Colonic Metastasis of Primary Lung Cancer

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Abstract
The colon is an uncommon secondary site for metastasis of lung adenocarcinoma. Distinguishing primary colonic carcinoma from metastatic spread of lung carcinoma can be difficult. We present a case of a patient with lung adenocarcinoma who, on abdominal computed tomography scan examination, was found to have a sigmoid tumor that was thought to represent a synchronous primary colorectal adenocarcinoma. Histological examination of endoscopic sigmoid tumor biopsies confirmed this to be metastasis from the lung adenocarcinoma. The patient subsequently developed major rectal bleeding and deteriorated significantly. This case also illustrates the poor prognosis association with colorectal metastasis of lung cancer.

Introduction
The mortality of lung cancer ranges from 18 to 23\% \cite{1} and up to 50\% of patients present with metastasis at the time of diagnosis \cite{2}. The common sites for metastasis are lymph nodes (48\%), liver (45\%), adrenal glands (41\%), bone (31\%), and brain (25\%) \cite{3}. However, metastasis to colorectum is quite uncommon \cite{4}. Kim et al. \cite{5} reported only 10 (0.19\%) out of 5,239 patients with lung cancer had metastasis to the colon and rectum. A literature review of 15 case reports of metastatic lung cancer to the colon demonstrated that squamous cell carcinoma is the most common subtype and that adenocarcinoma, as in the patient presented...
here, is less likely to metastasize to the colon [6]. Here, we are reporting a rare case of colonic metastasis of primary lung adenocarcinoma.

**Case Report/Case Presentation**

A 61-year-old male patient presented with a 3-week history of progressive dyspnea, neck, and facial swelling. He had a history of 40-pack years of smoking and prostate cancer treated with radiotherapy 5 years ago. He also had a sibling with EGFR-mutated lung adenocarcinoma. At that time, a contrast-enhanced computed tomography (CT) scan of thorax and liver showed a bulky mediastinal nodal mass invading the superior vena cava (SVC), the right main pulmonary artery, and the right main bronchus and indenting the right upper lobe bronchus. A 7 mm hypodense area was noted in the liver concerning for hepatic metastasis (Fig. 1a). Bronchoscopy showed extrinsic compression of the right upper lobe bronchus without an endobronchial tumor. Bronchoalveolar lavage, right upper lobe bronchial brushings, and transbronchial needle aspiration confirmed primary pulmonary adenocarcinoma, TTF1 positive, and P63-negative. The tumor harbored EGFR (exon 19) and KRAS mutations.

The patient was started on treatment for SVC obstruction. He received high-dose steroids and palliative mediastinal radiotherapy; this was followed by clinical improvement. He was then started on EGFR-targeted therapy with gefitinib. A positron emission tomography (PET)-CT scan showed metabolic activity in the right upper lobe tumor, mediastinal and cervical lymph nodes, and soft tissue masses in the caecum and sigmoid colon. The corresponding CT scan showed a decrease in the size of right hilar, cervical nodal masses, and circumferential thickening in the region of the descending/sigmoid colon was likely colonic primary tumor (Fig. 1b).

Subsequent colonoscopy showed a circumferential necrotic sigmoid mass (Fig. 2) which was biopsied and histology reported a poorly differentiated adenocarcinoma diffusely infiltrating the submucosa and the lamina propria between nondysplastic colonic crypts (Fig. 2). The tumor was diffusely positive for TTF1 and focally positive for cytokeratin 7 and pancytokeratins AE1/AE3 and MNF116. The tumor was negative for CDX2, CK20, PSA, PSAP, P504S, PAX-8, and Napsin A (Fig. 3). The features were consistent with metastatic adenocarcinoma of pulmonary origin.

**Fig. 1.** Axial CT thorax (a) with contrast showing a lobulated 7.3 cm soft tissue right paratracheal mass extending from the origin of the SVC to the superior aspect of the right atrium. The tumor invades the posterior wall of the superior vena cava and proximal right main pulmonary artery anterior/apical branches. Enlarged subcarinal lymph nodes are also seen. Axial CT Abdomen (b) showing circumferential thickening in the region of the descending/sigmoid colon was likely colonic primary tumor. CT, computed tomography; SVC, superior vena cava.
A decision was made to laparoscopically resect the sigmoid mass and to continue with gefitinib as he was showing partial radiological response. However, and before such a resection was performed, he developed worsening SVC obstruction syndrome and became unresponsive to high-dose steroid therapy. This was thought to be due to either SVC thrombosis or radiation-induced stricture. Patient’s condition deteriorated rapidly secondary to major per rectal bleeding, and he was deemed unsuitable for thrombolysis for possible SVC thrombus. Palliative care team started end-of-life care and patient died in few days.

**Discussion/Conclusion**

The incidence of gastrointestinal metastasis of primary lung cancer ranges from 0.3 to 1.7% [7]; however, in postmortem studies, the incidence ranges from 4.6 to 14% [7, 8]. This discrepancy indicates that most of the patients have asymptomatic gastrointestinal metastases. Adenocarcinoma of lung can metastasize to any gastrointestinal location from the oral cavity to the anus through lymphatic and hematogenous pathways being the probable routes of spread [9, 10]. Intestinal obstruction, perforation, and hemorrhage are some of the reported acute complications [11]. Gastrointestinal complications usually occur after

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**Fig. 2.** Colonoscopy showing (a) a circumferential necrotic sigmoid mass. Microscopic views (b) of embedded parts. There is a poorly differentiated tumor diffusely infiltrating the lamina propria in-between nondysplastic colonic crypts. High power view (c) showing poorly differentiated adenocarcinoma with occasional signet ring cells (arrows).

**Fig. 3.** On IHC staining, the tumor cells show strong diffuse nuclear positivity with TTF1 (a) and are also focally positive for cytokeratin 7 (b). c The tumor is negative for CDX2, while the background colonic crypts show normal strong nuclear expression. IHC, immunohistochemical staining.
the diagnosis of lung cancer is established as in the patient reported here; sometimes they can occur early in the course of the disease or even before the diagnosis of lung cancer is made [12–14].

A high degree of suspicion in lung cancer patients can yield early diagnosis of colorectal metastasis. CT scan is a commonly used modality for diagnosis of gastrointestinal lesions with an estimated sensitivity rate of 72% [15]. The most common CT findings of colorectum include wall thickening, as in patient presented here, and intraluminal polypoid masses. Despite that, CT scan can miss small asymptomatic gastrointestinal lesions which can be detected with PET-CT scan [16, 17]. In the patient reported here, PET-CT showed increased metabolic activity in caecum and sigmoid colon. The role of PET-CT is however unclear due to the paucity of cases of gastrointestinal metastasis of primary lung cancer [18]. Colonoscopy is Gold standard for colonic lesions and shows a variable morphology ranging from sub centimeter lesions to more larger masses. Colonoscopy in this patient showed a circumferential colonic mass. Immunohistochemical staining with TTF1, CDX2, cytokeratin 7 (CK7), and cytokeratin 20 (CK20) is valuable in differentiating pulmonary from colorectal adenocarcinoma [19]. Primary pulmonary adenocarcinoma is usually positive for TTF1 and cytokeratin 7 and is negative for CDX2 and CK20, as in our patient. Primary colorectal adenocarcinoma shows an opposite immune profile being positive for CDX2 and CK20 and negative for TTF1 and CK7 [19, 20].

The most important decision is which lesion needs to be treated first. It depends on the extent of colonic metastasis and the nature of presentation. For patients with complicated colonic metastasis, proper surgical treatment provides better outcomes in terms of reducing hospital stay, quality of life, and palliation. Colonic metastasis of lung cancer has a survival time of 5 weeks to 1 year and most patients die within the first 6 months [20]. In our case, chemotherapy was used for palliation. This patient survived roughly for 3 months. In conclusion, colonic metastasis of primary lung adenocarcinoma is a rare and can be accurately differentiated from synchronous colon cancer with immunohistochemical staining. This case also demonstrates the poor prognosis associated with such occurrence.

Statement of Ethics

The article describes a case report. Therefore, no additional permission from our Ethics Committee was required. Written informed consent was obtained from the patient’s legal guardian for publication of this case report and any accompanying images. Information revealing the subject’s identity was avoided. All identifying information has been removed from this case report to protect patient privacy.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Writing-original draft preparation: Salman Idrees Bhutta and Yasar Ahmed; writing-review-editing: Talal Zahid, Habib ur Rehman, and Tariq Mahmood; validation: Habib ur Rehman, Talal Zahid, and Mutaz M. Nur provided the pathology images; supervision: Paula Calvert. Formal Analysis: Tariq Mahmood, Habib ur Rehman, and Talal Zahid. Salman Idrees Bhutta wrote the manuscript, approved the final version, and is the article guarantor.

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