Melaena: A Rare Complication Of Duodenal Metastases From Primary Carcinoma Of The Lung
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Citation

Abstract
Small bowel metastases from primary carcinoma of the lung are very uncommon and occur usually in patients with terminal stage disease. These metastases are usually asymptomatic but may present as perforation, obstruction, malabsorption, or haemorrhage.

Haemorrhage as a first presentation of small bowel metastases is extremely rare and is related to very poor patient survival especially when these are located in the duodenum.

We describe the case of 61 year-old patient with primary adenocarcinoma of the lung , presenting with melaena as the first manifestation of small bowel metastasis.

Upper gastrointestinal endoscopy performed with a colonoscope revealed active bleeding from a metastatic tumour involving the duodenum and the proximal jejunum. Histological examination and immunohistochemical staining of the biopsy specimen strongly supported the diagnosis of metastatic lung adenocarcinoma.

INTRODUCTION
Metastases affecting the small bowel and originating from carcinoma of the lung are a rare occurrence, but recent reports suggest that they may be more frequent than previously thought as they rarely produce symptoms.

The majority of patients with metastases of the small bowel referred to in the literature, present with bowel perforation.

Overt gastrointestinal hemorrhage has been described in a few cases as a prelude to bowel perforation, whilst it has been described only rarely as the main presentation.

We present a case of a 61 year old patient with upper gastrointestinal bleeding due to duodenal metastases from a primary adenocarcinoma of the lung with secondary deposits in the abdominal lymph nodes. Metastatic involvement of the duodenum presenting with melaena has been described extremely rarely in the literature.

CASE REPORT
A 61 year old man was admitted to our hospital with a two day history of melaena. He reported a 4-month history of weakness, anorexia, 5kg loss of weight, cough, dyspnoea on exertion, and blood stained sputum; and a two month history of fatigue and altered bowel habit.

He was a cigarette smoker with a history of arterial hypertension and chronic obstructive airway disease.

On examination he was pale, with normal blood pressure and pulse rate, had wheezy breathing and decreased breath sounds in the upper right lung region. Digital examination proved positive for melaena. Haematocrit was 35% and haemoglobin 9.5g/dl.

Chest x-ray revealed a density in the upper region of the right lower lobe.

Endoscopy of the upper gastrointestinal tract up to the secondpart of the duodenum revealed erosive antral gastritis without an active bleeding site.

Computerized axial tomography (CAT) scanning of the thorax revealed an irregularly shaped, nodular mass measuring 4 cm in diameter, in the upper region of the right lower lobe of the lung.
Bronchial biopsy revealed the presence of blood clots and desquamated bronchial epithelial cells, without signs of malignancy.

The results of cytological examination of bronchial excretions however, proved positive for non-small cell carcinoma of the lung.

Staging of the disease followed by CAT scanning of the upper and lower abdomen and of the retroperitoneal space showed multiple, enlarged bilateral para-aortic, and mesenteric lymph nodes. The patient was started on combined chemotherapy with cisplatin and hydrochloric gemcitabine. His bowel motions had become normal by the third day of hospitalization and he was subsequently discharged, denying further investigation.

During admission for the second round of chemotherapy and one month after diagnosis, the patient complained of diffuse abdominal pain and abdominal tenderness. Shortly afterwards this was accompanied by haemodynamic instability and tachypnea.

Digital examination was positive for melaena. Haematocrit had fallen from 34% to 26%, haemoglobin from 9g/dl to 6g/dl, and serum urea/creatinine ratio was greater than 40 (urea 60mg/dl and creatinine 1.3mg/dl).

Plain abdominal X-ray showed no abnormalities and the patient underwent endoscopy of the upper and lower gastrointestinal tract using a Pentax 160 cm colonoscope. In the 4th part of the duodenum three irregular, nodular protrusions of the mucosa measuring 0.5-1.5 cm in diameter were observed. These were noted to be friable and slightly haemorrhagic. At the proximal jejunum there was a larger polypoid haemorrhagic mass about 2.5 cm in diameter (Fig. 1).

Biopsies of these lesions revealed gatherings of poorly differentiated neoplastic cells invading the mucosal bed and extending into the intestinal villae with sparing of the superficial epithelium. Infiltration of the lymph vessels was also noted. These findings were consistent with metastatic disease.

Immunohistochemical staining for keratin 8, 18, 19 and TTF 1 as well as histochemical staining PAS strongly supported the diagnosis of poorly differentiated metastatic adenocarcinoma of the lung (Fig. 2 and 3).
Figure 3
Figure 3: Embolus of neoplastic cells in the lymph vessels of the intestinal villae.

Radiological examination of the small bowel was not completed due to patient discomfort.

The patient was transfused with 3 units of packed erythrocytes and 3 units of fresh frozen plasma. Only four cycles of chemotherapy were carried out due to the generally poor condition of the patient. In addition he received 4000 U of erythropoetin per week. Three months after his last episode of melaena the patient continued to have occult upper gastrointestinal bleeding and was admitted on several occasions for blood transfusion. The patient died seven months after the diagnosis of his condition from end stage cancer of the lung.

DISCUSSION
Primary carcinoma of the lung is the leading cause of mortality from cancer in men as well as in women. Lung cancer may present with non-specific respiratory symptoms, paraneoplastic syndromes, and/or with symptoms occurring as the result of local or distant metastases. Approximaty 50% of patients have metastatic disease at the time of presentation. Metastases from primary carcinoma of the lung may occur in all tissues. The sites more commonly involved are lymph nodes (48%), liver (45%), adrenals (41%), bone (31%), and brain (25%). More rarely metastases may occur in the kidneys, stomach, large bowel, and peritoneum.

According to the literature, small bowel metastases usually originate from primary carcinomas of the gastrointestinal or genital organs, and more specifically from the large bowel, the uterus, the cervix, the ovaries, and the testes. Thoracic malignancies metastasize less frequently to the small bowel. Apart from carcinoma of the lung, these also include malignant melanoma, carcinoma of the breast, carcinoma of the salivary glands, carcinoma of the oesophagus, and rhabdomyosarcoma of the lung.

A review of the literature reveals few studies of patients with lung cancer and metastases to the small bowel. The object of these studies is to describe the histology of the neoplasm, the stage of the disease, the presence of concurrent metastases in other organs, and the length of patient survival.

An extensive eleven year study of patients with primary lung cancer revealed that at autopsy, 46 out of 431 patients (10.6%) had secondary deposits in the small bowel. These patients had an average of 4.8 metastatic sites, whilst small bowel metastases were discovered in 39% of cases of large cell carcinomas, 12% of adenocarcinomas, 8% of small cell carcinomas, and 7.5% of epidermoid carcinomas. A more recent study of patients with non-small cell carcinoma of the lung revealed small bowel metastases in 4.6% of cases. It should be emphasized that all these cases were adenocarcinomas, with a disease stage greater than IIIA, as well as a minimum of two other metastatic sites before the development of bowel metastases. Another large study involved 1,399 patients with lung cancer who underwent surgical resection of the primary tumour. This study revealed a much smaller percentage (0.5%) of symptomatic patients having small bowel metastases.

In direct contrast to the previous study which concludes that adenocarcinoma is the cell type resulting more frequently in small bowel metastasis, this study concludes that squamous cell carcinoma is the more frequent cause, representing 61% of cases.

Patients with primary lung cancer with metastases to the small bowel are usually asymptomatic. Less frequently these metastases can cause symptoms which vary according to the way the metastatic tumour invades the bowel wall. Rapid tumour growth leads to symptoms of obstruction, although it seems that perforation occurs more commonly and is probably due to central tumour necrosis.

According to the literature most cases of primary lung cancer and small bowel metastasis present with small bowel perforation. When ulceration of the mucosa occurs the metastatic tumour may bleed, whilst large extension of tumour may lead to symptoms of malabsorption.
Haemorrhage from a metastatic tumour in the small bowel is an uncommon occurrence, explaining the absence of large studies on this issue. A small number of isolated cases however have been described. They describe patients over the age of 55 years, with primary lung carcinoma of large or small cell types, who have already developed distant metastases. These patients usually present with acute haemorrhage from ulceration of the metastatic tumour, and less frequently with iron deficiency anaemia, or with non-specific abdominal symptoms before the onset of melaena. In one case report, the patient presented with iron-deficiency anaemia and melaena, and the diagnosis of primary lung cancer was made after surgical resection of the intestinal metastasis, as no tumour evidence was found on chest x-ray. The presence of small bowel metastases in this patient were confirmed with CAT scan, as upper and lower gastrointestinal endoscopies were negative.

A very small number of cases of upper gastrointestinal bleeding due to duodenal metastases from lung cancer have been reported. Small intestinal metastases have been reported to occur more frequently in the jejunum and the terminal ileum than the duodenum. Our patient is one of very few cases described where melaena as the first manifestation of small bowel metastasis, had arisen from the duodenum and jejunum. Also interesting to note is the short time interval between diagnosis of cancer and metastasis to the small bowel, as the patient presented with melaena before the establishment of the diagnosis of lung carcinoma and was still in a good general state of health. The diagnosis of metastatic involvement of the small bowel was suspected but was not confirmed at the beginning. This emphasizes the importance of considering the presence of small bowel metastases in a patient with lung cancer displaying symptoms of haemodynamic instability, melaena, or abdominal symptoms such as dyspepsia, distention, pain, even if the time elapsed from the time of diagnosis of cancer is short.

It must be noted that occult gastrointestinal bleeding must be suspected if laboratory investigations reveal iron deficiency anaemia, or a fall in haematocrit or haemoglobin, even in an asymptomatic patient. This will be confirmed by persistently positive faecal occult-blood tests. Gastrointestinal haemorrhage can usually be managed conservatively with intravenous fluids and red blood cell transfusion until the patient is haemodynamically stable and haemorrhage ceases. There have however been cases requiring surgical resection of small bowel in order to control massive haemorrhage. Only a few patients have survived more than 9 months after surgical intestinal resection of intestinal metastases, with the exception of one patient who survived 22 months after peritonitis.

Perioperative mortality has decreased considerably, and the question remains whether surgery should be considered as palliative therapy, and not only for symptomatic patients. After haemorrhage from small bowel metastases, patient survival varies between several weeks to several months. It seems that haemorrhage originating from small bowel metastases, is related to a very poor patient survival. The patient we have presented survived for a considerably long time i.e., 6 months after his first bleeding episode. During this period of time he continued to have microscopic haemorrhage requiring frequent blood transfusions. Active gastrointestinal bleeding from small bowel metastases has never been described as the cause of death in patients suffering from carcinoma of the lung.

In conclusion, small bowel metastases from primary carcinoma of the lung occur usually in patients with terminal disease and rarely produce symptoms. Haemorrhage as a first presentation of small bowel metastases is extremely rare, especially when these are located in the duodenum and is a poor prognostic sign of survival. Gastrointestinal bleeding from a metastatic tumour should be included in the differential diagnosis of gastrointestinal blood loss in a patient with a known bronchogenic tumor.

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