

Case Report

Capsule Endoscopy-Based Diagnosis of Lung Squamous Cell Carcinoma Associated with Abdominal Pain and Metastasis to Small Intestine: A Case Report

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Keywords

Abdominal pain · Lung squamous cell carcinoma · Metastasis · Small intestine · Capsule endoscopy

Abstract

Gastrointestinal metastases of lung cancer are relatively uncommon, yet occur at a higher frequency than would be expected among patients that exhibit a longer survival interval. Metastases that arise in the small intestines are often associated with no or few symptoms such that their early diagnosis can be challenging. In this report, we describe an extremely rare case of a lung squamous cell carcinoma that had metastasized to the small intestine and was associated with symptoms of abdominal pain. The patient underwent capsule endoscopy which detected an irregular mass in the distal ileum that was hemorrhagic, after which laparoscopic ileal resection and anastomosis in parallel with partial bladder resection were performed. Subsequent pathological biopsy confirmed that the intestinal mass was consistent with metastatic squamous cell carcinoma. With surgery and subsequent maintenance therapy with targeted drugs, the survival of the patient was more than 6 months. As a noninvasive testing strategy, capsule endoscopy can be easily performed to support etiological diagnostic efforts in cases where other diagnostic options are lacking. Early diagnosis and therapeutic intervention can contribute to better prognostic outcomes for GMLC patients.

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Introduction

Lung cancer remains the second most common form of cancer globally and was the leading cancer-related cause of death as of 2020, with an estimated 2.2 million diagnoses and 1.8 million deaths per year. As of 2040, lung cancer rates are forecast to rise by ~64%, while the number of deaths is expected to increase by ~67% [1]. The high incidence and mortality rates associated with lung cancer thus make it a pressing threat to global public health [2, 3]. The gastrointestinal tract is a relatively uncommon site of metastatic progression in individuals with advanced lung cancer [4]. As these patients have generally undergone multiple rounds of intensive treatment, their overall health tends to be poor such that any emergent gastrointestinal symptoms are often discounted or misdiagnosed [5]. Clinically, gastrointestinal metastases of lung cancer (GMLC) are often only identified when serious symptoms such as bowel perforation, obstruction, or hematochezia develop [6], at which time the optimal therapeutic window has passed. Here, we report the case of a patient with metastatic lung squamous cell carcinoma who experienced abdominal pain as their primary symptom. Capsule endoscopy identified a small intestinal mass in this patient that was subsequently confirmed via postoperative pathological biopsy to correspond to a small intestinal metastasis of lung squamous cell carcinoma. Following maintenance therapy with oral targeted drugs, this patient survived for more than 6 months, emphasizing the importance and value of capsule endoscopy as a means of examining the small intestine in lung cancer patients.

Case Presentation

A 55-year-old male that had previously been diagnosed with stage IVB lung squamous cell carcinoma was admitted to our hospital on September 3rd, 2021, due to 1-month history of abdominal pain. The patient had no smoking habit but had been working as a stonemason for a long time. Twenty months prior to admission the patient had undergone the radical resection of the left lower lung via a thorascopic approach in our hospital. Intraoperative findings showed that the tumor (3.6 × 2.5 × 2.5 cm) was located in the left lower lung lobe, the pleura was depressed, and no cross-lobe growth was observed. The left oblique fissure is incomplete, and the pleura is adherent. No pleural thickening, no metastatic nodules, no obvious pleural effusion. Postoperative pathological analyses revealed a keratinized squamous cell carcinoma of the left lower lung with vascular invasion (+), nerve invasion (+), p40 (+), and lymph node metastasis (1/9) (Fig. 1a, b). Therefore, the pathological diagnosis was left lower lung squamous cell carcinoma stage IIIA (pT_{2a}N₂M₀). In June 2020, this patient underwent an initial round of TP chemotherapy (albumin paclitaxel 400 mg D1 + nedaplatin 110 mg D1). Upon discharge, the patient incidentally identified a peanut-sized nodule on his scalp that was identified as a metastatic lesion upon biopsy at a local hospital. In July 2020, he was diagnosed with bone metastases via whole-body bone imaging in our hospital. The patient's diagnosis was thus revised to left lower lung squamous cell carcinoma stage IVB (rT_{2a}N₂M_{1c}, scalp, bone). He continued to undergo TP chemotherapy combined with carrelizumab (200 mg) for 5 cycles, followed by maintenance treatment with carrelizumab until the present admission.

Routine hematological examination revealed moderate anemia after admission and fecal examination revealed positivity for occult blood. Abdominal enhanced CT imaging revealed local thickening of the wall of the small intestine together with mesenteric lymph node enlargement potentially consistent with lymphoma or primary tumor metastasis (Fig. 2a, b). Gastrointestinal imaging following barium swallow failed to reveal any definitive obstruction, stenosis, or filling defects. The patient was considered to exhibit a low risk of capsule retention such that a capsule endoscopy was performed which revealed an irregular mass in the distal ileum occupying half of

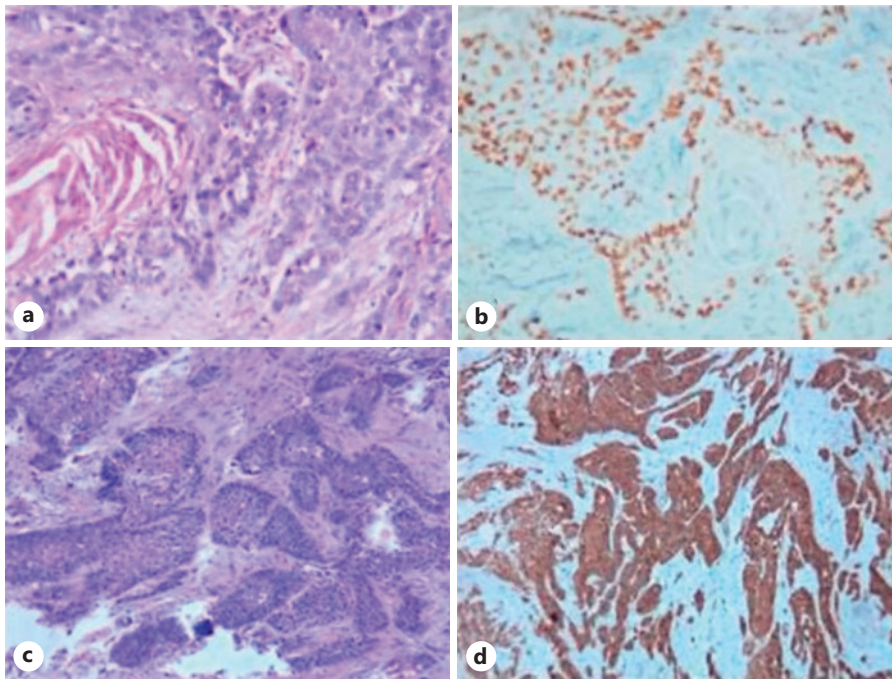


Fig. 1. Pathological findings of the lung primary tumor and the small intestinal metastatic tumor. **a** Hematoxylin-eosin staining of the lung squamous cell carcinoma. **b** Immunohistochemical analysis indicated the lung squamous cell carcinoma was positive for P40. **c** Hematoxylin-eosin staining of the small intestine metastatic tumor cells. **d** Immunohistochemical analysis indicated the small intestine metastatic tumor cells were positive for CK5/6.

the lumen with a rough, ulcerated surface that was actively bleeding (Fig. 3). This patient was advised to undergo either surgery or double-balloon enteroscopy to confirm the diagnosis and elected to undergo surgical resection. Laparoscopic exploration under general anesthesia revealed a small intestinal mass 70 cm from the ileocecal area adhering closely to the pelvic wall, consistent with the invasion of the pelvic wall. The tumor was also closely associated with the bladder suggesting potential bladder invasion. As such, the patient underwent partial ileal resection and anastomosis in parallel with partial cystectomy. Histological analysis was performed on the surgical specimen, revealing the small intestine to be 9 cm long with a circumference of 5 cm. A gray mass (5 × 4 × 2 cm) was observed on the intestinal wall 1.5 cm away from the cutting edge on one side and 6 cm away from the cutting edge on the other side. The mass was solid in nature and had visibly invaded the whole layer under direct visualization, occupying half of the intestinal lumen. Small amounts of bladder tissue (4 × 3 × 0.4 cm) were observed on the serosal surface of the small intestine. There were 3 palpable lymph nodes in the peri-intestinal adipose tissue that were 0.3–0.8 cm. Postoperative immunohistochemical analyses revealed the small intestinal tumor cells to be positive for p40 and CK5/6, but negative for cytokeratin 7 (CK7), CK20, and thyroid transcription factor-1 (TTF-1) (Fig. 1c, d), consistent with a metastatic squamous cell carcinoma, potentially of pulmonary origin. As such, the mass was diagnosed as a lung squamous cell carcinoma small intestinal metastasis.

At 3 months post-surgery, abdominal enhanced CT reexamination revealed significant thickening of the small intestinal anastomosis and mass formation, together with an additional mass on the left side of the pelvic cavity above the bladder suggestive of postoperative tumor recurrence (Fig. 2c, d). The patient began undergoing afatinib treatment (40 mg, orally, once per day) to control tumor growth. At 6 months post-surgery, the patient was unable to come to our hospital for a follow-up review owing to the impact of the COVID-19 pandemic.

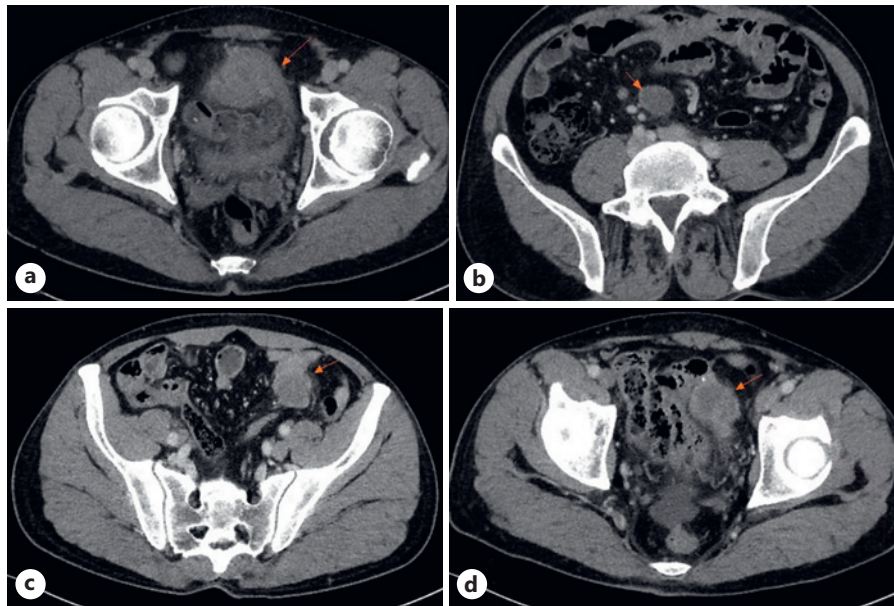


Fig. 2. CT findings of the small intestinal metastatic tumor: **a** Local thickening of the small intestine wall at the pelvic entrance level was about 1.3 cm, and the lesion length was about 5.7 cm **b** Multiple lymph nodes can be seen at the mesentery root, and the larger ones are about 2.7×2.3 cm in size. **c** Anastomosis was significantly thickened with mass formation, and the size of the mass was about 3.0×3.2 cm in size. **d** On the left side of the pelvic cavity, there was another mass above the bladder, about 2.8×3.2 cm in size.

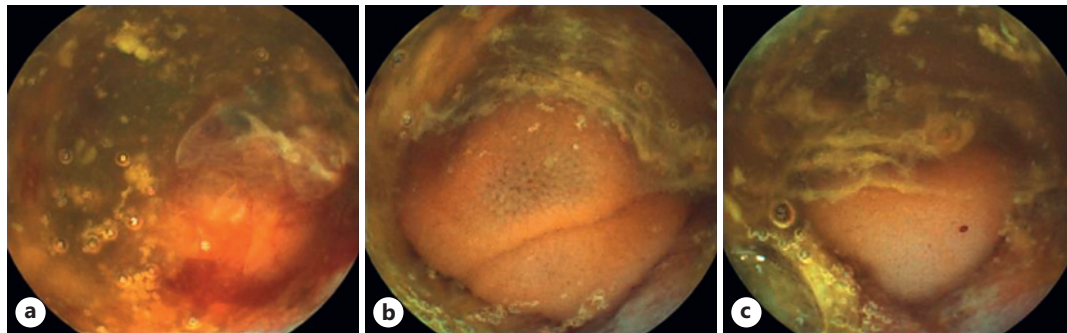


Fig. 3. SBCE findings of the small intestinal metastatic tumor. An irregular mass in the distal ileum, involving 1/2 circle (**a**), with rough surface (**b**), ulceration, and active bleeding (**c**).

Through telephone-based follow-up, he complained of a persistent dull pain in the lower abdomen that was less severe than his preoperative pain and indicated that he had not experienced any bloody stools. The CARE Checklist has been completed by the authors for this case report, attached as in online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529060).

Discussion

As lung cancer incidence continues to rise and treatments for this condition continue to advance, GMLC has become increasingly common [7]. As most GMLC cases occur during the terminal stages of the disease, there are significant differences in GMLC incidence rates

reported in clinical studies as compared to rates detected upon autopsy (2% vs. 5–14%), suggesting that the majority of GMLC cases are asymptomatic or mild and subclinical, often resulting in misdiagnosis or missed diagnosis thereof [8, 9]. The small intestines are the most frequently impacted organ in GMLC cases owing to their abundant blood supply [5, 10]. Within the small intestine, metastases occur most often in the jejunum followed by the ileum and duodenum [11]. Typical clinical symptoms in affected patients include perforation (42.0%), hemorrhage (24.6%), and obstruction (20.4%) [5]. In the present case, abdominal pain was the primary symptom reported by the patient, and routine stool examinations revealed the presence of fecal occult blood, while routine hematological testing revealed moderate anemia. While this presentation was not typical of a small intestinal metastasis, when underlying gastrointestinal bleeding that cannot be explained by chemotherapy or primary lung cancer is observed, GMLC should be considered as a potential diagnosis.

The small intestine is 5–8 m in length and accounts for 70–75% of the total length of the overall gastrointestinal tract, forming multiple intestinal loops freely located within the abdominal cavity connected by the mesentery. Given its distance from both the mouth and anus, traditional gastrointestinal endoscopes cannot access the small intestine such that it was once considered a blind spot in the context of digestive tract examination. While the double-balloon enteroscopy can enable a largely complete examination of the small intestine, it must be performed via both the oral and anal routes, which is time-consuming and associated with anesthesia-related risk, limiting its value in the context of routine examination. Small bowel capsule endoscopy (SBCE) has been shown to exhibit similar diagnostic rates to dual-balloon enteroscopy when assessing small intestinal lesions (55.3% vs. 60.5%) [12]. As such, SBCE represents a safe, efficient, and noninvasive approach to intestinal examination that can rapidly yield an etiological diagnosis, making it well-suited as a first-line approach to examining the small intestine [13, 14]. While abdominal enhanced CT imaging revealed the thickening of the intestinal wall, imaging following a barium swallow did not reveal any abnormalities in this patient. As such, SBCE was performed to guide further diagnostic efforts. Small intestinal metastases observed via SBCE are often characterized by diffuse mucosal injury, multiple nodules with or without mucosal ulcers, or isolated volcanic neoplasms [15]. It is thus important to gauge the risk of intestinal lesion-related capsule retention prior to examination.

In this patient, SBCE confirmed the presence of a small intestinal mass. While the mass could have been evaluated via either double-balloon enteroscopy or surgery, the patient elected to undergo surgical resection. Immunohistochemical pathological diagnostic analyses are the only reliable approach to differentiating between primary and secondary lesions or determining the tissue of origin for small intestinal tumors [15, 16]. CK20 positivity is a hallmark of a primary intestinal malignancy, while lung squamous cell carcinoma cells generally exhibit a p40+ and CK5/6 + staining profile, whereas primary lung adenocarcinoma cells are generally TTF-1+ and CK7+ [17, 18]. The three most common histological subtypes observed in cases of GMLC include squamous cell carcinoma (28.5%), adenocarcinoma (27.6%), and large cell carcinoma (20.9%). A comparison of this histological distribution with that of primary lung cancer suggests that large cell carcinoma and adenocarcinoma are, respectively, associated with the highest and lowest risk of gastrointestinal metastasis [5, 19]. Median GMLC patient survival is just 2.8 months, with early detection, diagnosis, and treatment being critical to the prolongation of patient survival [20, 21]. In the present case, abdominal enhanced CT reexamination revealed tumor recurrence in the bladder and anastomosis site. The patient has since been undergoing oral targeted drug maintenance therapy and has survived for over 6 months. Therefore, with the continuous breakthrough of lung cancer treatment pattern, whether targeted therapy or immunotherapy, patients with advanced lung cancer can benefit from it [22–24]. Meanwhile, the prognosis of the patient

supported advanced age, parenteral metastasis, and intestinal perforation as negative prognostic indicators for GMLC patients, while abdominal surgery was a positive prognostic factor [5, 25]. Therefore, surgical intervention may be one of the most effective means to prolong the survival of patients with GMLC.

Conclusion

In summary, while the gastrointestinal tract remains an uncommon site of lung cancer metastasis, GMLC should be considered as a potential diagnosis in lung cancer patients exhibiting gastrointestinal symptoms or unexplained gastrointestinal bleeding, with particular attention being paid to the small intestine [26]. SBCE is the preferred approach to examining the small intestine in addition to routine gastrointestinal endoscopy. In this subset of at-risk patients, we recommend that thorough multidisciplinary analyses, targeted surgery, and systematic treatment be applied in order to improve patient survival and quality of life.

Statement of Ethics

This study protocol was reviewed and the need for approval was waived by the Ethics Committee of our hospital (Chongqing University Cancer Hospital). The written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Zhong Yihua was a major contributor in writing the manuscript, drafted the manuscript, took part in the literature search, and treated the patient. Tang Xianjun analyzed and interpreted the patient data, performed the histological examination of the tumors, and provided the pictures of tumor pathology. Deng Bowen participated in the diagnosis and treatment decisions and provided the writing assistance and radiology pictures. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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