



## Case report

## Iron deficiency anemia as initial presentation of a non-small cell lung carcinoma: A case report



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## ABSTRACT

Duodenal metastases secondary to lung cancer are very rare and most of the time asymptomatic. When symptomatic they usually present with bowel obstruction or perforation. We here describe the case of a 68 year-old man with a solitary metastasis in the duodenum from a non-small cell lung carcinoma (NSCLC). The patient presented with reduced exercise tolerance and iron deficiency anemia without clinical gastrointestinal blood loss. Further investigation showed a tumor in the left upper lung lobe and a duodenal metastasis for which he received chemotherapy. To the best of our knowledge this is the first case report of iron deficiency anemia as initial presentation of a duodenal metastasis from a NSCLC.

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## 1. Introduction

Lung cancer is responsible for the majority of cancer-related death among males worldwide and females in developed countries. Approximately 50% of these patients develop metastatic disease [1]. Primary non-small cell lung carcinoma (NSCLC) usually metastasizes to the mediastinal lymph nodes, liver, brain, adrenal glands and bone. Spread to the small intestine (with a prevalence between 2.6 and 10.7%) is uncommon [2]. Duodenal metastases have been described in only a few case reports.

Most of the small bowel metastases are asymptomatic but autopsy studies suggest that asymptomatic metastases may be more frequent than previously thought with a prevalence up to 4.6% [3,4]. Metastases of the small bowel usually presents with obstruction or bowel perforation [2]. Gastrointestinal hemorrhage, or anemia from occult bleeding of small bowel metastases have been described in a small number of cases of primary NSCLC [5,6]. Even less common is a metastasis so presenting with no obvious primary lung tumor [7]. We describe a case of a 68 year-old man with

anemia as the presenting symptom of a duodenal metastasis from a primary NSCLC.

## 2. Case report

A 68-year-old man, with a history of hypertension, vestibular neuritis and a benign vocal cord polyp, was referred by his General Practitioner to the outpatients of our Department of Internal Medicine. He complained of a progressive reduction in his capacity to exercise probably resulting from an iron deficiency (hemoglobin: 7.73 g/dL, mean corpuscular volume: 73 fL, ferritin: 12 µg/L). Laboratory findings further revealed a creatinine level of 126 µmol/L for which the cause remains undiscovered.

Patient had noticed bright red blood in the stools likely caused by known hemorrhoids but never melaena. He had reduced his cigarette smoking 9 years ago (40 pack-years) to 2 cigars a day. Examination of the lungs showed weak vesicular breath sounds but further physical examination was normal.

Gastroduodenoscopy revealed a tumor in the duodenum which was biopsied. On chest roentgenogram a mass of 8 cm was visible in the left lung apical for which the patient was referred to a pulmonologist. Additional total body F-18-fluoro-positron emission tomography (FDG-PET)/computed tomography (CT) scan showed a solitary circular mass with a diameter of 7.4 cm at the dorsal side of

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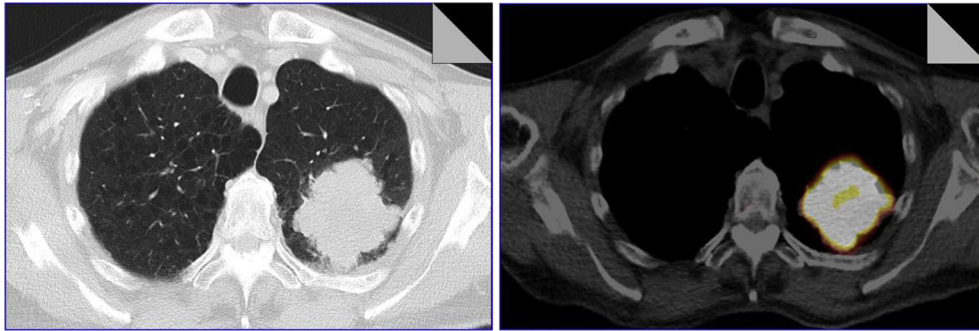


Fig. 1. Blanco-CT and FDG-PET/CT of the thorax showing a circular mass at the dorsal side of the left upper lobe with a diameter of 7.4 cm.

the left upper lobe (Fig. 1). There was also a circular process present in the duodenum (Fig. 2). There were no signs of lymph node, liver, bone or adrenal gland metastases. Shortly after the start of therapy magnetic resonance imaging (MRI) of the brain was performed which shows signs of small ischemic events but no clear metastases.

Histopathological study of CT guided perthoracal needle biopsy of the tumoral process in the left upper lung showed a poorly differentiated adenocarcinoma (Fig. 3A). Immunohistochemical analysis revealed the tumor cells to be positive for cytokeratin 7 and thyroid transcription factor 1 (TTF-1). There was also nuclear expression in the P53 gene which strongly supported the diagnosis of a poorly differentiated adenocarcinoma. Cytokeratin 20, CDX2, P63, S-100 and PSA proved negative.

The histopathological outcomes of the duodenum biopsy matched the NSCLC (Fig. 3B). Immunohistochemical analysis was positive for cytokeratin 7, TTF-1 and CEA. Cytokeratin 20, CDX2 and PSA proved negative. Thus the immunohistochemical profile too, was comparable with that of the lung tumor, allowing the conclusion to be drawn that the duodenal lesion was a metastasis of the primary NSCLC. Additional molecular diagnostics of the NSCLC revealed the tumor was pan-negative.

In conclusion this patient had a pT3N0M1b NSCLC. Induction chemotherapy consisted of Carboplatin and Pemetrexed in a 3-week cycle. Carboplatin was chosen because of the reduced kidney function. The patient will receive 2 such cycles after which evaluation by CT will take place. If response is adequate, resection of both tumors will be planned.

### 3. Discussion

Patients diagnosed with metastases in the small bowel from primary lung cancer are usually asymptomatic [4]. Primary NSCLC with undiagnosed small bowel metastasis presents typically with small bowel obstruction or perforation. In most cases rapid tumor

growth leads to obstruction, however central tumor necrosis seems more likely to result in perforation [4]. To the best of our knowledge this is the first case report of a duodenal metastasis from an undiagnosed primary NSCLC presenting as iron deficiency anemia.

Solitary small bowel metastases of NSCLC are rare. The jejunum (followed by the ileum), seems to be the most common small bowel location in the reported cases [8]. Early diagnosis and treatment of small bowel metastases are difficult because symptoms are absent or vague. Screening for small bowel metastases using CT of the abdomen has a low sensitivity. The use of total-body FDG-PET/CT for staging of lung cancer might increase the detection of gastrointestinal metastases [9]. Recent studies discuss the role of FDG-PET/CT in detecting gastrointestinal metastases from – for example – lung cancer [10]. At present there is insufficient knowledge about sensitivity and specificity of FDG-PET/CT data to aid diagnose of small bowel metastases.

All NSCLC tumor cell types can produce small intestinal metastases. Adenocarcinoma, large cell carcinoma and squamous cell carcinoma are suggested to be the most common [5]. Although the formation of gastrointestinal metastases is commonly considered to be hematogenous, the precise way these metastases form remains to be determined. Some studies document cancer cells filling the lymphatic vessels of the intestine [11]. These cases suggested a lymphatic route for formation of solitary small bowel metastases.

According to McNeill et al. all his patients with lung cancer and small bowel metastases had metastases in other organs including the more common adrenal gland, liver and kidney [12]. This could indicate that small bowel metastases are a late symptom of lung cancer and may be a indicator of poor prognosis for metastasized lung cancer.

Most patients described in the literature with small bowel metastasis from NSCLC, underwent surgical resection of the small bowel process or the affected part of the bowel because of life-threatening complications such as perforation. Fifty-seven case reports and three retrospective studies included by Di et al. showed

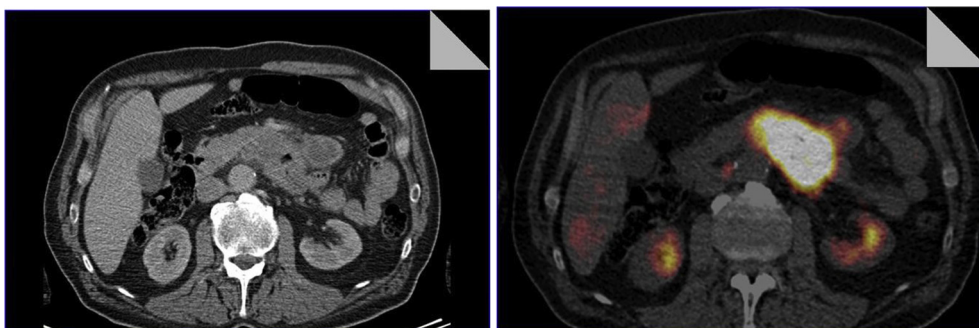
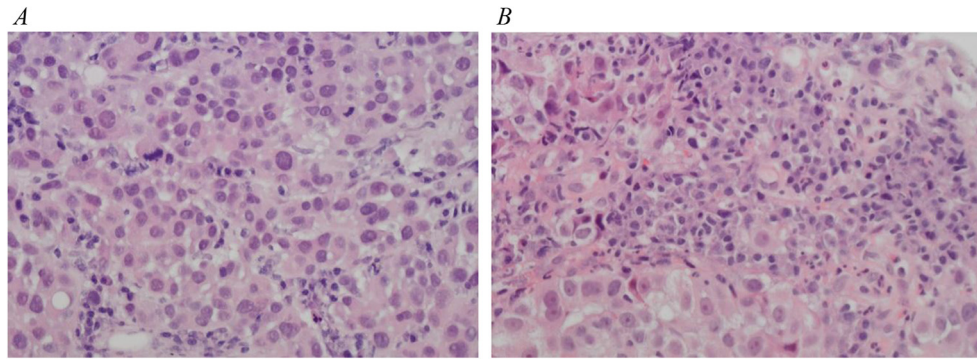


Fig. 2. Blanco-CT and FGD-PET/CT of the abdomen showing a solitary mass in the duodenum.



**Fig. 3.** Microscopic images of the primary NSCLC (A) and the duodenal metastasis (B). H&E, 400X. A: solid fields of polymorphic epithelial cells with enlarged nucleoli and a large amount of eosinophilic cytoplasm consistent with NSCLC. B: solid fields of large polymorphic epithelial cells with enlarged eosinophilic nucleoli and a large amount of eosinophilic cytoplasm, consistent with primary NSCLC.

a median survival of 2.3 months. Some case reports describe survival of more than a year [13]. Survival of patients with small bowel metastases from NSCLC thus remains uncertain.

#### 4. Conclusion

Duodenal metastases secondary to NSCLC are probably more frequent than expected, and physicians should always keep this in mind despite most being asymptomatic. The rarity and variety of solitary small bowel metastases as shown in the comprehensive review by Di et al. makes it difficult to analyze these patients in a randomized controlled trial. Without evidence-based medicine a tailored approach is important for patients with NSCLC and suspected small bowel metastasis.

#### Conflicts of interest

The authors state that they have no Conflict of interest.

#### References

- [1] L.A. Torre, F. Bray, R.L. Siegel, J. Ferlay, J. Lortet-Tieulent, A. Jemal, Global cancer statistics, 2012, *CA Cancer J. Clin.* 65 (2) (2015) 87–108.
- [2] J.Z. Di, J.Y. Peng, Z.G. Wang, Prevalence, clinicopathological characteristics, treatment, and prognosis of intestinal metastasis of primary lung cancer: a comprehensive review, *Surg. Oncol.* 23 (2) (2014) 72–80.
- [3] L.E. Stenbygaard, J.B. Sorensen, Small bowel metastases in non-small cell lung cancer, *Lung Cancer Amsterdam Neth.* 26 (2) (1999) 95–101.
- [4] A. Hillenbrand, J. Strater, D. Henne-Bruns, Frequency, symptoms and outcome of intestinal metastases of bronchopulmonary cancer. Case report and review of the literature, *Int. Semin. Surg. Oncol.* 2 (2005) 13.
- [5] W. Liu, W. Zhou, W.L. Qi, Y.D. Ma, Y.Y. Xu, Gastrointestinal hemorrhage due to ileal metastasis from primary lung cancer, *World J. Gastroenterol.* 21 (11) (2015) 3435–3440.
- [6] E. Hinoshita, H. Nakahashi, K. Wakasugi, S. Kaneko, M. Hamatake, K. Sugimachi, Duodenal metastasis from large cell carcinoma of the lung: report of a case, *Surg. Today* 29 (8) (1999) 799–802.
- [7] M.C. Mulder, J.W. Kist, E.C. Consten, P.M. Verheijen, Gastrointestinal metastasis as the first presentation of lung carcinoma, *Int. J. Colorectal Dis.* 27 (6) (2012) 839–840.
- [8] R.A. Garwood, M.D. Sawyer, E.J. Ledesma, E. Foley, J.A. Claridge, A case and review of bowel perforation secondary to metastatic lung cancer, *Am. Surg.* 71 (2) (2005) 110–116.
- [9] E.A. Usmanij, L.F. de Geus-Oei, J. Bussink, W.J. Oyen, Update on F-18-fluorodeoxy-glucose-PET/computed tomography in nonsmall cell lung cancer, *Curr. Opin. Pulm. Med.* 21 (4) (2015) 314–321.
- [10] C.G. Cronin, J. Scott, A. Kambadakone, O.A. Catalano, D. Sahani, M.A. Blake, et al., Utility of positron emission tomography/CT in the evaluation of small bowel pathology, *Br. J. Radiol.* 85 (1017) (2012) 1211–1221.
- [11] N. Ise, H. Kotanagi, M. Morii, O. Yasui, M. Ito, K. Koyama, et al., Small bowel perforation caused by metastasis from an extra-abdominal malignancy: report of three cases, *Surg. Today* 31 (4) (2001) 358–362.
- [12] P.M. McNeill, L.D. Wagman, J.P. Neifeld, Small bowel metastases from primary carcinoma of the lung, *Cancer* 59 (8) (1987) 1486–1489.
- [13] K.M. Kant, V. Noordhoek Hegt, J.G. Aerts, A patient with four-year survival after nonsmall cell lung carcinoma with a solitary metachronous small bowel metastasis, *J. Oncol.* 2010 (2010) 616130.