

Perforation of small intestine secondary to metastatic lung adenocarcinoma

A case report

Jian Wang, MS^a, Yimeng Chen, BS^c, Sisi Zhang, MS^{b,*}, Qingyong Chen, MD^{b,*}

Abstract

Rationale: About 50% of patients with a diagnosis of nonsmall cell lung carcinoma exhibit metastatic disease at the time of diagnosis. The preferential sites of extrapulmonary spread are the lymph nodes, liver, brain, adrenal glands, and bones; gastrointestinal tract perforation secondary to metastatic lung cancer is extremely rare.

Patient concerns: A 60-year-old male nonsmoker patient presented with a 20-day history of facial, neck, and right upper limb edema. Physical examination revealed a 3.5 cm mass in his right chest. Computed tomography (CT) revealed a 4 cm mass near the right lung hilum.

Diagnosis: Biopsy of the right chest wall mass revealed low differentiated lung adenocarcinoma. Additionally, retroperitoneal lymphadenopathy, pericardial effusion, metastases in the mediastinum, bilateral adrenal gland, and right thoracic wall nodule, as well as multiple bone metastases were also found.

Interventions: Since the patient was diagnosed with multiple metastatic lung cancer, chemotherapy was started. One week after chemotherapy, he experienced a sudden acute abdominal pain. Abdominal CT examination indicated the possibility of intestinal perforation. Hence, the patient underwent an emergency operation. During the surgical procedure, 2 perforations of size 1 × 1 cm² were discovered at 110 cm and 140 cm of the jejunum from Treitz's ligament. Then, an intestinal resection and end-to-end anastomosis were performed. The pathological diagnosis of the resected specimen revealed that it was a metastatic lung adenocarcinoma of small intestine.

Outcomes: The patient died 10 days after operation and 19 days following the cancer diagnosis due to septic shock.

Lessons: Gastrointestinal tract metastasis from the lung is uncommon, but the survival rate is extremely low; therefore, it should be considered as a possibility in patients who present with any of the gastrointestinal symptoms.

Abbreviation: CT = computed tomography.

Keywords: chemotherapy, metastatic lung adenocarcinoma, perforation, small intestine cancers

1. Introduction

About 50% of patients with a diagnosis of nonsmall cell lung carcinoma exhibit metastasis at the time of diagnosis. The preferential sites of extra pulmonary spread are the lymph nodes,

liver, brain, adrenal glands, and bones.^[1] Gastrointestinal metastases are really rare.^[2] We report a case of patient who presented with acute abdomen due to small bowel perforation from lung cancer metastasis, a very rare complication in the natural history of this cancer.

Editor: N/A.

The authors have no conflicts of interest to disclose.

^a Department of The Third General Surgery, People's Hospital of Xiangzhou, Xiangyang City, ^b Department of Emergency Surgery, Union Hospital, ^c Grade 2015, 8 Years of Clinical Medicine, Tongji Medical College, Huazhong University of Science and Technology, Wuhan City, China.

* Correspondence: Qingyong Chen, Department of Emergency Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Wuhan 430022, China (e-mail: chenqy68@163.com), Sisi Zhang, Department of Emergency Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Wuhan 430022, China (e-mail: lxzsl@163.com).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2018) 97:49(e13469)

Received: 26 September 2018 / Accepted: 5 November 2018

http://dx.doi.org/10.1097/MD.00000000000013469

2. Case presentation

A 60-year-old male nonsmoker patient presented with a 20-day history of facial, neck, right upper limb edema. Physical examination revealed a 3.5 cm mass on his right chest. Computed tomography (CT) revealed a 4 cm mass near the right lung hilum. Besides, retroperitoneal lymphadenopathy, pericardial effusion, metastases in the mediastinum, bilateral adrenal gland, and right thoracic wall nodule, as well as multiple bone metastases were also found (Fig. 1). The fecal examination for occult blood had strongly positive results, while no obvious tumor or perforation was found in the abdominal CT examination. Biopsy of the right thoracic wall nodule metastases showed low differentiated lung adenocarcinoma (Fig. 2). Therefore, the patient was treated with pemetrexed and nedaplatin for chemotherapy. One week later, he experienced a sudden acute abdominal pain, which was considered to be acute peritonitis. Abdominal CT scan revealed free air and massive ascites in the peritoneal cavity (Fig. 3). Although the site of perforation was not identified, he was

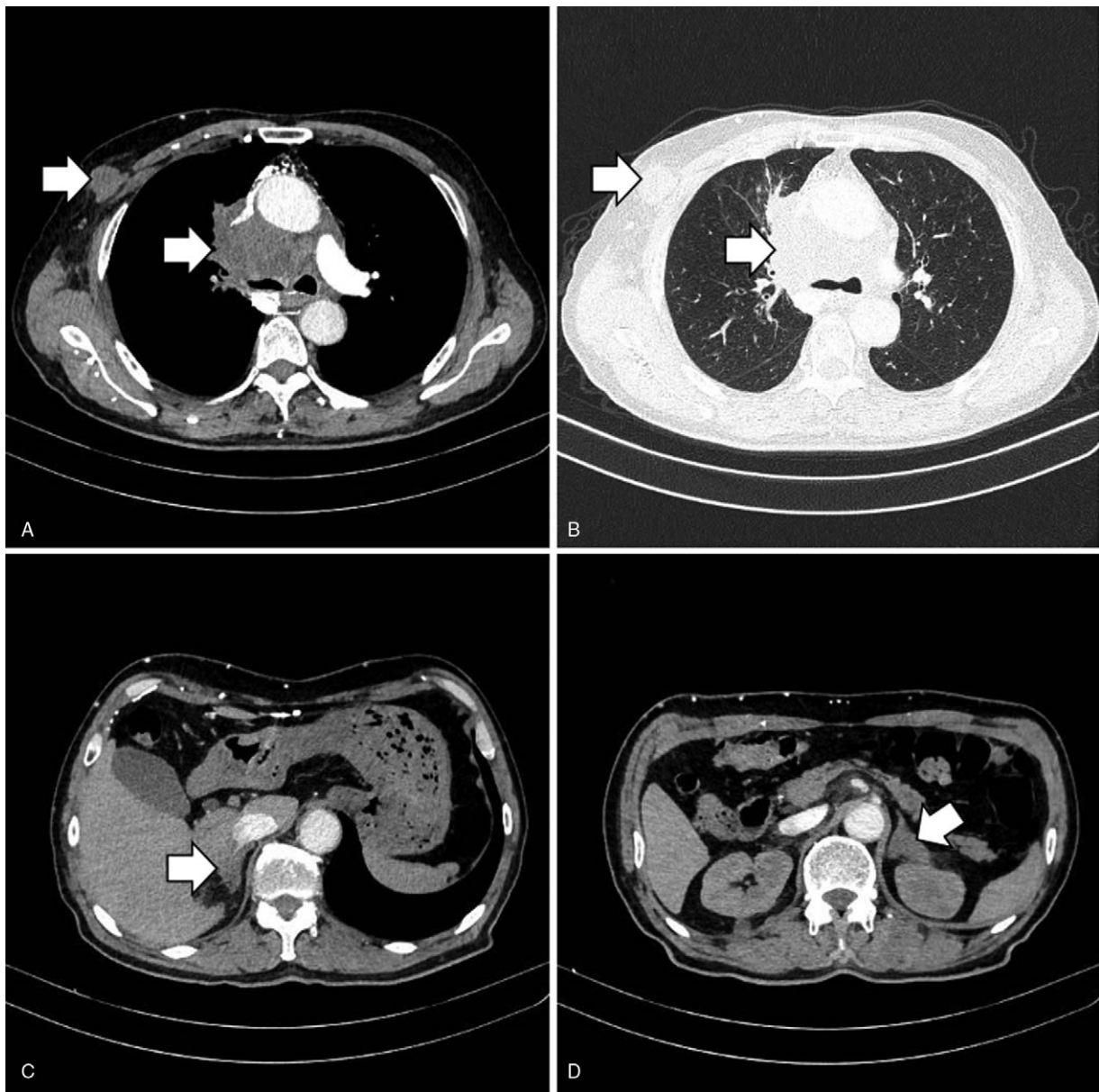


Figure 1. Computed tomography scan: (A, B) High-density mass in right upper lobe; (C, D) Bilateral adrenal tumors.

diagnosed with acute peritonitis with gastrointestinal perforation, and underwent emergency surgery. During the surgical procedure, a large amount of dirty ascites was found. Hyperemia and edema were noted in the small intestinal wall, and pus adhesion was noted in the omentum and small intestine surface. Many grey nodules were noted in the mesentery. Moreover, 2 perforations of size $1 \times 1 \text{ cm}^2$ were discovered at 110 cm and 140 cm of the jejunum from Treitz's ligament, and 2 other suspicious perforations of the serous membrane were noted at about 90 cm and 160 cm inside the jejunum from the Treitz's ligament. Hence, an intestinal resection of approximately 70 cm and end-to-end anastomosis were performed. The pathological diagnosis of the resected specimen indicated a metastatic lung adenocarcinoma of small intestine (Fig. 2). Immunohistochemical analysis showed that the tumor cells were positive for CK7 and TTF-1, indicating a metastasis from primary lung carcinoma. Unfortunately, the patient died 10 days after surgery and 19 days following the

cancer diagnosis, due to septic shock. Written informed consent was obtained from the patient's family for the publication of this case report and accompanying images.

3. Discussion

Lung cancer is the most common cancer in the world, accounting for 19.4% of all the cancer-related deaths.^[3] Besides, lung cancer has a high rate of metastasis. The most common metastatic sites are the other lung (50%), liver (37%), adrenal gland (31%), bone (29%), kidneys (18%), and brain (12%).^[1] Furthermore, in various reports, the incidence of gastrointestinal metastasis has been reported to be as low as 0.2% to 1.7%.^[2,4-7] Autopsy studies reveal higher rates of metastatic disease.^[4] According to several autopsy studies, gastrointestinal metastasis of primary lung cancer occurs in 4.7% to 14.0% of all cases.^[8,9] Metastatic lung cancer has been known to be highly malignant, and has been

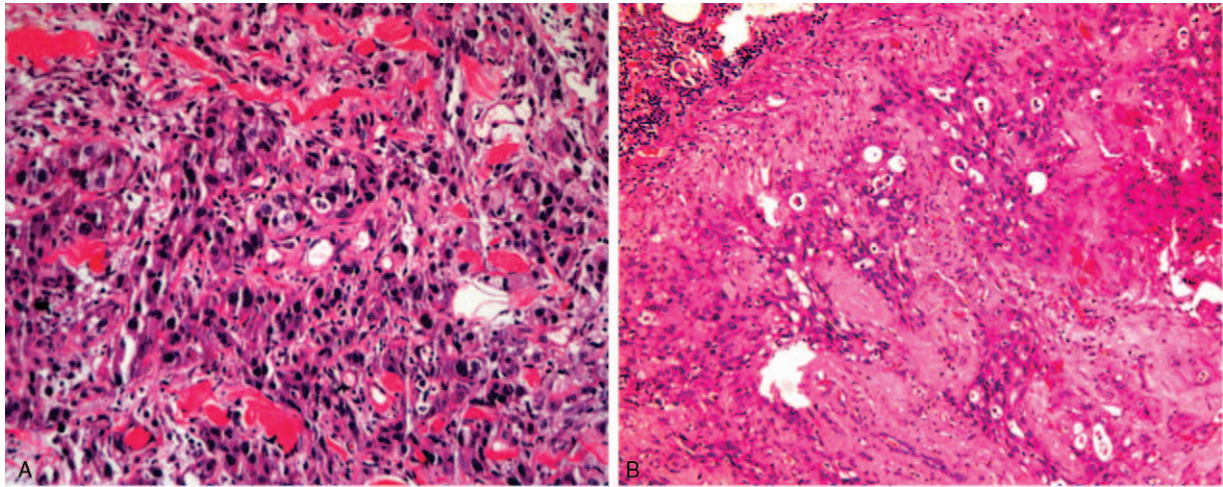


Figure 2. Microscopic findings: (A) Biopsy of the right chest wall mass (H&E, ×200); (B) Pathological examination of part of small intestine perforation (H&E, ×200).

noted to have spread to any location, from the oral cavity to the anus.^[10] Liu et al^[11] reported that in the 64 documented cases, 57 patients displayed metastasis. The jejunum was the most common site, as noted in 50.9% (29/57) of patients, followed by the ileum, in 33.3% (19/57), and the duodenum, in 15.8% (9/57). The general route of gastrointestinal metastasis has been thought to be hematogenous metastasis through the spinal veins or lymphogenous metastasis, from the mediastinum through the retroperitoneum and mesentery.^[12]

Small bowel metastasis may occur in every cell type of primary lung cancer. Immunohistochemical staining of the tissue is useful in streamlining the diagnosis.^[13] All adenocarcinomas including lung adenocarcinoma do not express TTF-1; therefore, TTF-1 is an important marker for distinguishing primary adenocarcinoma from metastatic adenocarcinoma.^[14] Nevertheless, Antler et al^[9] reported that squamous cell and undifferentiated large cell

carcinomas lead to gastrointestinal metastasis more frequently than other histological types. McNeil et al^[8] and Yoshimoto et al^[4] also showed that large cell carcinoma was the more frequent histological type. However, in contrast, Garwood et al^[15] reported that small bowel perforations were most often caused by adenocarcinoma (23.7%), squamous cell carcinoma (22.7%), large cell carcinoma (20.6%), and small cell carcinoma (19.6%). Therefore, the histological type predominantly associated with gastrointestinal metastasis is still not clear. The prevalence of small bowel perforation secondary to a given primary lung carcinoma histology may varied by region.

Metastatic intestinal tumors from lung cancer present with various symptoms. In one study, metastasis presented as perforation (46%), obstruction (35%), and gastrointestinal bleeding (16%).^[16] Besides these, bowel perforation is one of the commonly reported acute complications.^[17] Previous studies

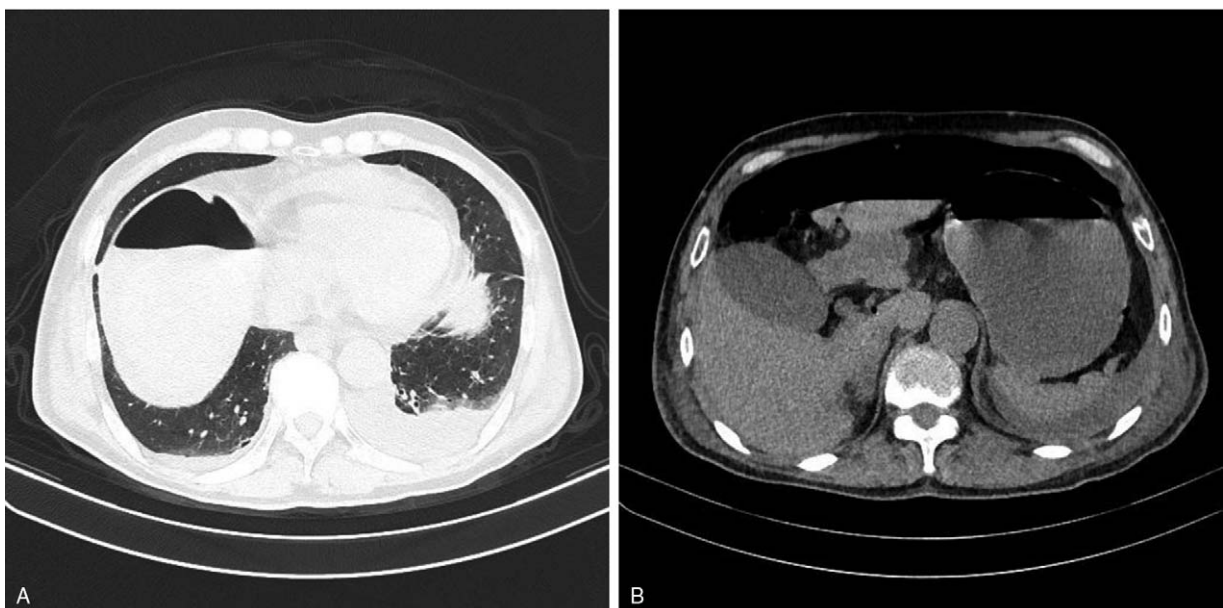


Figure 3. Abdominal computed tomography scans: free intraperitoneal gas is seen.

have also reported that the small bowel is the most common gastrointestinal metastatic site of lung cancer.^[15,18] The incidence of metastatic intestinal tumors from lung cancer is higher in men than in women, and at a mean age of 64.5 years.^[23] The prognosis of tumor in this location is worse than that in other locations,^[15,18] and emergency surgery has been described as treatment option, especially in small bowel lesions, to prevent further complications. However, the prognosis is still considered to be very poor; in one study, the cumulative survival rate for perforation was about 1.7 months.^[24] The 1-year survival rate in patients who underwent surgery for the perforation was 12%.^[24] In the present case, the patient died about 10 days after surgery due to septic shock.

This may be due to the fact that small bowel metastasis is typically associated with widespread disease. Stenbygaard et al^[1] reported that gastrointestinal metastases are typically observed in other widely metastatic disease. In the present study, intraoperative findings showed multiple metastatic nodules in the mesentery, and the cause of mortality therefore was thought to be the following: first, patients with advanced lung cancer accompanied by cardiopulmonary function based state poorer; second, patients who undergo septic shock before the operation, with severe abdominal infection; third, patients with superior vena cava pressure, which causes upper limb, facial, and brain edema; And finally, patients receiving assisted breathing through breathing machines in the intensive care unit after operation, who have a high risk of pulmonary infection. So, the patient's death was possibly caused by the comprehensive factors. The possible mechanisms responsible for his perforation may have been ischemia of the intestinal wall resulting from a blood or tumor thrombus, the necrosis of the intestinal wall, as a result of chemotherapy, etc.^[19] Previous studies have reported chemotherapy-induced small intestinal perforation as a complication of treatment for lung cancer.^[20] According to this case, chemotherapy-induced necrosis of metastatic tumors may lead to small bowel perforation.

When lung cancer patients with gastrointestinal metastasis exhibit an acute abdomen, abdominal CT has a high value in diagnosing gastrointestinal metastases, and surgical intervention is required. Laparoscopic surgery has not only the advantages of less trauma, less blood loss and quicker recovery, but also has a huge diagnostic potential. Due to the unclear clinical symptoms in some patients with small bowel metastases, early diagnosis and treatment are difficult and an important matter. Therefore, prolonging a patient's life with positron emission computed tomography is thought to be possible,^[21] and capsule endoscopy has the capability of providing visual images of the bowel.^[22] These examinations can provide help in identifying the presence of small intestinal metastasis when a patient with positive occult-blood tests.

4. Conclusion

In short, we experienced a rare case of multiple perforation of a small bowel metastatic tumor caused by lung cancer. This case indicates that metastasis to the gastrointestinal tract should be considered as a differential diagnosis. To our knowledge, the prognosis of metastatic intestinal tumors from lung cancer is very poor, and the survival rate is extremely low. Therefore, when patients with advanced lung cancer develop an acute abdomen or if the fecal occult-blood tests show persistently positive results, it is necessary to keep in mind the possibility of a gastrointestinal metastatic tumor.

Author contributions

JW, YC, and SZ are the co-first authors, and contributed equally to this work. JW and YC contributed to the literature search and the writing of the manuscript. QC and SZ contributed to the review and revision of the manuscript.

References

- Stenbygaard LE, Sorensen JB, Larsen H, et al. Metastatic pattern in non-resectable non-small cell lung cancer. *Acta Oncol* 1999;38:993–8.
- Taira N, Kawabata T, Gabe A, et al. Analysis of gastrointestinal metastasis of primary lung cancer: clinical characteristics and prognosis. *Oncol Lett* 2017;14:2399–404.
- Mao Y, Yang D, He J, et al. Epidemiology of lung cancer. *Surg Oncol Clin N Am* 2016;25:439–45.
- Yoshimoto A, Kasahara K, Kawashima A. Gastrointestinal metastases from primary lung cancer. *Eur J Cancer* 2006;42:3157–60.
- Kim SY, Ha HK, Park SW, et al. Gastrointestinal metastasis from primary lung cancer: CT findings and clinicopathologic features. *AJR Am J Roentgenol* 2009;193:W197–201.
- Gitt SM, Flint P, Fredell CH, et al. Bowel perforation due to metastatic lung cancer. *J Surg Oncol* 1992;51:287–91.
- Lee PC, Lo C, Lin MT, et al. Role of surgical intervention in managing gastrointestinal metastases from lung cancer. *World J Gastroenterol* 2011;17:4314–20.
- McNeill PM, Wagman LD, Neifeld JP. Small bowel metastases from primary carcinoma of the lung. *Cancer* 1987;59:1486–9.
- Antler AS, Ough Y, Pitchumoni CS, et al. Gastrointestinal metastases from malignant tumors of the lung. *Cancer* 1982;49:170–2.
- Al-Tarakji M, Feilchenfeldt J, Haidar A, et al. Rare occurrence of metastasis from lung cancer to the anus: case report and review of the literature. *World J Surg Oncol* 2016;14:157.
- Liu W, Zhou W, Qi WL, et al. Gastrointestinal hemorrhage due to ileal metastasis from primary lung cancer. *World J Gastroenterol* 2015;21:3435–40.
- Ogata R, Tanio Y, Takashima J, et al. Retrospective analysis of immediate cause of death in lung cancer—two case reports of lung cancer deaths due to bowel necrosis (in Japanese). *Gan To Kagaku Ryoho [Jpn J Cancer Chemother]* 2011;38:987–90.
- Lin HC, Yu CP, Lin HA, et al. A case of lung cancer metastasized to the gastrointestinal anastomosis site where the primary gastric cancer was resected 17 years ago. *Lung Cancer* 2011;72:255–7.
- El Hag M, Schmidt L, Roh M, et al. Utility of TTF-1 and Napsin-A in the work-up of malignant effusions. *Diagn Cytopathol* 2016;44:299–304.
- Garwood RA, Sawyer MD, Ledesma EJ, et al. A case and review of bowel perforation secondary to metastatic lung cancer. *Am Surg* 2005;71:110–6.
- Di JZ, Peng JY, Wang ZG. Prevalence, clinicopathological characteristics, treatment, and prognosis of intestinal metastasis of primary lung cancer: a comprehensive review. *Surg Oncol* 2014;23:72–80.
- Berger A, Cellier C, Daniel C, et al. Small bowel metastases from primary carcinoma of the lung: clinical findings and outcome. *Am J Gastroenterol* 1999;94:1884–47.
- Yang CJ, Hwang JJ, Kang WY, et al. Gastro-intestinal metastasis of primary lung carcinoma: clinical presentations and outcome. *Lung Cancer* 2006;54:319–23.
- Ise N, Kotanagi H, Morii M, et al. Small bowel perforation caused by metastasis from an extra-abdominal malignancy: Report of three cases. *Surg Today* 2001;31:358–62.
- Suzaki N, Hiraki A, Ueoka H, et al. Gastric perforation due to metastasis from adenocarcinoma of the lung. *Anticancer Res* 2002;22(2b):1209–12.
- Kelly RF, Tran T, Holmstrom A, et al. Accuracy and cost-effectiveness of [18F]-2-fluoro-deoxy-D-glucose-positron emission tomography scan in potentially resectable non-small cell lung cancer. *Chest* 2004;125:1413–23.
- Leduc C, Prim N, Mennecier B, et al. Diagnosis of jejunal metastases from lung cancer using capsule endoscopy. *Case Rep Oncol* 2016;9:526–9.
- Nakagawa K, Yasumitsu T, Kotake Y, et al. Seven operated cases of metastasis to the small intestine from lung cancer and a review of the Japanese literature (in Japanese). *Haigan (Lung Cancer)* 1996;36:319–24.
- Narikiyo M, Boku S, Nakatani K, et al. A case of acute peritonitis due to perforated metastatic lesion of small intestine from lung cancer (in Japanese). *Nihon Fukubu Kyukyu Igakukai Zasshi [Jpn J Abdom Emerg Med]* 1997;17:1081–108.