Case Report

Lung Cancer with p53 Expression and a Solitary Metastasis to the Stomach: A Case Report

Motoharu Hamatake, MD, Teruyoshi Ishida, MD, Koji Yamazaki, MD, Hideo Baba, MD, Yoshihiko Maehara, MD, Kenji Sugio, MD, and Keizo Sugimachi, MD

Lung cancer with a solitary metastasis to the stomach occurred in a 65-year-old man, surgically treated for gastric metastasis was followed by pulmonary resection. The gastric metastasis was accompanied by upper gastrointestinal hemorrhage. After total gastrectomy to control this hemorrhage, a left lower lobectomy with a partial resection of the lingular segment and combined resection of the chest wall were done. Histopathological features of both the primary tumor in the left lower lobe and the gastric tumor were poorly differentiated adenocarcinoma, and showed the same immunoreactivities of p53 protein, carcinoembryonic antigen and keratin. These results indicate that the gastric tumor was a metastasis originating from the lung cancer. (Ann Thorac Cardiovasc Surg 2001; 7: 162–5)

Key words: lung cancer, gastric metastasis, p53, hematemesis

Introduction

Lung cancer commonly metastasizes to bones, brain, contralateral lung, adrenals, or liver. However, a metastasis to the gastrointestinal tract is uncommon, hence, is rarely diagnosed during the patient's lifetime and these patients are often asymptomatic. We treated a patient with lung cancer with solitary gastric metastasis, diagnosed by the occurrence of hematemesis. Pulmonary resection was done 21 days after total gastrectomy. The histopathology and immunohistochemical analyses are useful biomarkers to diagnose whether the gastrointestinal lesion is metastasis or not.

Case Report

A 65-year-old Japanese man who was a smoker was admitted to a private clinic with a complaint of back pain and hemosputum, and was treated with antibiotics under the diagnosis of pneumonia. Three months later, he showed an acute hematemesis. Emergency endoscopy revealed a bleeding gastric ulcer and then a blood transfusion and an H_2-receptor antagonist were administered. Since chest X-ray and computed tomography (CT) showed a cavitating mass in the left lower lobe, the patient was referred to Kyushu University Hospital for further evaluation of the lung tumor and for treatment of the bleeding from the stomach.

On admission, the patient had chest pain in the left lateral region, an area where was dullness on percussion with decreased breathing sounds. Laboratory data showed a hematocrit level of 30.3% and hemoglobin of 10.3 g/dl. The serum carcinoembryonic antigen (CEA) level was 36.7 ng/ml. Chest X-ray and CT showed a solitary round mass in the left lower lobe measuring 4.5×3.0 cm, with invasion into the chest wall (Fig. 1). Bronchoscopic brushing cytology indicated the possibility of an undifferentiated carcinoma. Gastroscopy demonstrated a hemorrhagic tumor with massive coagulum on the posterior wall of the mid-stomach. Blood counts revealed progressive anemia with occult blood in the stool.

A laparotomy was done first to control the bleeding, based on a diagnosis of a bleeding gastric ulcer. A hard mass about 3 cm with obvious serosal invasion into the posterior wall of the corpus and enlarged regional lymph nodes were identified, indicating gastric cancer macroscopically. Therefore, total gastrectomy with lymph node

From the Department of Surgery II, Faculty of Medicine, Kyushu University, Fukuoka 812-8582, Japan

Received October 10, 2000: accepted for publication January 22, 2001.

Address reprint requests to Kenji Sugio, MD: Department of Surgery II, Faculty of Medicine, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.

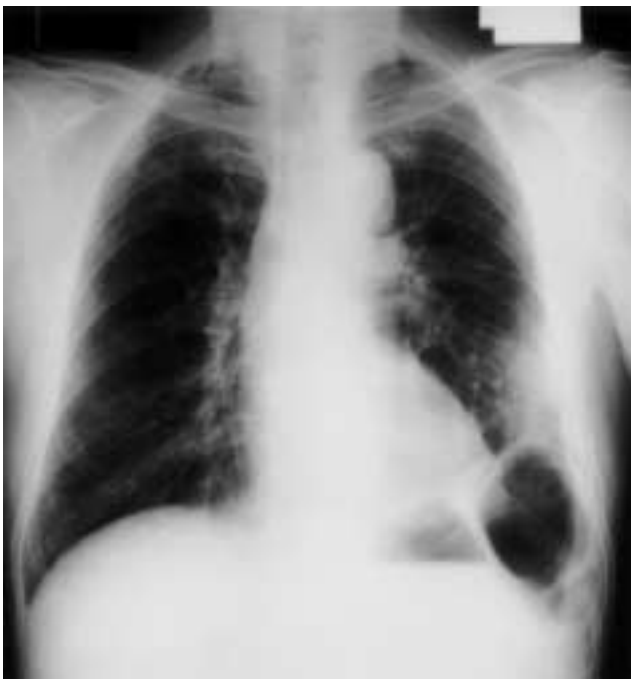


Fig. 1. Chest X-ray shows mass shadow in the left lower lobe.

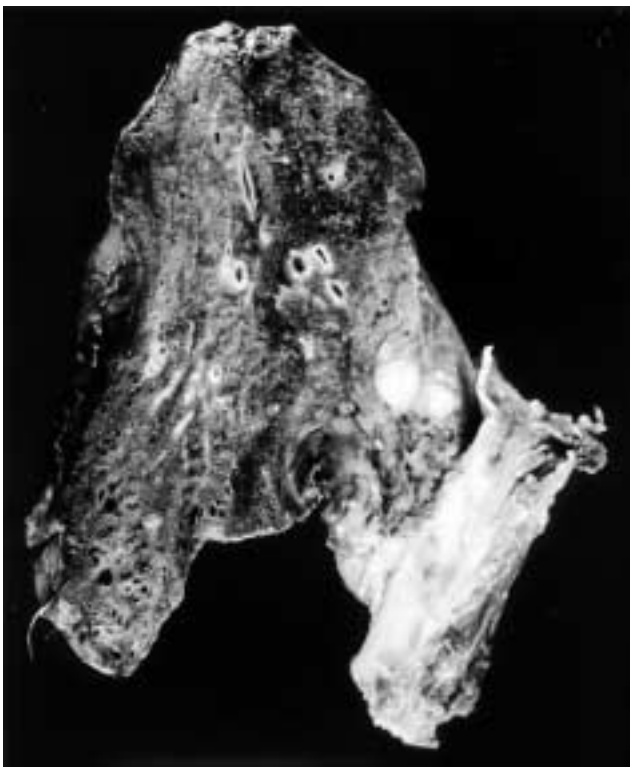


Fig. 2. Gross appearance of the left lower lobe of the lung shows a peripheral solid mass involving the chest wall.

dissection was done. The postoperative course was uneventful. Then 21 days after the gastrectomy, a left lower lobectomy with a partial resection of the lingular segment and combined resection of the chest wall were done, with mediastinal lymph node dissection. Postoperatively the patient did well for approximately three months, but he died of cardiorespiratory failure 126 days after the pulmonary resection.

Gross appearance of the left lower lobe showed a hard mass, 4.2×2.8×1.4 cm, which directly invaded the left lingular segment and chest wall (Fig. 2). Histologically, the tumor of the lung revealed a poorly differentiated adenocarcinoma (Fig. 3a). The tumor tissue had a papillary pattern and undifferentiated diffuse proliferation, findings compatible with those of gastric specimens.

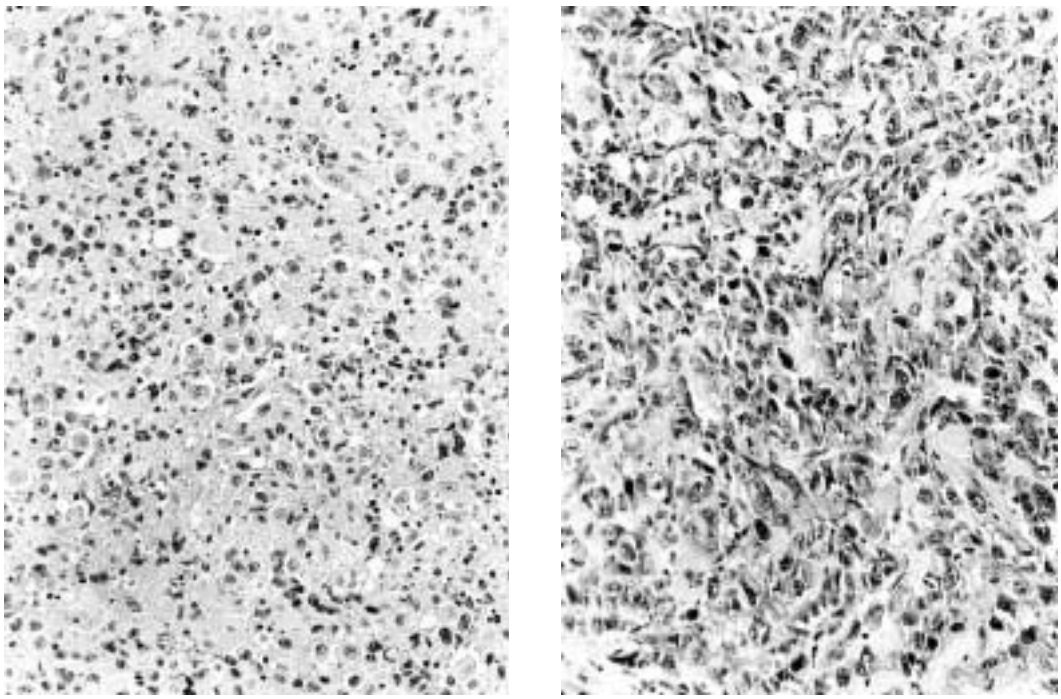
Gross appearance of the gastric lesion showed a hard mass with ulceration of about 3 cm with obvious serosal invasion into the posterior wall of the corpus. The histopathological features of the tumor were an undifferentiated carcinoma. The cells had large nuclei containing prominent nucleoli proliferated in solid nests or diffusely, and partly in a papillary pattern (Fig. 3b). The lesion revealed a submucosal growth pattern with a wide range of necrosis. A few cancer cells contained alcian blue-positive intercellular vacuoles.

The resected specimens were fixed in 10% buffered formalin, dehydrated and embedded in paraffin. Sections 4 μm thick were stained with hematoxylin and eosin, periodic acid-Schiff (PAS) and alcian blue. An immunoperoxidase study was done using the streptoavidin-biotin-peroxidase complex method and antibodies to keratin (CAM5.2, Becton Dickinson, California, USA), carcinoembryonic antigen (Dako, Denmark) and p53 protein (CM-1, Novocastra, Newcastle, UK).

In the immunohistochemical examinations, most tumor cells from both the lung and stomach were positive for the p53 protein, which is exclusively limited to the nucleus (Fig. 4a, b). Epithelial markers, carcinoembryonic antigen and keratin, were present in the both tumors. These positive reactions were diffuse throughout the cytoplasm and the membrane. These findings were shown in both the lung tumor and gastric tumor.

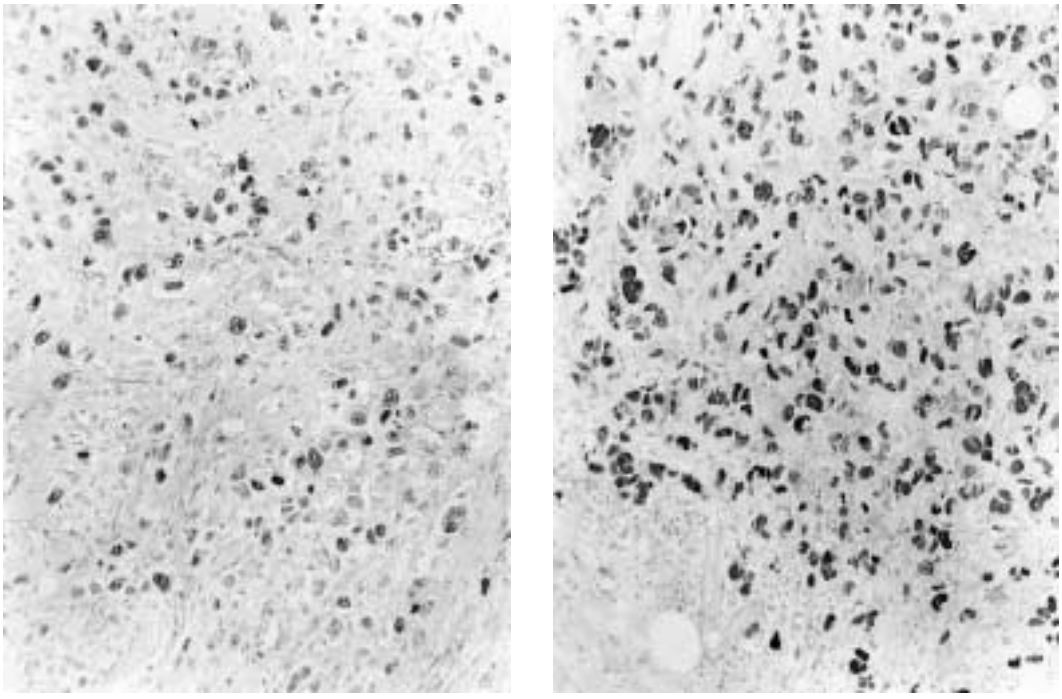
Discussion

Gastrointestinal metastasis from lung cancer is uncommon. The incidence of gastric metastasis in an autopsy series was reported to be 0.5-9%.[1-4] Gastric metastases usually are not detected during the life time of the patient. Hematogenous metastases are generally situated



a b

Fig. 3. Photomicrographic view of a specimen obtained from pulmonary resection shows a papillary pattern and undifferentiated diffuse proliferation, suggesting poorly differentiated adenocarcinoma (a). Photomicrographic view of a specimen obtained from gastrectomy demonstrates undifferentiated diffuse proliferation and partly a papillary pattern (b). (Hematoxylin & eosin stain, ×290)



a b

Fig. 4. Immunohistochemistry for the p53: p53 immuno-positivity can be observed strongly in the nuclei of the tumor cells in both lung cancer (a) and metastatic gastric lesion (b). (Hematoxylin & eosin stain, ×250)

in the submucosa and often remain asymptomatic unless the mucosa becomes involved.[5] However, nausea, vomiting, hematemesis, melena, anemia, epigastric pain, gastric perforation and pyloric obstruction have been reported.[1,3,5-8] Breast cancer, melanoma and lung cancer tend to spread to the stomach most commonly, even with a wide variety of histologic types of lung cancer.[1,2]

Mutations of the tumor suppresser gene p53 lead to neoplastic transformation. The half-time of the mutated p53 protein is longer than that of the wild-type protein and mutations of the p53 gene usually lead to stabilization and accumulation of mutated protein in the tumor cells.[9] Therefore, mutated p53 protein will lead to detectable levels by immunohistochemistry. In the literature, the incidence of p53 immunoreactivity in the lung cancers was reported to be 43-70%.[9-11] For our patient, immunohistochemical studies were done to detect accumulated p53 protein in the pulmonary and gastric tumors, using a polyclonal antibody CM-1 raised against both the wild-type and the mutated p53 proteins. A similar pattern of p53 positivity was noted.

It is difficult to diagnose metastases from a primary lung cancer to the stomach, when the histology is adenocarcinoma. In our patient, the gastric lesion appeared macroscopically as a solitary mass, with ulceration. Pathological findings of the resected specimen of the gastric tumor revealed marked proliferation of cancer cells mainly in the submucosa and were much like those of the lung cancer. Primary gastric cancer is not usually accompanied with a wide range of necrosis, and frequently cause lymphogenous metastases to the lungs and pleural effusion, and rarely cause single or multiple nodules greater than a few millimeters in diameter. In addition, the immunohistochemical examinations which are useful in characterizing biological behavior of tumors, showed a similar staining pattern in both primary and secondary tumors. All these findings suggested that these two tumors were from same origin, and the lung tumor was the primary site.

In general, no surgical therapy is indicated for a distant metastatic lesion originated from lung cancer. However, gastrectomy for cases with gastric metastasis is sometimes indicated, to control bleeding or to avoid stenosis.

References

1. Antler AS, Ough Y, Pitchumoni CS, Davidian M, Thelmo W. Gastrointestinal metastases from malignant tumors of the lung. *Cancer* 1982; **49**: 170–2.
2. Burbige EJ, Radigan JJ, Belber JP. Metastatic lung carcinoma involving the gastrointestinal tract. *Am J Gastroenterol* 1980; **74**: 504–6.
3. Higgins PM. Pyloric obstruction due to metastatic deposit from carcinoma of bronchus. *Cancer J Surg* 1962; **5**: 538–41.
4. Green LK. Hematogenous metastases to the stomach: a review of 67 cases. *Cancer* 1990; **65**: 1596–600.
5. Menuck LS, Amberg JR. Metastatic disease involving the stomach. *Am J Dig Dis* 1975; **20**: 903–13.
6. Fletcher MS. Gastric perforation secondary to metastatic carcinoma of the lung: a case report. *Cancer* 1980; **46**: 1879–82.
7. Rubin SA, Davis M. “Bull’s eye” or “target” lesions of the stomach secondary to carcinoma of the lung. *Am J Gastroenterol* 1985; **80**: 67–9.
8. Telerman A, Gerard B, Van den HB, Bleiberg H. Gastrointestinal metastases from extra-abdominal tumors. *Endoscopy* 1985; **17**: 99–101.
9. Iggo R, Gatter K, Bartek J, Lane D, Harris AL. Increased expression of mutant forms of p53 oncogene in primary lung cancer. *Lancet* 1990; **335**: 675–9.
10. Quinlan DC, Davidson AG, Summers CL, Warden HE, Doshi HM. Accumulation of p53 protein correlates with a poor prognosis in human lung cancer. *Cancer Res* 1992; **52**: 4828–31.
11. Brambilla E, Gazzeri S, Moro D, et al. Immunohistochemical study of p53 in human lung carcinomas. *Am J Pathol* 1993; **143**: 199–210.