gastric mucosal barrier after growing in the acidic conditions of the lower stomach. The gastric mucosal barrier acts as a physical barrier and plays an active role in host defense by secreting a mucin layer and bactericidal peptides and can be compromised by various factors. The secretion of gastric mucin decreases with age, and in patients with DM, the gastric mucosal barrier can be broken down by oxidative stress-induced damage to the mucosa (18, 19). To our knowledge, there have been no reports of intra-abdominal abscesses caused by non-perforated gastric ulcers. The patient's blood glucose levels should have been controlled prior to ESD, which might have resulted in a better outcome. It is important to ascertain the status of underlying diseases in advance and ensure that they are well controlled. In patients with DM, blood glucose should be controlled prior to the performance of ESD.

Asayama et al. (20) reported a case of gastric wall abscess in which endoscopic ultrasound (EUS)-guided drainage was safely performed because the stomach and the abscess were contiguous. We also considered performing EUS-guided transgastric drainage. However, our case was more

challenging because there was a risk of leakage of the intra-abdominal abscess after it was punctured. The abscess was also technically difficult to handle because the puncture lines between the stomach and the abscess passed through the liver. Therefore, we performed laparoscopic irrigation and inserted a drain. In this case, EUS-guided transgastric drainage was challenging.

According to the Japan Gastroenterological Endoscopy Society guidelines, it is not recommended to use prophylactic antibiotics for gastric ESD (21). In patients with DM or cancer and the elderly, immunocompetence should be determined before performing ESD. The administration of prophylactic antibiotics as a measure against abscess formation should be considered in special and high-risk cases.

In conclusion, we encountered a case of intraperitoneal abscess that developed as a postoperative complication of gastric ESD. The postoperative status should be carefully monitored when ESD is performed in patients with underlying conditions.

The authors state that they have no Conflict of Interest (COI).

References

1. Kakushima N, Fujishiro M, Kodashima S, et al. Technical feasibility of endoscopic submucosal dissection for gastric neoplasms in the elderly Japanese Population. *J Gastroenterol Hepatol* **22**: 311-314, 2007.
2. Tokioka S, Umegaki E, Murano M, et al. Utility and problems of endoscopic submucosal dissection for early gastric cancer in elderly patients. *J Gastroenterol Hepatol* **27**: 63-69, 2012.
3. Suzuki H, Takizawa K, Hirasawa T, et al. Short-term outcomes of multicenter prospective cohort study of gastric endoscopic resection: 'Real-world evidence' in Japan. *Dig Endosc* **31**: 30-39, 2019.
4. Tsunada S, Ogata S, Mannen K, et al. Case series of endoscopic balloon dilation to treat a stricture caused by circumferential resection of the gastric antrum by endoscopic submucosal dissection. *Gastrointest Endosc* **67**: 979-983, 2008.
5. Coda S, Oda I, Gotoda T, Yokoi C, Kikuchi T, Ono H. Risk factors for cardiac and pyloric stenosis after endoscopic submucosal dissection, and efficacy of endoscopic balloon dilation treatment. *Endoscopy* **41**: 421-426, 2009.
6. Isomoto H, Ohnita K, Yamaguchi N, et al. Clinical outcomes of endoscopic submucosal dissection in elderly patients with early gastric cancer. *Eur J Gastroenterol Hepatol* **22**: 311-317, 2010.
7. Iizuka H, Kakizaki S, Sohara N, et al. Stricture after endoscopic submucosal dissection for early gastric cancers and adenomas. *Dig Endosc* **22**: 282-288, 2010.
8. Akasaka T, Nishida T, Tsutsui S, et al. Short-term outcomes of endoscopic submucosal dissection (ESD) for early gastric neoplasm: multicenter survey by Osaka University ESD Study Group. *Dig Endosc* **23**: 73-77, 2011.
9. Venkatesh KR, Halpern A, Railey LB. Penetrating gastric ulcer presenting as a subcapsular liver abscess. *Am Surg* **73**: 82-84, 2007.
10. Jung JY, Kim JS, Kim BW, et al. Perigastric abscess as a complication of endoscopic submucosal dissection for early gastric cancer: first case report. *Korean J Gastroenterol* **67**: 142-145, 2016.
11. Dohi O, Dohi M, Inoue K, Gen Y, Jo M, Tokita K. Endoscopic transgastric drainage of a gastric wall abscess after endoscopic submucosal dissection. *World J Gastroenterol* **20**: 1119-1122, 2014.
12. Suzuki H, Oda I, Sekiguchi M, et al. Management and associated

- factors of delayed perforation after gastric endoscopic submucosal dissection. *World J Gastroenterol* **21**: 12635-12643, 2015.
13. Lim JH, Kim SG, Choi J, Im JP, Kim JS, Jung HC. Risk factors of delayed ulcer healing after gastric endoscopic submucosal dissection. *Surg Endosc* **29**: 3666-3673, 2015.
 14. Cheung AH, Wong LM. Surgical infections in patients with chronic renal failure. *Infect Dis Clin North Am* **15**: 775-796, 2001.
 15. Hanaoka N, Uedo N, Ishihara R, et al. Clinical features and outcomes of delayed perforation after endoscopic submucosal dissection for early gastric cancer. *Endoscopy* **42**: 1112-1115, 2010.
 16. Reid-Lombardo KM, Khan S, Sclabas G. Hepatic cysts and liver abscess. *Surg Clin North Am* **90**: 679-697, 2010.
 17. Oda I, Gotoda T, Hamanaka H, Eguchi T. Endoscopic submucosal dissection for early gastric cancer: technical feasibility, operation time and complications from a large consecutive series. *Dig Endosc* **17**: 54-58, 2005.
 18. Suzuki H, Nishizawa T, Tsugawa H, Mogami S, Hibi T. Roles of oxidative stress in stomach disorder. *J Clin Biochem Nutr* **50**: 35-39, 2012.
 19. Kemmerly T, Kaunitz JD. Gastroduodenal mucosal defense. *Curr Opin Gastroenterol* **30**: 583-588, 2014.
 20. Asayama N, Nagata S, Yukutake M, et al. A rare case of delayed perigastric abscess after curative resection of early gastric cancer by uncomplicated endoscopic submucosal dissection: successful treatment with endoscopic ultrasound-guided drainage. *Intern Med* **60**: 1383-1387, 2021.
 21. Ono H, Yao K, Fujishiro M, Oda I. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc* **28**: 3-15, 2016.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).