

Single Case

Small-Intestinal Metastasis from Lung Carcinoma

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Keywords

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Abstract

A 62-year-old man was referred to our hospital because of abdominal pain. Computed tomography revealed an approximately 7-cm-diameter tumor in the left abdomen with metastatic lymph nodes, an approximately 1-cm-diameter round tumor in contact with the subclavian artery in the apical lobe of the right lung, and mediastinal lymph node enlargement in contact with the superior vena cava. Esophagogastroduodenoscopy and colonoscopy revealed no abnormalities. Double-balloon endoscopy revealed a whole circumferential ulcer in the jejunum approximately 20 cm from the ligament of Treitz. Biopsy analysis of an ulcer specimen revealed a poorly differentiated carcinoma. Immunohistochemical staining of the specimen showed that it was positive for thyroid transcription factor 1 and cytokeratin 7 and negative for cytokeratin 20, GATA-binding protein 3, caudal-type homeobox protein 2, and paired box 8. Positron emission tomography revealed positive findings in the small-intestinal tumor, nearby mesenteric lymph nodes, lymph nodes around the abdominal aorta, lung tumor, and mediastinal lymph node in the apical lobe of the right lung. Accordingly, the patient was diagnosed as having a lung carcinoma with small-intestinal metastasis (T1b, N3, M1c; cStage IVB). Pathological examination helped distinguish the primary small-intestinal tumor from the metastatic small-intestinal tumor and detect the tumor origin.

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Introduction

Among all neoplasms, lung cancer has the highest mortality rate worldwide. Despite advances in lung cancer prevention, approximately 50% of patients present with metastases at the time of diagnosis. However, owing to advances in diagnosis and treatment, patient survival has increased in the last few years, which unfortunately facilitates the development of long-term metastases [1]. Distant metastases are usually found in the adrenal glands, bone, liver, brain, and kidney; however, metastases in the gastrointestinal tract are relatively rare [2] and account for only a small number of cases [2]. Small-intestinal metastases are usually detected after the onset of serious complications such as perforation, obstruction, or massive hemorrhage, and the prognosis of the patient is extremely poor because of advanced progressive lesions. When a lung tumor and a small-intestinal tumor are found simultaneously, it is difficult to determine which is the primary tumor and which is the metastasis solely on the basis of diagnostic imaging techniques such as computed tomography (CT) and endoscopy. In such cases, pathological examination is helpful in diagnosing the primary lesion. Here, we report a case of a lung cancer with small-intestinal metastasis in which the initial diagnosis of the tumor origin was difficult by using CT and enteroscopy and in which pathological examination was helpful in determining the primary carcinoma.

Case Report

A 62-year-old man without a medical history was referred to our hospital because of abdominal pain. However, he did not complain of markable melena or hematochezia, which could be related to gastrointestinal bleeding. His family history was unremarkable. The physical examination findings were unremarkable, and initial laboratory data were as follows: hemoglobin, 9.0 g/dL; hematocrit, 28.7%; serum iron, 17 µg/dL; and ferritin, 13.6 ng/mL, suggesting iron deficiency anemia. The levels of tumor markers such as carcinoembryonic antigen and carbohydrate antigen 19-9 were within normal limits (1.3 ng/mL and 20 U/mL, respectively). Other laboratory parameters were also within normal limits.

However, abdominal CT revealed a tumor approximately 7 cm in diameter in the left abdomen (Fig. 1a) with nearby swollen mesenteric lymph nodes and lymph node enlargement around the abdominal aorta (Fig. 1b). The abdominal tumor contained air in the central portion and was considered to have originated from the small intestine. Chest CT revealed a round tumor approximately 1 cm in diameter in contact with the subclavian artery in the apical lobe of the right lung (Fig. 1c) and mediastinal lymph node enlargement in contact with the superior vena cava (Fig. 1d). Esophagogastroduodenoscopy and colonoscopy revealed no abnormalities. Enteroscopy was performed after intubation into the jejunum from the nose to shorten the jejunum for facilitating the procedure. Enteroscopy using double-balloon endoscopy revealed a whole circumferential ulcer in the jejunum approximately 20 cm from the ligament of Treitz (Fig. 2a, b). However, because of tumor stenosis, the enteroscope could not pass through the stenosis. Therefore, the anal side of the ulcer and the whole ulcer could not be observed. On the basis of the CT findings, the ulcer was considered to be an exposed part of the tumor. Positron emission tomography revealed positive findings in the small-intestinal tumor (Fig. 2c), nearby mesenteric lymph nodes (Fig. 2d), lymph nodes around the abdominal aorta (Fig. 2d), lung tumor, and mediastinal lymph node in the apical lobe of the right lung (Fig. 2e).

Analysis of a biopsy specimen obtained from the ulcer revealed a poorly differentiated carcinoma (Fig. 3a) consistent with a lung origin. Immunohistochemical staining of the specimen showed that it was positive for thyroid transcription factor 1 (TTF1) (Fig. 3b) and

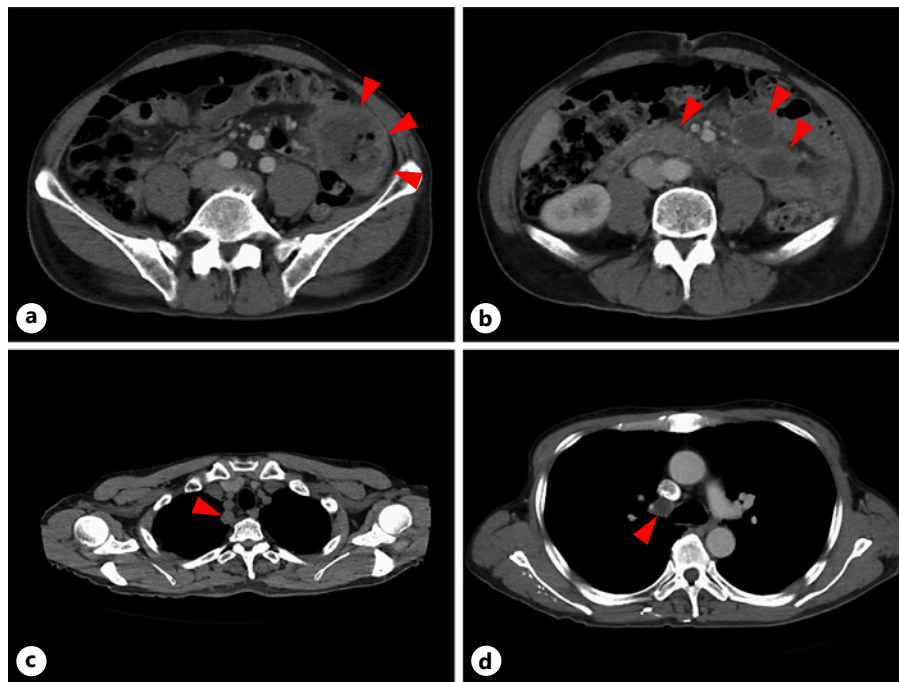


Fig. 1. Abdominal CT shows a tumor measuring approximately 7 cm in diameter in the left abdomen (**a**, arrowheads) with nearby swollen mesenteric lymph nodes and lymph node enlargement around the abdominal aorta (**b**, arrowheads). Chest CT shows a round tumor measuring approximately 1 cm in diameter in contact with the subclavian artery in the apical lobe of the right lung (**c**, arrowhead) and mediastinal lymph node enlargement in contact with the superior vena cava (**d**, arrowhead).

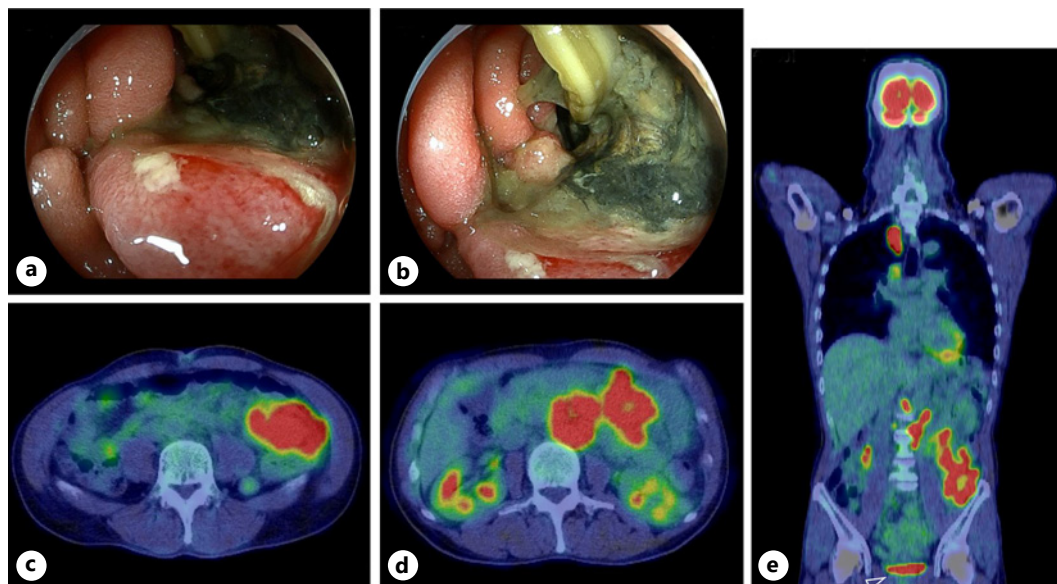


Fig. 2. Enteroscopy shows a whole circumferential ulcer is seen in the jejunum approximately 20 cm from the ligament of Treitz. **a** Anal side of the ulcer. **b** A whole circumferential dirty ulcer. PET shows accumulations in the small-intestinal tumor (**c**), nearby mesenteric lymph nodes (**d**), lymph nodes around the abdominal aorta (**d**), lung tumor (**e**, arrowhead), and mediastinal lymph node in the apical lobe of the right lung (**e**, arrow). PET, positron emission tomography.

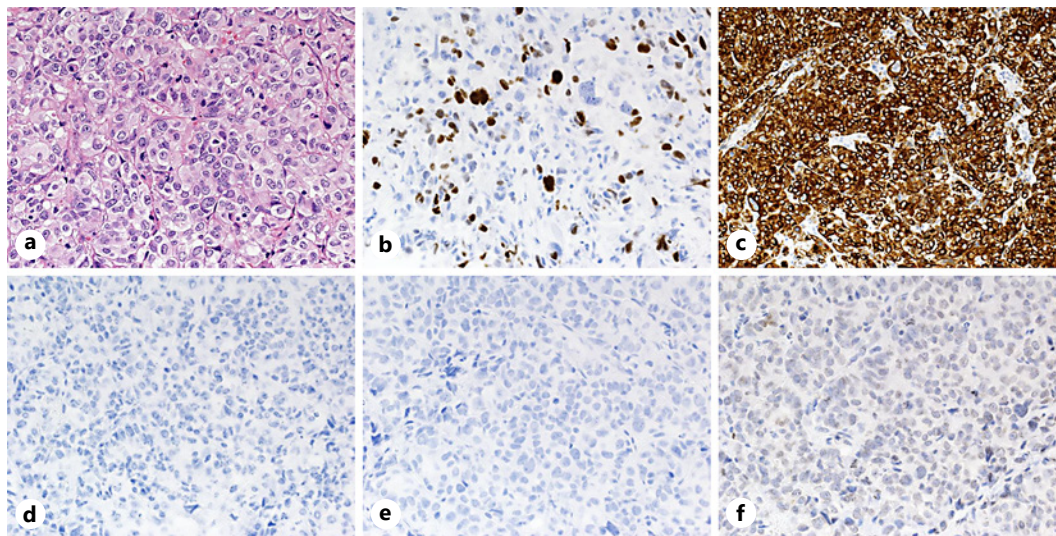


Fig. 3. Pathological examination. Hematoxylin and eosin staining reveals the tumor is a poorly differentiated adenocarcinoma (a). Immunohistochemical staining for TTF1 (b) and CK7 (c) is positive. Immunohistochemical staining for CK20 (d), CDX2 (e), and PAX8 (f) is negative. Original magnification, $\times 400$.

cytokeratin 7 (CK7) (Fig. 3c) and negative for cytokeratin 20 (CK20) (Fig. 3d), GATA-binding protein 3 (GATA3), caudal-type homeobox protein 2 (CDX2) (Fig. 3e), and paired box 8 (PAX8) (Fig. 3f).

Accordingly, the patient was diagnosed as having a lung carcinoma with small-intestinal metastasis (T1b, N3, M1c; cStage IVB). The Eastern Cooperative Oncology Group performance status [3] of the patient was 3. As chemotherapy, nanoparticle albumin-bound paclitaxel (160 mg/day) was intravenously administered once a week (day 1: nanoparticle albumin-bound paclitaxel, 100 mg/m²/day; days 2–7, none) for a period of 3 weeks (which equates to 1 course of chemotherapy). However, after 1 course (i.e., approximately 1 month) of chemotherapy, the patient's condition deteriorated, and chemotherapy was discontinued. Unfortunately, 2 months after the discontinuation of chemotherapy, the patient died.

Discussion

Metastases to the gastrointestinal tract are rare in patients with lung cancer and are more commonly encountered in the advanced stages of the disease. Yang et al. [4] reported that the incidence of symptomatic gastrointestinal metastases from primary lung cancer was 1.77%. However, the prevalence at autopsy is much higher, ranging from 4.7% to 14% [5]. The most frequently observed symptoms without associated complications are abdominal pain (in 50% of patients) and weight loss [6, 7]. The most frequent complications are small-bowel perforation and intestinal obstruction, occurring as a result of an occlusive tumor or invagination of a tumor [8, 9]. On endoscopy, lung cancer metastases to the intestine exhibit no specific features and usually appear as diffuse involvement of the intestinal mucosa, multiple nodules with/without mucosal ulceration, or as a solitary “volcano-like” tumor of the intestine [10].

In our case, the small-intestinal tumor (approximately 7 cm in diameter) was larger than the lung tumor (approximately 1 cm in diameter), and the swollen mesenteric lymph nodes and lymph node enlargement around the abdominal aorta were larger than the mediastinal lymph node enlargement. In other words, the metastatic small-intestinal tumor progressed

more rapidly than did the primary lung tumor. Moreover, the intestinal tumor had no features of lung cancer metastases to the intestine. Therefore, the small-intestinal tumor was initially diagnosed as a primary carcinoma or lymphoma of the small intestine with lung and lymph node metastases. Further, it was difficult to distinguish a primary small-intestinal tumor from a metastatic tumor derived from the lung on the basis of the enteroscopic examination findings. Pathological diagnosis using immunohistochemical staining is the only reliable method to differentiate a primary small-bowel malignancy from a metastatic lesion derived from the lung [11]. Primary lung carcinomas usually exhibit a CK7+/CK20– immunophenotype, as opposed to the usual CK7–/CK20+ immunophenotype of primary rectal or intestinal adenocarcinomas [5, 10]. Moreover, TTF1 is highly specific to adenocarcinomas of pulmonary origin, with a positive predictive value of >90% [10]. The expression of GATA3 is strongly associated with estrogen receptor- α expression in breast cancer, and evidence shows that GATA3 may be used to predict the response to hormonal therapy in patients with breast cancer. GATA3 has also been shown to be a novel marker for bladder cancer [12, 13]. CDX2 encodes an intestine-specific transcription factor, expressed in the nuclei of epithelial cells throughout the intestine, from the duodenum to the rectum. The expression of CDX2 has also been documented in primary and metastatic intestinal carcinomas [14]. PAX8 has been observed in the nuclei of normal adult thyroids, follicular adenomas, follicular thyroid cancers, and papillary thyroid cancers but not in undifferentiated thyroid cancers [15]. In our case, the tumor cells were positive for TTF1 and CK7, and their expressions were consistent with those in lung cancer. The lack of GATA3, CDX2, and PAX8 expressions indicated that the small-intestinal tumor did not metastasize from the breast, bladder, intestine, thyroid, or kidney.

Therefore, the small-intestinal tumor was finally diagnosed as a metastasis from a primary lung cancer. When a lung tumor and a small intestinal tumor are found simultaneously, it is difficult to determine which is the primary tumor and which is the metastasis solely on the basis of CT and endoscopic findings. In such cases, pathological examination may be helpful in distinguishing the primary small-intestinal tumor from the metastatic small-intestinal tumor and in detecting the tumor origin.

In conclusion, distinguishing a primary small-intestinal tumor from a metastatic tumor originating from the lung on the basis of the findings of enteroscopic examination, CT, and positron emission tomography is difficult. However, pathological examination has a high value in diagnosing such primary lesions. Therefore, we recommend performing confirmatory pathological examinations to distinguish the primary and metastatic small-intestinal tumors and to detect the tumor origin in cases in which imaging findings alone are inconclusive.

Statement of Ethics

All procedures were carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from the patient for publication of this case report and any accompanying images prior to his death. Written informed consent was also obtained from the next of kin of the patient for publication of the details of their medical case and any accompanying images. This case report was reviewed, and the need for approval was waived by the Ethics Review Committee of Aichi Medical University School of Medicine.

Conflict of Interest Statement

The authors declare no conflicts of interest pertaining to this manuscript.

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Author Contributions

Naotaka Ogasawara and Kunio Kasugai contributed to literature review and manuscript writing. Satoshi Ono, Kazunori Adachi, and Yoshiharu Yamaguchi had managed the patient during hospitalization. Satoshi Ono, Tomoya Sugiyama, Shinya Izawa, and Masahide Ebi performed endoscopic examinations. Yasushi Funaki and Makoto Sasaki contributed to final review of the manuscript. The final version of the manuscript was read and approved by Naotaka Ogasawara, Satoshi Ono, Tomoya Sugiyama, Kazunori Adachi, Yoshiharu Yamaguchi, Shinya Izawa, Masahide Ebi, Yasushi Funaki, Makoto Sasaki, and Kunio Kasugai.

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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