

Case Series Analysis of Diagnosis and Treatment of Gastrointestinal Metastasis in Lung Cancer Patients

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Objective: This study was designed to investigate the clinical, pathological, endoscopic, and imaging characteristics of gastrointestinal metastasis in patients with lung cancer.

Methods: The clinical data of 20 patients with primary lung cancer with gastrointestinal metastasis.

Results: This study included sixteen men and four women, ranging in age from 31 to 75 years. The time interval from the diagnosis of lung cancer to the detection of gastrointestinal metastasis ranged from 13 to 142 months. The most common sites of metastasis were the small intestine (eight cases), colon (four cases), and upper gastrointestinal tract (eight cases). The major symptoms included obstruction, perforation, abdominal pain, abdominal distension, anorexia, and anemia. The predominant pathological type was poorly differentiated adenocarcinoma (seventeen cases). A single ulcer was mostly seen on endoscopy, and some cases showed a slight depression of the intestinal wall. The CT and PET-CT scan revealed bowel wall thickening, intraluminal polypoid masses, and intestinal perforation.

Conclusion: Gastrointestinal metastasis of lung cancer is mainly observed in the small intestine, colon, and stomach, and is often detected when severe complications such as gastrointestinal obstruction and perforation occurred. Regular evaluation of gastrointestinal conditions during lung cancer diagnosis and treatment is recommended to improve the diagnostic accuracy and prevent misdiagnosis.

Keywords: lung cancer, gastrointestinal tract, metastasis, endoscopic biopsy

Introduction

Lung cancer is currently one of the malignant tumors with the highest morbidity and mortality in the world. The common metastatic sites of lung cancer are various, including the brain, bone, liver, and adrenal gland. However, gastrointestinal metastasis is relatively rare. Notably, gastrointestinal metastasis is mostly reported as case reports in the literature, with few large-scale reports. Therefore, there are different reports on the incidence of gastrointestinal metastasis of lung cancer. The clinical incidence of gastrointestinal metastasis is approximately 0.3%–1.77%,^{1–3} but the incidence found at autopsy can be as high as 11.9%–13.7%.^{4,5} According to the literature, gastrointestinal metastasis of lung cancer can occur in the stomach,⁶ duodenum,⁷ biliary tract,^{8,9} colon,¹⁰ perianal and rectal regions,¹¹ and small intestine,^{4,12} and even in multiple sites at the same time.¹³ Of them, small intestine, colon, and stomach are the common sites of metastasis. Gastrointestinal metastasis of lung cancer is asymptomatic in the early stages, and most cases are detected when severe gastrointestinal complications occur. In this study, 20 cases of primary lung cancer with gastrointestinal metastasis were retrospectively analyzed. The clinical understanding of gastrointestinal metastasis of lung cancer was enhanced by summarizing the clinical manifestations, pathological results, and the interval between the diagnosis of lung tumors and the detection of metastasis detection, thus improving the early diagnosis and treatment.

Materials and Methods

General Information

A total of 20 patients with lung cancer with gastrointestinal metastasis were hospitalized at Guangdong Provincial People's Hospital from January 2013 to December 2023. There were sixteen males and four females with ages ranging from 31 to 75 years. The basic information and medical records of patients were detailed, and the imaging data of preoperative and postoperative follow-up were complete. All patients were informed about the surgical process and signed the informed consent form. The data of each case were retrospectively analyzed, and the study subjects were determined based on the inclusion and exclusion criteria. The observed markers included the site and pathological type of primary lung cancer, the clinical manifestation and site of gastrointestinal metastasis, diagnostic bases such as the imaging results, gastrointestinal endoscopy results and surgical outcomes, and the time interval between the diagnosis of lung cancer and the detection of gastrointestinal metastasis.

Inclusion Criteria

The patients (1) were aged ≥ 18 years; (2) were diagnosed with lung cancer by imaging and pathology of biopsy/surgical specimen (the 8th edition of the American Joint Committee on Cancer); and (3) had the pathology of the gastrointestinal metastasis of lung cancer confirmed to be consistent with that of the primary lung cancer through gastrointestinal endoscopic biopsy or surgical resection of gastrointestinal lesions.

Exclusion Criteria

The pathology of the gastrointestinal lesions could not be confirmed to be consistent with the pathology of primary lung cancer.

Treatment Methods

According to the specific pathological type and Tumor, Node, Metastases staging, the study subjects were treated with multidisciplinary comprehensive treatment for lung cancer including surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapy. The gastrointestinal lesions were primarily treated symptomatically. Surgical treatment was performed based on the condition of the patient if severe complications such as gastrointestinal obstruction and perforation occurred.

Evaluation Criteria

The imaging, endoscopy, and pathological results were evaluated and reviewed by two specialist physicians, respectively.

Statistical Analysis

The data analysis was conducted using the SPSS 22.0 statistical software. The Chi-square test was used to compare the enumeration data. $P < 0.05$ was considered statistical significance.

Results

Clinical Data

Of the 20 patients, there were four cases in the left upper lung, four in the lower left lung, ten in the upper right lung, and two in the lower right lung. The time interval between the diagnosis of lung cancer and the detection of gastrointestinal metastasis ranged from 13 months to 142 months.

Gastrointestinal Symptoms, Metastasis Sites, and Diagnosis

Among the 20 patients, the sites of gastrointestinal metastasis were various. Of them, there were eight cases in the small intestine (five in the jejunum, two in the ileum, and one in the jejunum and ileum), three cases in the colon (one in the right colon, one in the transverse colon, and one in the left colon), and one case in the small intestine combined with a left colon. Besides, eight cases were observed in the upper gastrointestinal metastasis, including seven in the stomach and one

Table 1 Summary of Immunohistochemistry Staining Profiles

| Case Type | CK7 | TTF-1 | CK20 | CDX-2 | Syn | CgA | CD56 | Other Markers |
|-------------------------|------|-------|------|-------|-----|-----|------|---|
| Adenocarcinoma (n=17) | ++++ | ++++ | — | — | NA | NA | NA | - |
| Small Cell Carcinoma 1 | + | ++ | - | - | ++ | - | ++ | SSTR2 (+), Ki67 (80%+) |
| Small Cell Carcinoma 2 | - | +++ | - | - | +++ | - | +++ | Ki67 (90%+), P63 (-), CK5/6 (-), CAM5.2 (-) |
| Adenosquamous Carcinoma | +++ | + | - | - | NA | NA | NA | P63 (sqCC+), P40 (sqCC+), CAM5.2 (+++) |

Notes: "+" indicates a positive staining result, with more "+" symbols representing stronger or more widespread positivity. "-" indicates a negative staining result. "NA" indicates that the marker was not applicable or not assessed in that particular case.

in the stomach combined with duodenum. Regarding gastrointestinal symptoms, obstruction was observed in eight cases and perforation in two cases. The sites of these symptoms occurred in the small intestine, which was confirmed by surgical pathology. A total of two cases of abdominal pain with severe anemia occurred in the jejunum (confirmed by pathological biopsy of enteroscopy) and the transverse colon (confirmed by pathological biopsy of colonoscopy), respectively. Additionally, seven cases occurred in the upper gastrointestinal were presented with various symptoms, including abdominal pain, abdominal distension, and anorexia, which was confirmed by the pathological biopsy of gastroscopy. Furthermore, one case occurred in the stomach had no obvious gastrointestinal symptoms, which was discovered by follow-up positron emission tomography (PET)/computerized tomography (CT) and confirmed by the pathological biopsy of gastroscopy.

Pathological Diagnosis Data of Gastrointestinal Metastasis of Lung Cancer

There were seventeen cases of adenocarcinoma in the 20 patients, all of which were poorly differentiated. The immunohistochemical (IHC) results were summarized in Table 1. Notably, cytokeratin (CK) 7 was positive in sixteen cases, and thyroid transcription factor 1 (TTF-1) was positive in thirteen cases. However, CK20 and caudal-type homeobox 2 (CDX-2) were negative in all cases (Figure 1A).

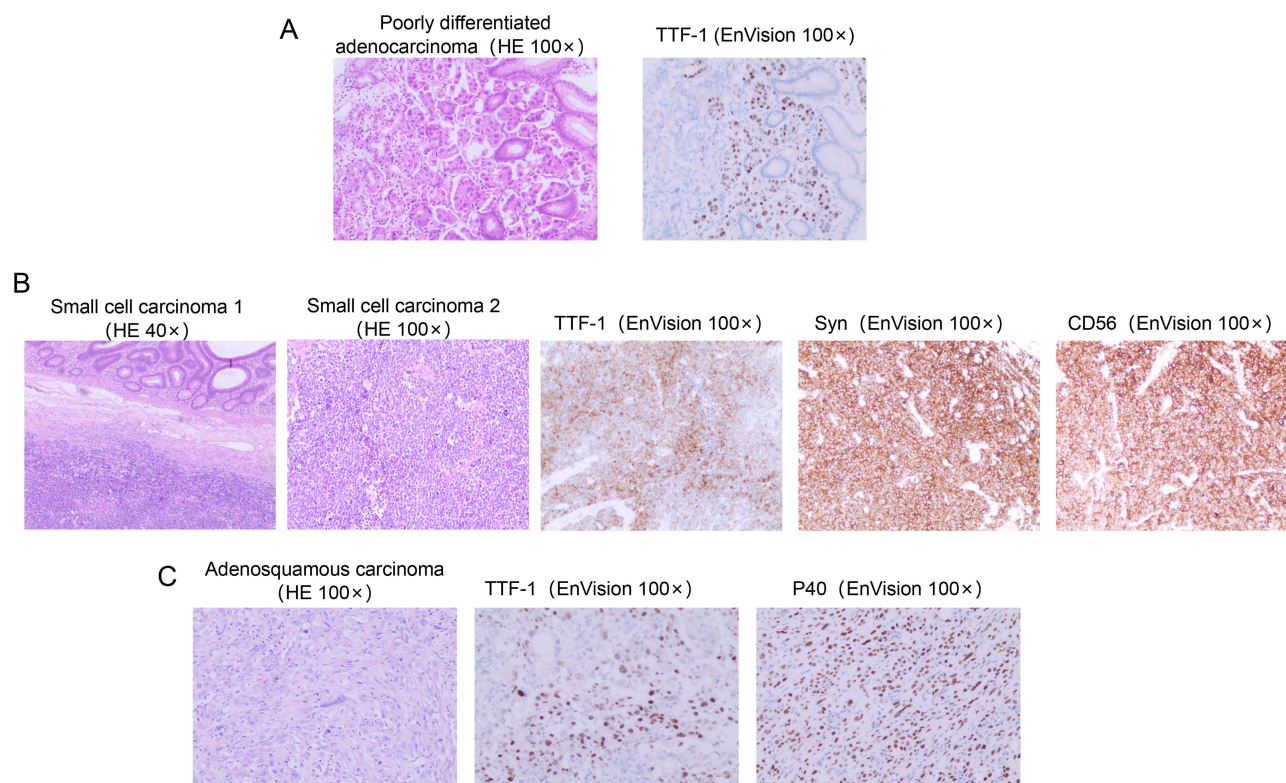


Figure 1 Histopathological characteristics and immunohistochemical phenotype of patients with lung cancer with gastrointestinal metastasis (A) Hematoxylin and eosin (H&E) staining of adenocarcinoma (100x magnification) and immunohistochemistry (100x magnification). (B) H&E staining of small cell carcinoma (40x, 100x magnification) and immunohistochemistry (100x magnification). (C) H&E staining of adenosquamous carcinoma (100x magnification) and immunohistochemistry (100x magnification).

For small cell carcinoma (two cases), the IHC results (Figure 1B) were as follows:

Case 1: CK7 (+), CK20 (-), TTF-1 (++), CDX-2 (-), synaptophysin (Syn) (++), chromogranin A (CgA) (-), neural cell adhesion molecule 1 (CD56) (++), somatostatin receptor 2 (+), Ki67 (approximately 80%+).

Case 2: Syn (+++), CgA (-), CD56 (+++), CK5/6 (-), CK7 (-), TTF-1 (+++), CAM5.2 (-), tumor protein 63 (P63) (-), Ki67 (90%+).

There was one case of adenosquamous carcinoma, with the following IHC results: CK (+++), CAM5.2 (+++), CK7 (+), CK20 (-), P63 (squamous cell carcinoma+), P40 (squamous cell carcinoma+), TTF-1 (adenocarcinoma+) (Figure 1C).

The above results indicated that most tumor markers, such as CK7 and TTF-1, were positive in most cases, while CK20 and CDX-2 were less expressed, suggesting that these gastrointestinal metastases primarily originated from primary lung tumors.

Endoscopic Data

The endoscopic lesions confirmed by one enteroscopy and one colonoscopy showed deep, large depressed ulcers with a black eschar in eight patients with upper gastrointestinal metastasis of lung cancer (Figure 2A). Of them, one case occurred simultaneously in the descending portion of the duodenum, presenting as a single, depressed ulcer with dirty eschars (Figure 2B). Three cases showed only localized flat elevated or slightly depressed areas under gastroscopy (Figure 2C). The endoscopic findings in five cases exhibited single, irregular, deep and large, depressed ulcers covered with dirty eschars, primarily located in the gastric body (Figure 2D and E).

Imaging Examination Data

The CT and PET-CT signs of gastrointestinal metastasis of lung cancer included localized thickening of the bowel wall, intraluminal polypoid masses, localized swollen lymph nodes, intussusception, and intestinal perforation (Figure 3).

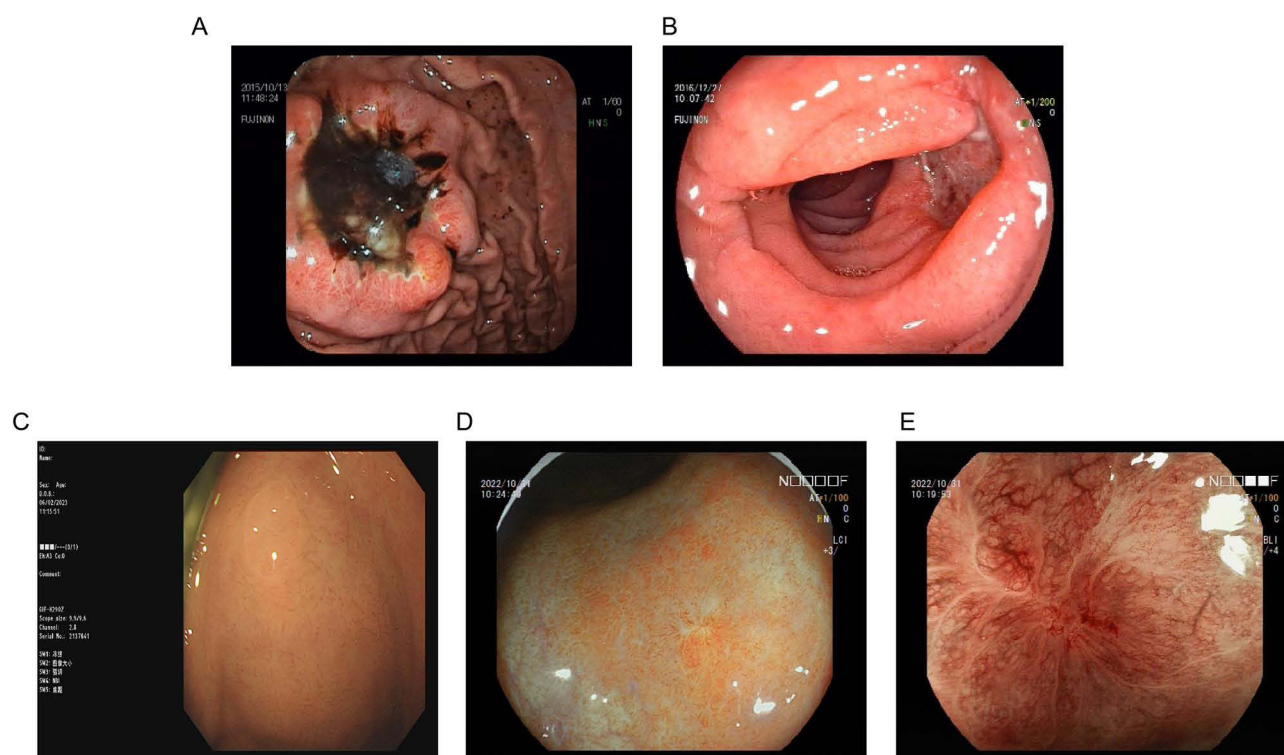


Figure 2 Endoscopic findings of upper gastrointestinal metastasis of lung cancer (A) Large depressed ulcers with black eschars at the junction of the gastric fundus and body. (B) Depressed ulcers with dirty eschars in the descending portion of the duodenum. (C) Change of localized flat elevated area in the gastric fundus. (D) A slightly depressed stellate change in the middle of the gastric angle, with an absent boundary line and irregular thickening of microvessels observed by magnifying endoscopy with narrow-band imaging. (E) Irregular, erythematous mucosal changes with subtle nodularity observed in the gastric antrum, suggesting possible metastatic infiltration.

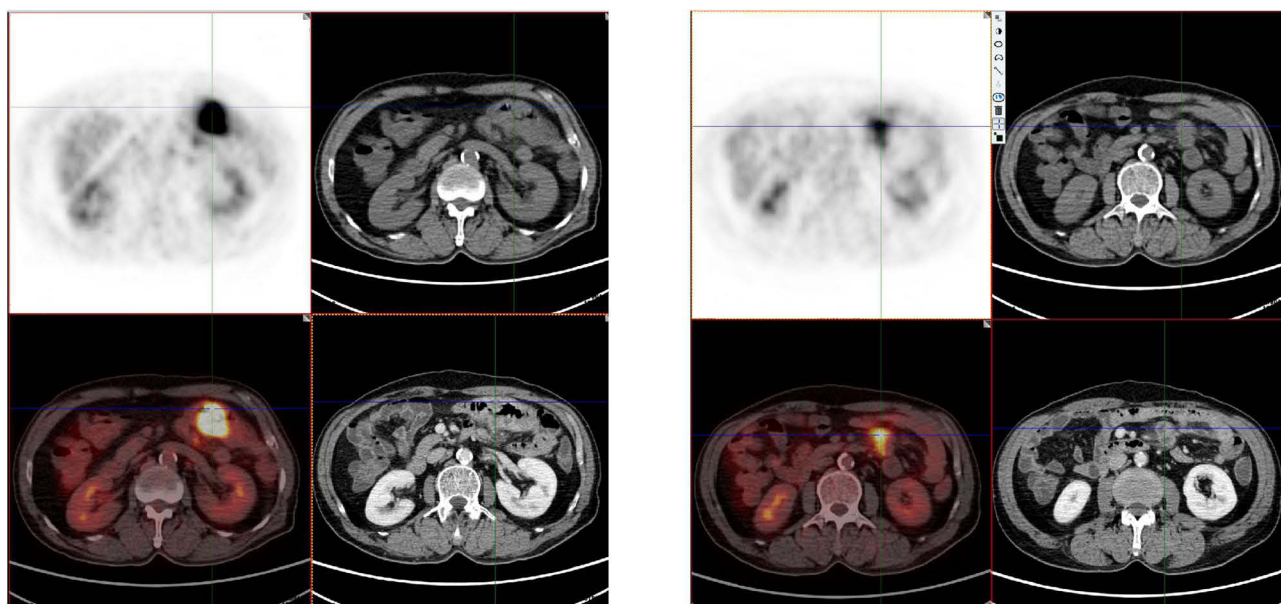


Figure 3 Imaging comparisons of patients with lung cancer with gastrointestinal metastasis.

Discussion

In our case series, we identified that the small intestine and stomach are the most common sites of gastrointestinal metastasis in patients with primary lung cancer, consistent with the findings of previous studies.¹⁴ The small intestine, in particular, is frequently affected, which aligns with a retrospective study in 2018 where the small intestine (59.6%) was the most commonly affected organ in the gastrointestinal tract, followed by the colorectum (25.5%).¹⁵

A significant finding in this study is that adenocarcinoma was the predominant pathological type, accounting for 85% of the cases. These adenocarcinomas were poorly differentiated, which correlates with their highly malignant behavior. This observation is crucial as it underscores the aggressive nature of gastrointestinal metastasis when it originates from poorly differentiated adenocarcinoma of the lung.

Immunohistochemical analysis in our cases revealed a consistent pattern where CK7 and TTF-1 were positive, and CK20 and CDX-2 were negative. This immunophenotype is characteristic of gastrointestinal metastasis originating from lung adenocarcinoma, as also reported by Rossi G et al.¹⁶ In contrast, cases of small cell carcinoma demonstrated positivity for neuroendocrine markers such as CD56 and Syn, further supporting the diagnosis of metastatic small cell lung cancer rather than primary gastrointestinal neuroendocrine tumors.¹⁷

Our study emphasized the importance of regular gastrointestinal evaluation in lung cancer, particularly in those with persistent gastrointestinal symptoms such as anemia, abdominal pain, hematemesis, or melena that could not be explained by the primary lung cancer or its treatment. Early detection through endoscopic biopsy combined with advanced imaging techniques like CT¹⁴ and PET-CT¹⁸ can significantly improve the diagnostic rate and help in managing these patients more effectively.

In conclusion, our findings highlighted the necessity for clinicians to maintain a high index of suspicion for gastrointestinal metastasis in lung cancer patients, especially when unexplained gastrointestinal symptoms are present. This approach could lead to earlier detection, appropriate treatment, and potentially improved outcomes for these patients.

Conclusion

Overall, gastrointestinal metastasis of lung cancer is usually asymptomatic in the early stages. Symptoms such as abdominal pain, anemia, and melena often appear only when complications occur, including intestinal obstruction and perforation. The small intestine and stomach are the most common sites of metastasis. The metastasis of lung cancer in

the gastrointestinal tract mainly involves squamous cell carcinoma, adenocarcinoma, and large cell carcinoma. Diagnostic methods include endoscopic biopsy and surgical pathology, and immunohistochemical staining such as CK7 and TTF-1 contributes to differentiating primary and secondary tumors. Endoscopic techniques are crucial for identifying gastrointestinal metastasis, and PET-CT is particularly valuable in the detection of asymptomatic metastases and systemic evaluation. In the management of lung cancer, it is the key to pay attention to the evaluation of gastrointestinal symptoms to avoid missed diagnosis of gastrointestinal metastasis.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (KY-Z-2021-626-01). All subjects signed the consent form before participation in the study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All patients were informed about the surgical process and signed the informed consent form.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests in this work.

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