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Gastric and colonic metastases from primary lung adenocarcinoma: A case report and review of the literature

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Abstract. Lung cancer is one of the leading causes of cancer-related mortality worldwide. Gastrointestinal metastasis from primary lung cancer is rare. Only a few reports have been published and the majority of described metastatic sites involved the small intestine. In the present study, we report the first case of primary lung adenocarcinoma with both gastric and colonic metastases. We also review the published literature of primary lung cancer with gastrointestinal metastasis.

Introduction

Lung cancer is one of the most prevalent cancers in Taiwan and also plays a leading role in cancer-related mortality. The major histological cell types include adenocarcinoma, squamous cell carcinoma, small cell carcinoma and large cell carcinoma. Advanced lung cancer may spread to extrathoracic sites, the most frequent sites being the liver, adrenal glands, bones and brain. Gastrointestinal (GI) metastasis from primary lung cancer is rare, although it is a recognized phenomenon in the literature. Certain case reports have been published (1-5), including cases of symptomatic GI metastasis as well as asymptomatic cases discovered unintentionally. When patients have malignant lung and GI lesions at the same time, the primary site among these lesions is often difficult to establish, particularly when both the lung and GI lesions have the same histologic cell type. It is essential to make a differential diagnosis of the primary origin among these lesions since these results may lead to a different choice of treatment.

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Case report

A 41-year-old female fish vendor with a smoking history presented at Chang Gung Memorial Hospital, Keelung, Taiwan, with diffused abdominal pain and fullness. Written informed consent was obtained from the patient prior to the study. The patient had also had a chronic cough for 5 months. An abdominal computed tomography (CT) scan was performed to rule out peritonitis, and this revealed mild ascites and peritoneal carcinomatosis. Panendoscopy revealed a 1.5-cm tumor with slight central ulceration in the patient's stomach (Fig. 1A). Colonfibroscopy was performed which revealed a 1-cm tumor with central ulceration in the transverse colon (Fig. 1B). Both gastric and colonic biopsies revealed an adenocarcinoma pattern using hematoxylin and eosin (H&E) staining (Fig. 2B-D). CT of the chest was later performed which revealed a left lower lobe tumor. Bronchoscopy was arranged and transbronchial biopsy was performed from LB 8 and 9. The transbronchial biopsy revealed adenocarcinoma (Fig. 2A). Tissue from biopsies including the stomach, colon and lung underwent immunohistochemical (IHC) staining (Fig. 3), from which lung cancer origin was diagnosed. An EGFR mutation test including L858R, exon 19 deletion, T790M, G719A, G719C and L861Q was negative. A bone scan also revealed multiple active bone lesions.

Following the diagnosis, the patient received chemotherapy with cisplatin (70 mg/m^2) and docetaxol (70 mg/m^2) on two occasions then switched to cisplatin (80 mg/m^2) and vinorelbine (30 mg/m^2). A brain MRI was performed when the patient complained of a headache which revealed both hematogenous and leptomengeal brain metastasis with mild obstructive hydrocephalus. The cytology of CSF also demonstrated positivity for malignant cells. The patient was administered targeted therapy with erlotinib 150 mg QD. A subsequent chest/abdominal CT scan revealed that the tumor was decreasing in size. A brain MRI revealed complete regression after 6 months of erlotinib treatment. However, after 11 months of erlotinib treatment, the patient complained of nausea, vomiting and headaches. A brain MRI then revealed marked progression of hydrocephalus and for this reason a ventriculoperitoneal (VP) shunt was implanted by a neurosurgeon. Unfortunately, the patient developed respiratory distress 2 months later due to

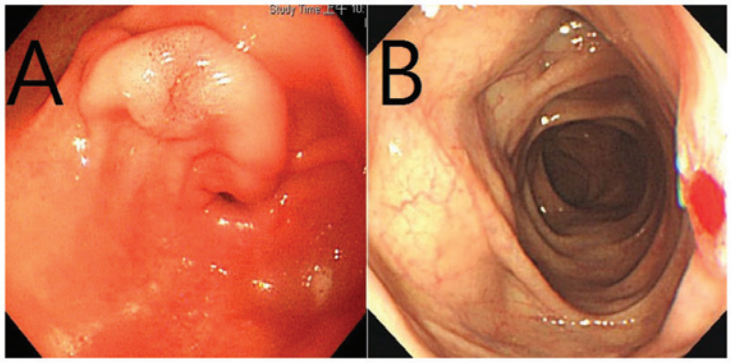

Figure 1. (A) Panendoscopy revealed a gastric tumor and (B) colonfibroscopy revealed an ulcerative tumor.

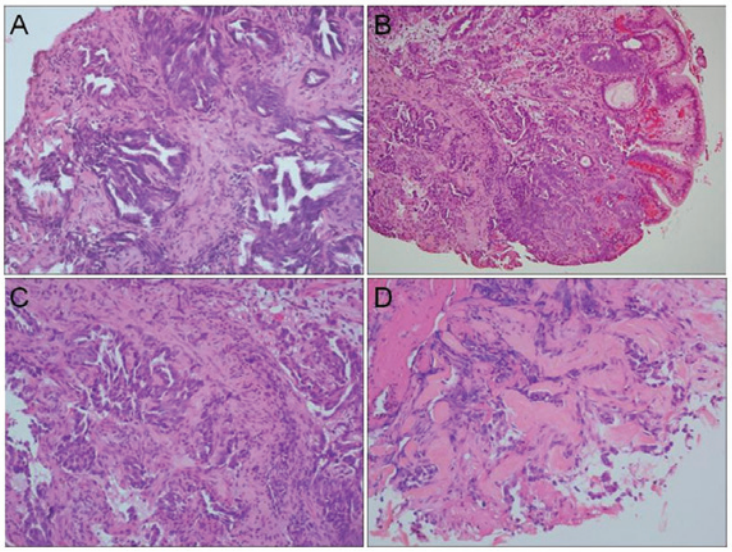

Figure 2. With hematoxylin and eosin (H&E) staining, (A) biopsy of primary lung tumor and (B and C) gastric biopsy show infiltrating neoplastic cells with similar glandular patterns and morphology. (D) Colonic biopsy shows scattered cauterizing hyperchromatic neoplastic cells.

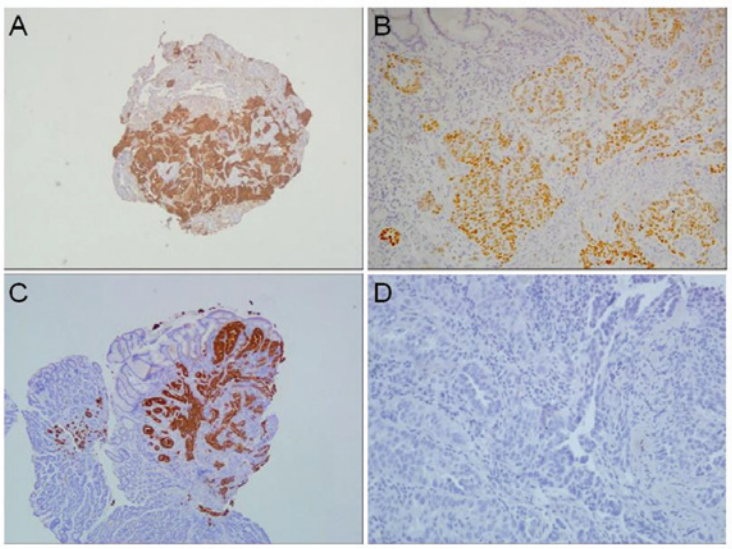

Figure 3. (A) Primary lung tumor shows diffuse strong TTF-1 nuclear immunostaining. Metastatic adenocarcinoma in the stomach shows positive (B) TTF-1, (C) CK7 and (D) negative CD20 immunostaining.

the progression of lung cancer. She succumbed to the disease 15 months after diagnosis.

Discussion

In women with ascites and peritoneal carcinomatosis, the most common origin is ovarian, colon, gastric or pancreatic cancer. In the case described above, three sites of adenocarcinoma were identified. Therefore a differential diagnosis including colon, gastric and lung adenocarcinoma should be considered. Synchronous lung and colon cancer has previously been reported (6). The possibility of synchronous lung, gastric and colon cancer should also be kept in mind. Different anti-malignancy strategies, including chemotherapy or targeted therapy, should be used depending on the different origins of the cancer cell line. The regimen for treating these three types of cancer is quite different. The response and prognosis are also different.

In the H&E-stained sections of biopsied tissue in the present case, both the primary lung tumor and metastatic gastric tumor revealed similar glandular patterns infiltrating in the stroma. However, only a few cauterized tumor cells were observed in the colonic biopsy (Fig. 2).

TTF-1 is a 38-40 kD transcription factor member of the NFx2 family which is normally expressed in thyroid and pulmonary epithelial cells (7). It is expressed in the nuclei of 60-75% of lung adenocarcinoma cases but seldom expressed in gastric and colonic adenocarcinoma (8). CK7 is expressed in both pulmonary and intestinal adenocarcinoma (9); but CK20 is expressed in 80% of gastric adenocarcinoma and 95% of colonic adenocarcinoma (10). In this case, the tumor cells in the gastric biopsy showed positive TTF-1 nuclear and CK7 staining in the IHC study, which is consistent with pulmonary origin. The possibility of gastrointestinal origin was excluded following the negative results of CK20 and CDX2 staining. The tumor cells of the lung and colonic biopsy both demonstrated positive TTF-1 staining. According to the above IHC results, the final diagnosis of the neoplastic glands was pulmonary origin. Therefore, the patient was treated as having non-small cell lung cancer. Initially, she had a positive response following targeted therapy with erlotinib. Her time to progression reached 6 months. Clinically, the patient's prognosis was also compatible with lung cancer.

GI tract metastasis from primary lung cancer has been described in certain previous case reports. The metastatic sites described have included the stomach (1-5), small bowel (11-13), appendix (14), colon (15) and anus (16). The clinical findings have included epigastric pain (9), anemia (17,18), upper gastrointestinal bleeding (7,19), bowel obstruction (11,13,20), bowel perforation (5,11), peritonitis (17) and polyp formation (16). These symptoms may require surgical intervention or palliative therapy, including chemotherapy or targeted therapy. Unfortunately, the prognosis was poor in these patients.

Certain patients were asymptomatic and the finding of GI tract metastasis was incidental. The actual incidence of non-small cell lung cancer metastasizing to the GI tract is uncertain. Autopsy reports have suggested that the prevalence is approximately 4.7-14% (12,21). Studies from Italy (22) and Taiwan (23) have suggested that 0.5-1.7% of patients with primary cancer developed GI tract metastasis. The cell type in Taiwan was squamous cell carcinoma (3/6) in the majority of cases, while large cell carcinoma (10/18) was dominant in Italy. The average time between the discovery of GI metastasis and mortality was only 130.3 days (range, 23-371 days). This may be due to multiple metastases. Compared with other lung cancer patients who developed GI tract metastasis, our patient lived considerably longer. In this patient, the survival time following diagnosis was 461 days. We presume that her anti-malignant therapy was effective during the first 12 months. Erlotinib demonstrated a definite significant benefit for this patient although the EGFR mutation test was negative. In cases such as this, the differential diagnosis of metastasis of lung cancer origin or GI malignancy is essential. Adequate treatment is dependent on a correct diagnosis.

Positron emission tomography (PET)-CT has been proven useful in the diagnosis of GI cancer (24). It is effective for the detection of distant metastasis except in the case of brain and liver metastasis (25). Certain studies have also revealed asymptomatic GI metastasis from lung cancer by PET-CT (26). A preoperative PET-CT may give a clinical indication of GI metastasis from lung cancer and improve the correctness of staging and further treatment. Therefore, PET-CT is crucial prior to the treatment of primary lung cancer.

In conclusion, GI tract metastasis of lung cancer is rare but well-documented. The prevalence rate is 0.5-14% according to clinical and autopsy reports. The common metastatic sites are the stomach, small intestine or colon. For the patient, both gastric and colon metastasis of lung cancer is very rare. Symptomatic GI metastasis should be treated by earlier surgical intervention or medical treatment. PET-FDG may provide the potential to increase the diagnosis of occult distant metastasis. If appropriate treatment can be provided earlier, these patients may have a better quality of life and also longer survival. The present case study is a good example of this. We hope that by sharing our experience we increase the confidence in the treatment of GI metastasis of primary lung cancer for both physicians and patients.

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