

Ileal Intussusception Due to Metastasis from Squamous Cell Carcinoma of the Lung Resected 12 Years Previously

Tomoki NAKAMURA^{*1}, Osamu CHINO^{*1}, Takayuki TAJIMA^{*2}, Yoichi TANAKA^{*1}, Daiki YOKOYAMA^{*1},
Tomoko HANASHI^{*1}, Sotaro SADAHIRO^{*2} and Hiroyasu MAKUUCHI^{*1,2}

^{*1}Department of Surgery, Tokai University Tokyo Hospital

^{*2}Department of Surgery, Tokai University School of Medicine

(Received April 2, 2015; Accepted August 20, 2015)

An 88-year-old woman, with a history of resection of stage IIA lung cancer in 1998, was referred to our hospital in August 2010 complaining of upper abdominal pain, vomiting, and dark brown stools. After endoscopic examination, she was admitted with a diagnosis of Mallory-Weiss syndrome. Vomiting recurred when food intake was resumed after fasting. Intestinal obstruction was suspected on abdominal radiography, and complete small bowel obstruction was confirmed by contrast-enhanced imaging after placement of an ileus tube. A small intestinal tumor with intussusception was detected by computed tomography.

At laparotomy, there was no ascites. Intussusception was found due to an ileal tumor located approximately 50 cm from the ileocecal valve, and we performed partial small bowel resection. The resected small intestine contained a submucosal tumor approximately 40 mm in diameter that had penetrated the bowel wall to reach the serosa. Pathological examination revealed a submucosal tumor that showed poor continuity with the surrounding mucosa, while the histology was squamous cell carcinoma. Immunohistochemistry showed that the tumor was CK7 positive, CK20 negative, TTF-1 negative, and CK10 positive. Based on these findings, we made a diagnosis of small intestinal metastasis at 12 years after radical resection of squamous cell carcinoma of the lung.

Key words: small intestinal metastasis, squamous cell carcinoma, lung cancer

INTRODUCTION

The mortality rate of lung cancer has increased 4- to 5-fold over approximately 60 years in both men and women [1]. Patients with Stage II non-small cell lung cancer only have a 50% chance of surviving for 5 years. Lung cancer is associated with high rates of both recurrence and metastasis, and it has been reported that the overall recurrence rate is > 50% [2]. The common sites of lung cancer metastasis are the lungs, liver, adrenal glands, bone, and brain, but metastasis to the small intestine is extremely rare [3, 4]. Postoperative recurrence of lung cancer usually occurs within 2 years of surgery, and recurrence at 5 years or later is very rare [5].

We present a patient with small intestinal metastasis that was identified because of ileal obstruction due to intussusception. The metastasis was considered to have occurred 12 years after resection of primary lung cancer.

Metastatic recurrence at 10 years or more after resection of primary lung cancer has been reported in 7 patients, but this is the first case of small bowel metastasis [6, 7]. Accordingly, we report this rare case of small intestinal metastasis at 12 years after radical surgery for squamous cell carcinoma of the lung.

CASE REPORT

In August 2010, an 88-year-old woman was referred to our hospital with abdominal pain, frequent vomiting, and dark brown stools. A bleeding gastric ulcer was suspected and Mallory-Weiss syndrome was diagnosed by emergency endoscopy. Physical examination at admission revealed surgical scars on the left side of the chest and abdomen. She had previously undergone left upper lobectomy for lung cancer (moderately differentiated squamous cell carcinoma, pT1N1M0, stage IIA [2]), laparoscopic cholecystectomy for cholelithiasis, and synechotomy plus hernia repair with Prolene mesh for adhesive ileus and an abdominal wall scar hernia in 1998, 1999, and 2001, respectively. Laboratory tests showed a mild inflammatory response with no biochemical abnormalities. The carcinoembryonic antigen (CEA) level was not elevated at 3.1 ng/ml (normal <5.0), but squamous cell carcinoma (SCC) antigen was increased to 2.9 ng/ml (normal <1.5). A plain abdominal X-ray film showed dilation of the small intestine with niveau formation. Recurrent adhesive ileus was suspected because of the patient's history, so an ileus tube was placed. Flow of contrast medium from the ileus tube was blocked on the anal side, suggesting small intestinal obstruction. A tumor was identified in the lower small intestine on abdominal contrast-enhanced CT scanning, confirming the results of ileus tube contrast imaging (Fig. 1). While small

intestinal cancer and malignant lymphoma were considered possible, the diagnosis could not be confirmed. Therefore, laparotomy was performed in September 2010. There was no peritoneal dissemination, enlargement of mesenteric lymph nodes, or abdominal ascites. The intestinal tract had a formed mass surrounded by dense adhesions, and intussusception was detected in the ileum approximately 50 cm oral to the ileocecal valve (Fig. 2A). Partial resection of the small intestine was performed, revealing a solid submucosal tumor approximately 40 mm in diameter (Fig. 2B).

Histologically, the tumor contained proliferating squamous cells, particularly in the muscle layer of the bowel wall, and extended from the mucosa to the serosal surface (Fig. 3A). The tumor exhibited poor continuity with the surrounding normal tissue (Fig. 3B).

While the main component of the tumor was squamous cell carcinoma, it included some areas of adenocarcinoma at the margins (Fig. 3C). Immunohistochemical analysis was performed, revealing that the lesion was positive for CK7 and negative for CK20 (Fig. 4A), which was indicative of a metastatic tumor. In addition, it was negative for TTF-1 and positive for CK10 (Fig. 4B), consistent with squamous cell carcinoma. The patient had a favorable postoperative course. Detailed postoperative examinations failed to identify a primary tumor. Based on the histopathological and immunohistochemical findings, the diagnosis was small intestinal metastasis of squamous cell lung cancer that had been resected 12 years previously.

We explained the standard chemotherapy regimen to the patient and her family, but they refused it due to her advanced age, so she was treated with oral tegafur/uracil.

In consideration of her age and general condition, low-dose oral adjuvant chemotherapy was discontinued after 1 month at the patient's request due to adverse reactions such as malaise. Gradually it began to repeat the aspiration and fever, and the pneumonia was recognized on the right lower lobe by X-ray. She died of aspiration pneumonia about 5 months postoperatively.

DISCUSSION

Metastatic small intestinal tumors often occur as part of systemic metastasis in patients with terminal malignancy. The primary tumors causing small intestinal metastasis are cancer of the stomach, pancreas, and lung in that order, but gastric and pancreatic cancer often spread by direct invasion while lung cancer usually causes hematogenous metastasis [8, 9]. This is because the abundant vascular/lymphatic networks in the lungs are constantly moving due to respiration, and there is a retroperitoneal pathway from the mediastinum to the mesentery as well as lymphatic routes to the peritoneal cavity via the pulmonary ligaments [10]. Since mediastinal or intraperitoneal lymphadenopathy was not observed in our patient, we considered that the tumor had arisen via hematogenous metastasis.

The 3 criteria for diagnosis of small intestinal metastasis are: 1) similarity of the pathologic findings to those of the primary tumor, 2) no intramucosal cancer in the small intestine, and 3) no evidence of development by contiguous growth from a primary

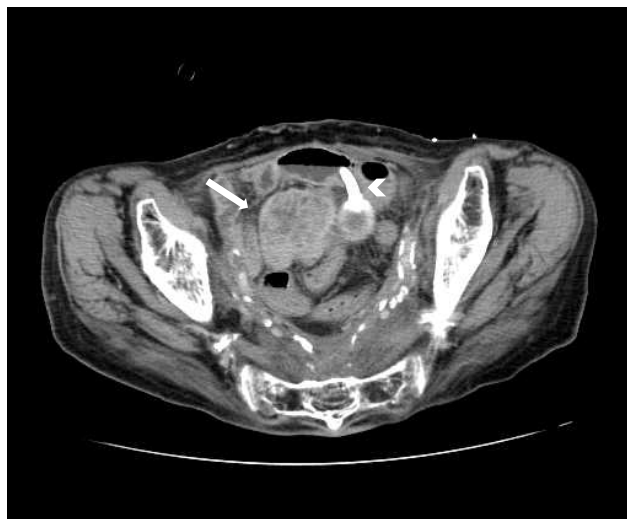


Fig. 1 Abdominal CT revealed a tumor (4 cm in size) in the distal small intestine. Arrowhead: MA tube balloon.

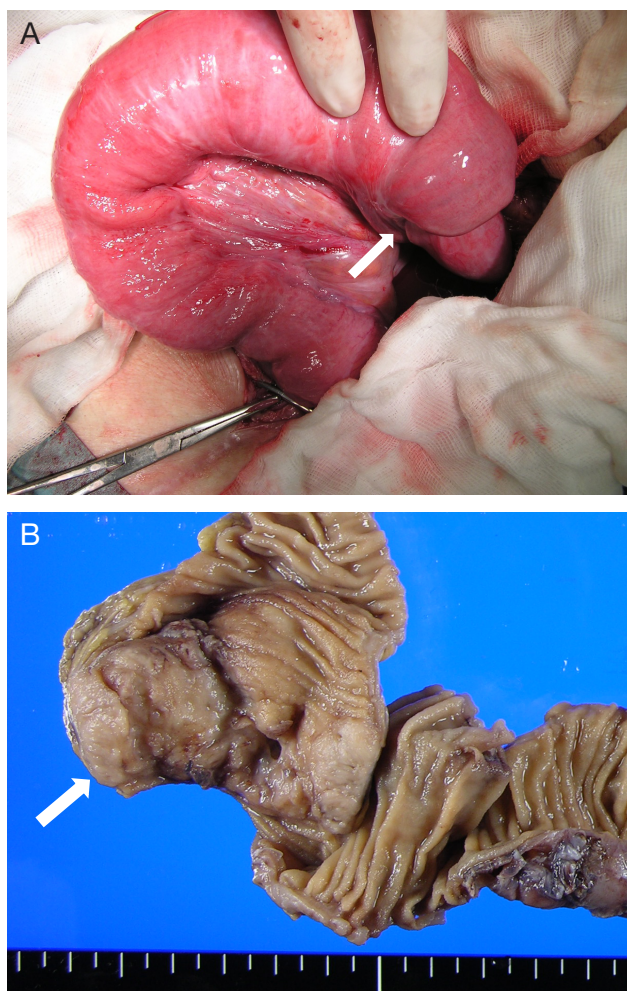
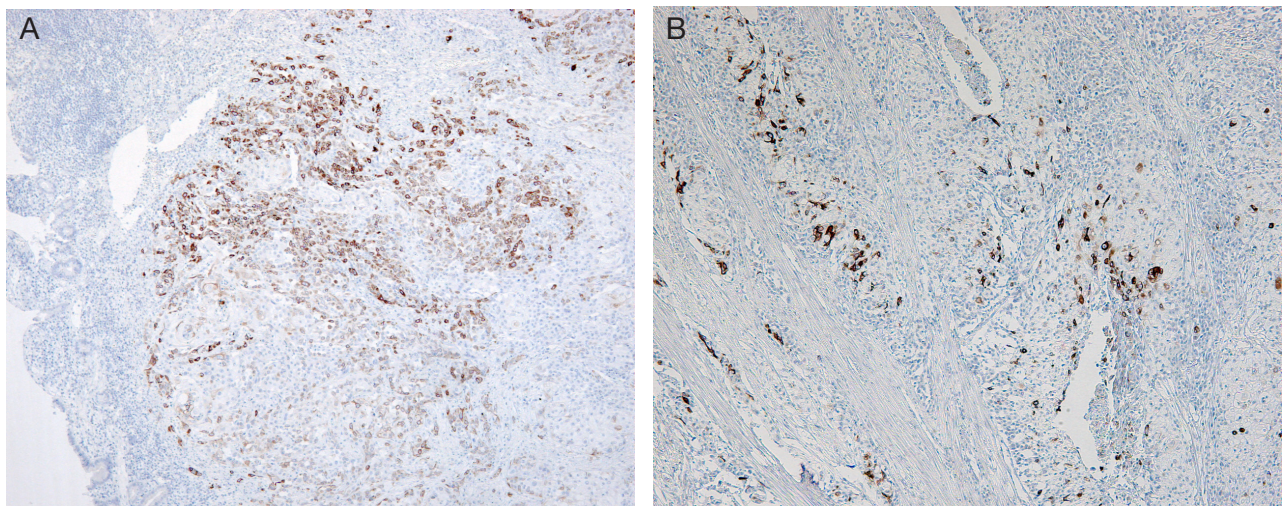
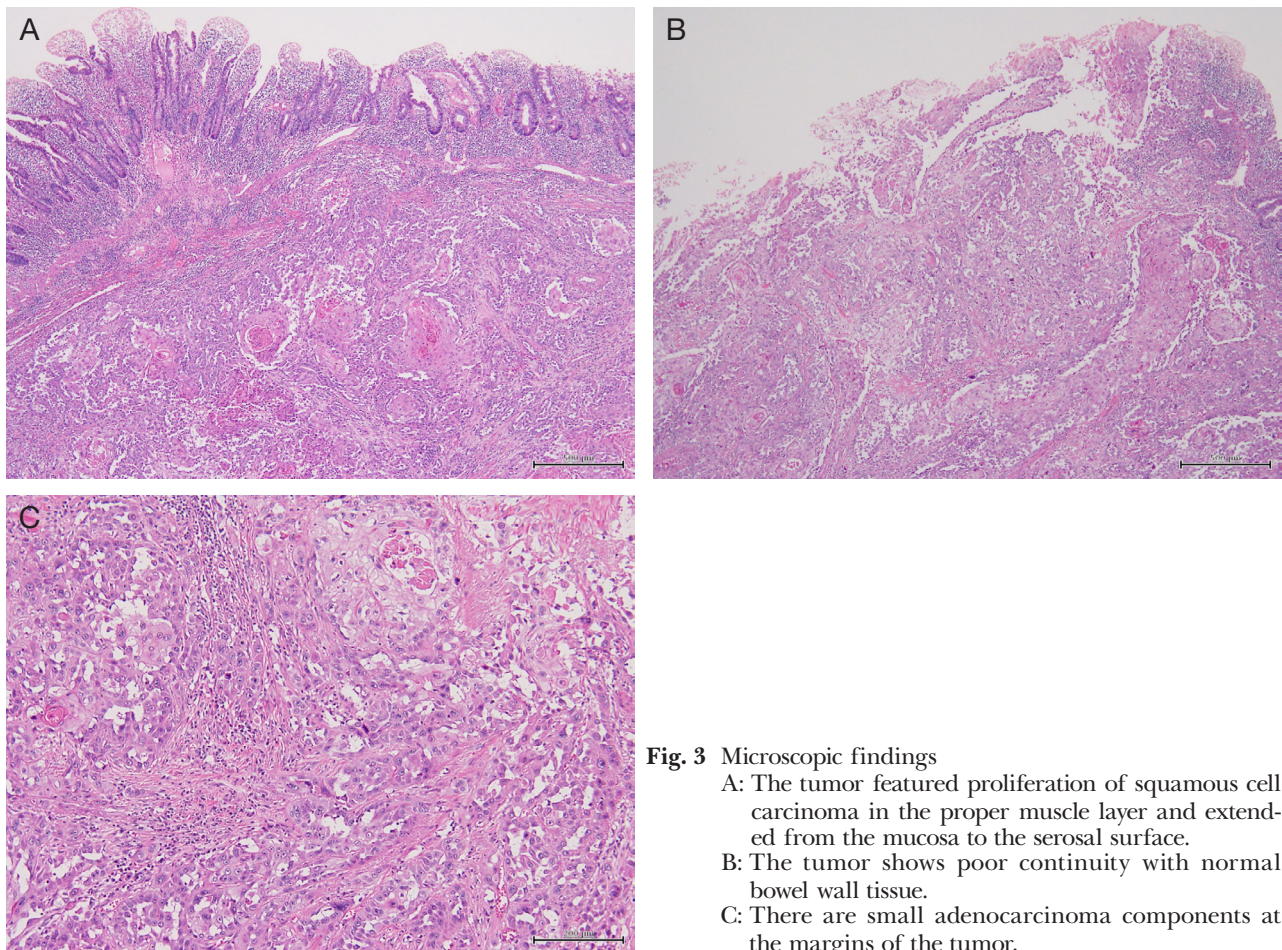


Fig. 2 A: The tumor was located approximately 50 cm oral to the ileocecal valve and caused intussusception. B: Macroscopic view of the resected specimen: part of the ileum containing a tumor.



small intestinal tumor or another metastasis [11]. It was impossible to compare histology with that of the primary tumor because lung cancer surgery had been performed 12 years previously in our patient and the resected specimens had been discarded. Since our patient's tumor met criteria 2) and 3) above, immunohistochemical analysis was performed to gain more information in relation to criterion 1). This revealed that the tumor was predominantly squamous cell carcinoma

because the lesion was CK7 positive, CK20 negative, TTF-1 negative, and CK10 positive [12, 13]. It has been reported that squamous cell cancer is CK7 negative/CK20 positive and adenocarcinoma of the lung is CK7 positive/CK20 negative, which is contrary to the findings in our patient [14]. When we examined the tumor in detail, we found adenocarcinoma-like components at some parts of the margins. Although the lesion was diagnosed as squamous cell carcinoma because that

was the main component, it was considered possible that CK7 was positive due to the adenocarcinoma component. It has been reported that adeno-squamous cell carcinoma, a mixture of adenocarcinoma and squamous cell carcinoma, accounts for 0.4–4% of lung primary lung cancers, and the above results are likely to be consistent with adeno-squamous cell carcinoma [15].

In addition, no other tumor was detected by systemic examination after surgery, so the lesion was considered to be a rare small intestinal metastasis from the lung cancer been resected 12 years previously.

The average period from resection of a primary lung tumor to postoperative recurrence is 13–15 months, and 65–70% of patients experience recurrence within 2 years [16, 17]. Our literature search identified 7 patients who developed metastatic recurrence at least 10 years after radical resection of the primary tumor. Intrapulmonary metastasis was reported in 5 patients, followed by cerebral metastasis in 3, lymph node metastasis in 3, and renal and cutaneous metastasis in 1 case each. There were no reports of metastasis to the gastrointestinal tract [6, 7]. The present case suggests that careful assessment with consideration of intraperitoneal metastasis lesion is necessary when abdominal symptoms occur after resection of lung cancer.

CONCLUSION

We presented a patient with small intestinal metastasis 12 years after resection of adeno-squamous cell carcinoma of the lung. The ileal tumor was revealed when intussusception led to small intestinal obstruction.

ACKNOWLEDGEMENT

We would like to express our deepest gratitude to Dr. Takuma Tajiri, Tomoko Sugiyama, and Shinichiro Hiraiwa (Department of Diagnostic Pathology, Tokai University Hachioji Hospital) for his guidance on histopathological diagnosis.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

REFERENCES

- 1) Health, Labour and Welfare Statistics Association. Journal of Health and Welfare Statistics. Tokyo: Health, Labour and Welfare Statistics Association, 2014/2015; 61: 63–7.
- 2) The Japan Lung Cancer Society. General rules for clinical and pathological recording of lung cancer. 7th ed. Tokyo: Kanehara & Co., Ltd., 2010.
- 3) Ryo H, Sakai H, Ikeda T, Hibino S, Goto I, Yoneda S, *et al.* Gastrointestinal metastasis from lung cancer. *Nihon Kyobu Shikkan Gakkai Zasshi* 1996; 34: 968–72.
- 4) McNeill PM, Wagman LD, Neifeld JP. Small bowel metastases from primary carcinoma of the lung. *Cancer* 1987; 59: 1486–89.
- 5) Martini N, Bains MS, Burt ME, Zakowski MF, McCormack P, Rusch VW, *et al.* Incidence of local recurrence and second primary tumors in resected stage I lung cancer. *J Thorac Cardiovasc Surg* 1995; 109: 120–9.
- 6) Kitamoto Y, Hayakawa K, Mitsuhashi N, Tsuchiya S, Saito R. Redevelopment of small cell lung cancer after a long disease-free period: a case report. *Jpn J Clin Oncol* 2002; 32: 30–32.
- 7) Matsui K, Sawa T, Suzuki H, Nakagawa K, Okamoto N, Tada T, *et al.* Relapse of stage I small cell lung cancer ten or more years after the start of treatment. *Jpn J Clin Oncol* 2006; 36: 457–61.
- 8) Masaoka I, Nakamura T. Metastatic neoplasms of the bowel. *Jpn J Clin Med* 1994; 612–5.
- 9) Haraoka S, Iwashita A, Nakayama Y. Metastatic tumor of the gastrointestinal tract. *Stomach & Intestine* 2003; 38: 1755–71.
- 10) Morris DM, Deitch EA. Clinically significant intestinal metastasis from a primary bronchogenic carcinoma. *J Surg Oncol* 1983; 23: 93–4.
- 11) Kudou A, Harada T, Nagasawa T. Two cases of metastatic small intestinal cancer after colon cancer surgery. *J Jpn Surg Assoc* 2009; 70: 2382–7.
- 12) Kojima K, Saito T, Tetumoto S, Konishi Y, Fushimi H. A case of metastatic intestinal cancer from lung causing intussusception. *Jpn J Diagn Pathol* 2007; 24: 83–5.
- 13) Fujita K, Kurihara T, Honda Y, Okimoto N. A case of small bowel metastasis from lung adenocarcinoma diagnosed by immunostaining for TTF-1. *Jpn J Lung Canc* 2004; 44: 49–54.
- 14) Chu P, Wu E, Weiss LM. Cytokeratin 7 and cytokeratin 20 expression in epithelial neoplasms: a survey of 435 cases. *Mod Pathol* 2000; 13: 962–72.
- 15) Travis W.D., Brambilla E., Muller-Hermelink H.K., Harris C.C. World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. Lyon: IARC Press, 2004: 51–2.
- 16) Yusa T, Yamaguchi Y, Saito Y, Yamakawa H, Obata S, Shiba M, *et al.* Clinical study on recurrence of lung cancer in patients who underwent curative surgical resection. *Jpn J Lung Canc* 1990; 30: 209–15.
- 17) Tsuchida A, Kimura K, Koyanagi Y, Aoki T, Kusama M, Nishida J, *et al.* A case of small intestine metastasis from lung cancer. *J Jpn Pract Surg Soc* 1991; 52: 2663–7.