


CASE REPORT

Non-small cell lung cancer with gastric metastasis and repeated gastrointestinal bleeding: A rare case report and literature review

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Introduction

The occurrence of gastrointestinal metastasis from lung carcinoma is rare. Compared with non-small cell lung cancer (NSCLC), small cell lung cancer more commonly results in this type of metastasis. Although unusual, gastrointestinal metastases may result in bleeding, obstruction, or even perforation.^{1,2}

Here, we report an unusual case of a patient with pulmonary (NSCLC) without evidence of distant metastasis initially who developed gastric metastasis five months after the initial diagnosis, despite the primary lung cancer showing partial response to radiotherapy and chemotherapy.

Case report

A 55-year-old man with a history of long-term smoking for 30 years (one pack of cigarettes per day for an average

Abstract

The occurrence of gastrointestinal metastasis from lung carcinoma is rare. Compared with non-small cell lung cancer (NSCLC), small cell lung cancer more commonly results in this sort of metastasis. Here, we report an unusual case of NSCLC initially without evidence of distant metastasis that developed into gastric metastasis five months after the initial diagnosis, despite the primary lung cancer having a partial response to radiotherapy and chemotherapy. Serial radiological examinations and endoscopic biopsies of the gastric tumor confirmed that it was a metastatic carcinoma originating from the lung. The patient received a total gastrectomy for gastric metastasis due to repeated gastrointestinal bleeding.

of 30 years) was diagnosed with right upper lung NSCLC (T3N0M0). The initial tumor size was 6.5 cm in size (Fig 1a). The initial presentation included chronic dry cough and dysphagia for three weeks, accompanied by poor appetite, general malaise, dizziness, and body weight loss of four kilograms within one month. The patient underwent computed tomography (CT)-guided biopsy and pathological examination revealed poorly differentiated NSCLC. Immunohistochemistry staining was negative for thyroid transcription factor-1 (TTF-1), p40, CD56, synaptophysin, chromogranin A, CD5, CD117, NUT and TdT. By means of whole-body CT examination, there was no evidence of distant metastasis in any sites, including the brain.

The patient received concurrent chemoradiotherapy (CCRT) in the six months following diagnosis, including 6600 cGy in 30 fractions to the lung tumor, one cycle of cisplatin and taxotere, which was shifted to two cycles of

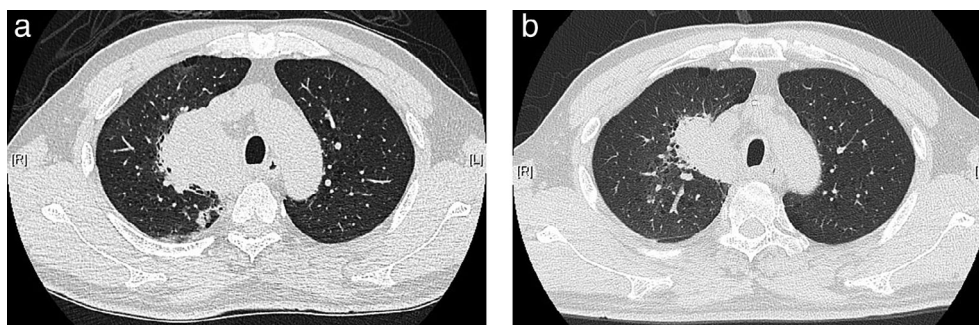


Figure 1 (a) The CT scan shows right upper lung non-small cell lung carcinoma (NSCLC) (T3N0M0). The initial tumor size was 6.5 cm. (b) Five months after initial diagnosis, computed tomography (CT) demonstrated partial response (PR) to CCRT, and the tumor had decreased in size to 3.5 cm in diameter.

IV vinorelbine and cisplatin and two cycles of oral vinorelbine and cisplatin due to acute pneumonitis because of hypersensitivity to taxotere. A subsequent CT scan of the chest five months after the initial diagnosis demonstrated partial response (PR) to CCRT, and the tumor size had decreased to 3.5 cm in size (Fig 1b).

However, approximately five months after the initial diagnosis of lung cancer, he suffered intermittent tarry stools. Indeed, the previous CT scan that revealed PR of the primary lung cancer had shown a gastric tumor (4.2 cm in size) (Fig 2a). However, the patient refused upper gastrointestinal endoscopy examination until seven months after diagnosis, when he visited the emergency department reporting tarry stools and mild dyspnea. A hemogram showed a significant decrease in hemoglobin level which was 5.0 g/dL, compared with the 9.3 g/dL value obtained half a month previously. Upper gastrointestinal endoscopy showed a massive (more than 5 cm) bleeding ulcerative mass in the anterior wall of the gastric high body (Fig 2b). A biopsy revealed poorly differentiated carcinoma. The cytomorphological histopathological features of this gastric tumor were similar to those of lung cancer, suggesting metastasis of lung carcinoma. Immunohistochemically, the tumor was negative for

CDX2, MUC5AC and MUC2. A CT scan at the same time revealed a bulky gastric mass at the greater curvature side of the high body of 10.9 cm in size with left gastric and splenic hilar lymphadenopathy (Fig 2c).

The patient received endoscopic hemostasis on two occasions, transarterial embolization (TAE) on one occasion, and radiotherapy for the stomach tumor (2400 cGy in seven fractions). However, his tarry stools persisted. Therefore, he received palliative total gastrectomy, cholecystectomy for gallstones, and feeding jejunostomy. During the operation, the perigastric lymph nodes were tightly attached to the greater and lesser curvatures; consequently, D1 lymph node dissection was inevitably performed.

The postoperative pathology showed poorly differentiated carcinoma with a volcano-like growth pattern, and the surface of the mass was broken (Fig 3a). Repeat immunohistochemistry analysis confirmed that the tumor was negative for TTF-1, CDX2 and MUC5AC (Fig 3b). Two out of 25 perigastric lymph nodes were positive for metastasis. The patient received the first cycle of palliative chemotherapy consisting of pemetrexed and carboplatin one month after the operation.

No more gastrointestinal bleeding occurred after total gastrectomy, and the patient received a total of three cycles

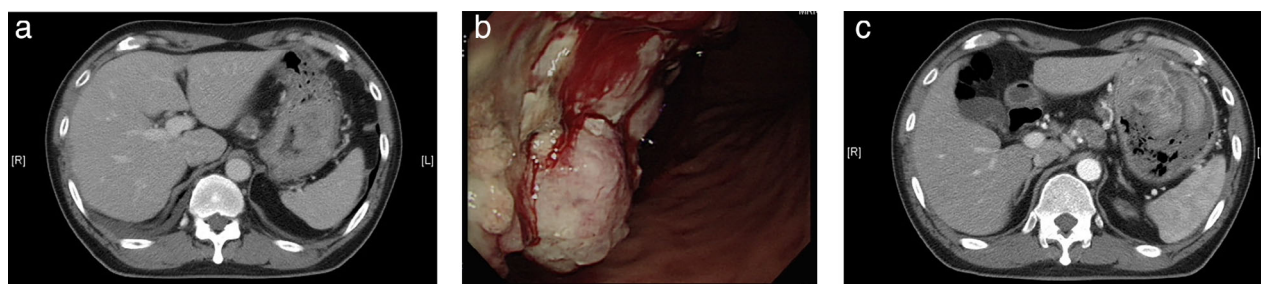


Figure 2 (a) Five months after the initial diagnosis of lung cancer, the computed tomography (CT) scan that revealed the partial response (PR) of the primary lung cancer also revealed a gastric tumor 4.2 cm in size. (b) Upper gastrointestinal endoscopy showed a massive (more than 5 cm), bleeding ulcerative mass in the anterior wall of the gastric high body. (c) Seven months after diagnosis, the CT scan revealed a bulky gastric mass at the greater curvature side of the high body 10.9 cm in size with left gastric and splenic hilar lymphadenopathy.

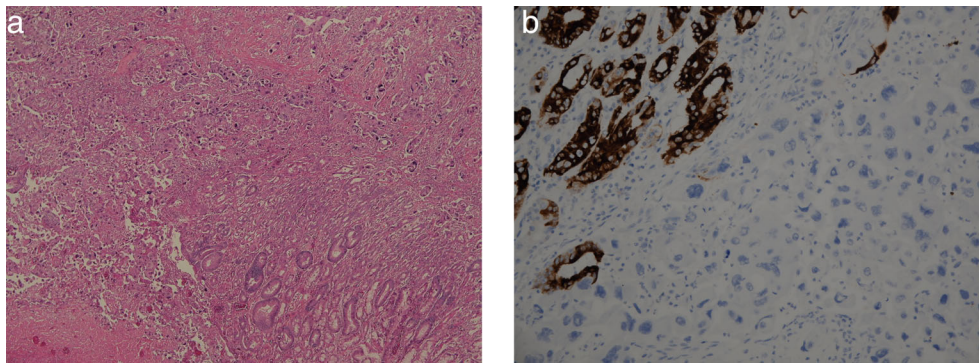


Figure 3 (a) The poorly differentiated tumor cells infiltrated underneath the mucosa and caused breaking of the surface. (b) The tumor lacked MUC5AC immunoreactivity, whereas normal gastric glands showed strong MUC5AC expression.

of palliative chemotherapy consisting of pemetrexed and carboplatin. Three months after the operation, the patient died of disease progression with respiratory failure.

Discussion

Primary lung cancer frequently metastasizes to the brain, liver, adrenal glands, and bones. In NSCLC, metastasis to soft tissues and the kidney, pancreas, spleen, peritoneum, intestine, bone marrow, eye, ovary, thyroid, heart, breast, tonsil, and nasal cavity have all been reported and tend to indicate a poor outcome.^{3,4} The occurrence of gastrointestinal metastasis from lung carcinoma is rare. Fujiwara *et al.* reported 0.58% gastrointestinal metastasis of NSCLC in a series.⁵ In this series, nine out of 1552 patients were diagnosed with NSCLC who received surgical treatment, and only one (0.06%) patient had gastric metastasis.

The most common primary cancer that metastasizes to the gastrointestinal tract is breast cancer.^{3,6,7} It has been reported that approximately 6% of women with advanced breast cancer developed gastric metastasis, especially those with lobular carcinoma.^{8–10} Other primary tumors that lead to gastric metastasis include rectal and endometrial cancers, according to a cohort published in 2019.³

Gastric metastasis is uncommon, and autopsy results have reported the incidence to range between 0.2 and 1.7% in different studies.^{11,12} Similar to this case, it has been reported that the median time between the diagnosis of lung cancer and the detection of gastric metastasis is five months.¹² Lung cancer with gastric metastasis tends to occur in male smokers aged between 45–90 years.^{13–16} Some reports have claimed that squamous cell carcinoma is the most common subtype of metastasis,^{1,17,18} but others have claimed that primary lung adenocarcinoma is the most common, followed by squamous cell carcinoma, small cell lung cancer, and pleomorphic carcinoma.¹² The

cases of gastric metastasis from primary lung squamous cell carcinoma previously reported in the English literature are summarized.

Lung cancer is hypothesized to result in gastric metastasis via swallowing sputum rich in cancer cells, which subsequently travel into the digestive tract; this mechanism is especially relevant in smokers who are more susceptible to gastric mucosal damage than nonsmokers.¹⁹ However, the validity of this hypothesis still needs to be confirmed.

Endoscopy with biopsy provides a diagnostic opportunity, especially in patients with gastrointestinal bleeding. Immunohistochemistry assists in identifying the origin of the primary tumor. Positive staining for cytokeratin 7 (CK-7) is consistent with either a gastrointestinal or pulmonary origin of the tumor, and positive staining for CK-14 and CK-18 suggests squamous cell carcinoma and adenocarcinoma, respectively. In addition, positive staining for TTF-1 indicates a thyroid or lung tumor origin.⁹ In our case, given that lung cancer was diagnosed five months before the gastric tumor presented and repetitive systematic radiological examinations provided no evidence of primary tumors at other sites, including the breast and rectum, we concluded that our patient's gastric tumor was a metachronous metastatic tumor originating from pulmonary NSCLC. Chemotherapy is the most important option in the treatment of recurrent or metastatic NSCLC. However, it has been previously reported to increase the risk of gastric bleeding or perforation, which may have resulted from tumor necrosis following chemotherapy.²⁰ Complete radical resection with metastasectomy for isolated metastasis may be beneficial. Ying *et al.* and Nemeto *et al.* reported aggressive surgical treatment for NSCLC with gastric metastasis, including lobectomy for primary pulmonary tumors and lymphadenectomy and gastrectomy for gastric metastasis.^{18,19} However, since only a small number of cases have been reported, the effect of aggressive surgery on long-term oncological outcome is still uncertain. In patients with intractable bleeding, perforation, or gastric

outlet obstruction, palliative resection is still indicated. In our patient, intractable bleeding deterred the patient from further chemotherapy and contributed to anemia; consequently, surgery was inevitable.

The prognosis of gastric metastasis in pulmonary carcinoma has been reported to be very poor. Kim *et al.* reported that the median survival time in pulmonary carcinoma with gastrointestinal metastasis was 94.5 days, ranging from 12 to 1907 days.²¹ Our patient had gastric metastasis three months before palliative gastrectomy and died three months thereafter, with a total survival after the diagnosis of gastric metastasis of six months (180 days).

In conclusion, lung cancer with gastric metastasis is rare and is reported less commonly in NSCLC than small cell lung cancer, but still occurs. A diagnosis can be made by means of systemic radiological examinations and immunohistochemistry studies. Surgical resection should be considered in patients with intractable bleeding, obstruction, or perforation and also be considered in those with resectable primary lung cancer with isolated gastric metastasis.

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Disclosure

The authors confirm that there are no conflicts of interest.

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