CASE REPORT

Small cell lung carcinoma presenting as a caecal polyp on surveillance colonoscopy

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Accepted 6 March 2014

SUMMARY

A 60-year-old man underwent surveillance colonoscopy that demonstrated five subcentimetre polyps, all of which were biopsied. One of the five polyps had histopathology consistent with small cell lung carcinoma (SCLC) metastasis from primary lung cancer. Subsequent imaging demonstrated a spiculated mass in the right upper lung lobe with metastasis to the brain, liver and spleen. He was immediately treated with palliative whole-brain irradiation followed by eight cycles of carboplatin and etoposide. Despite aggressive management, he had disease progression characterised by worsening performance status and development of transfusion-dependent anaemia, new blastic bone lesions and epidural disease. Given his liver failure, he was not considered a candidate for second-line topotecan. After discussion with the patient, family and palliative services, he was discharged with home hospice. This report describes a rare case of advanced SCLC presenting as a metastatic caecal polyp on surveillance colonoscopy.

Figure 1 Polyp noted in the transverse colon during screening colonoscopy.

BACKGROUND

Lung cancer remains the most common cause of cancer death in men and women.¹ Small cell lung carcinoma (SCLC), which accounts for only 15% of lung cancer cases, develops early with widespread metastases when compared with non-small cell lung cancer (NSCLC).^{2,3} The common sites of metastases include the contralateral lung, liver, adrenal glands, brain, bones and bone marrow.² Rarely, lung cancer can metastasise to the gastrointestinal (GI) tract, the most common site being the oesophagus.⁴ Of the metastatic lung cancers, NSCLC is more frequently diagnosed than SCLC.⁵ The finding of SCLC that was diagnosed with a metastatic lesion to the large bowel is an extremely rare manifestation of this disease and demonstrates the importance of immunohistochemistry in distinguishing carcinomas of different origins.

CASE PRESENTATION

A 61-year-old man with a medical history of type II diabetes mellitus, alcohol-related liver cirrhosis and transjugular intrahepatic portosystemic shunt (TIPS) for refractory ascites underwent colonoscopy for age-appropriate screening and evaluation of anaemia. His initial colonoscopy demonstrated a single tubular adenoma but was repeated 8 months later due to poor preparation. The surveillance colonoscopy revealed five polyps, one being a 3 mm polyp close to the ileocolic valve (figure 1). This

polyp had tumour morphology that stained positive for cytokeratin 7 (CK7), thyroid transcription factor-1 (TTF-1), chromogranin and synaptophysin, and negative for CK20 (figure 2). These results were consistent with a small cell carcinoma metastasis from primary lung cancer. The other polyps were tubular adenomas and hyperplastic in histology.

At the time of presentation to oncology clinic, the patient reported a 5-pound weight loss over the preceding 2 months despite good appetite, but denied fever, haemoptysis, dyspnoea, chest pain or any neurological symptoms. On social history, he indicated a 60 pack-year smoking history and heavy alcohol use, having quit both habits 6 years prior to presentation. On examination, he was found with obesity, scleral icterus, a hard but mobile 2×1 cm subcutaneous nodule on the left upper abdominal wall and a mildly enlarged prostate. His complete blood count was significant for anaemia (haemoglobin 12.0 g/dL) with a mildly elevated mean corpuscular volume (96.1 fL) and red blood cell distribution width (14.9%) and thrombocytopenia (50 000 per mm³). His chemistry was notable for low albumin (3.4 g/dL), elevated total bilirubin (3.0 mg/dL) and elevated alkaline phosphatase (202 IU/L). There was no evidence on history, examination or laboratory tests that suggested paraneoplastic syndrome, which can sometimes be the first clinical manifestation of malignancy.⁶

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To cite: Khan AM, Khan S, Dave V, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202624

Figure 2 Histological examination of the polyp located near the ileocolic valve. (A–C) H&E staining of increasing magnification demonstrating infiltrative cells with prominent nuclear moulding and high mitotic count. (D–H) These cells stained positive for CK7 (D), TTF-1 (E), chromogranin (F) and synaptophysin (G), and negative for CK20 (H).

INVESTIGATIONS

Imaging studies including CT, MRI, positron emission tomography (PET) and whole body bone scan (figure 3) were conducted. A CT of the chest demonstrated a 4.3×4.0×4.2 cm spiculated mass in the posterior segment of the right upper lobe surrounding the bronchus, extending into the right hilum and pretracheal space with lymphadenopathy (figure 3A). A CT of the abdomen and pelvis demonstrated a nodular liver with TIPS catheter in place, multiple low-density hepatic and splenic lesions (figure 3B). MRI of the brain demonstrated several lesions in the cerebellum and in the supratentorial region (the largest in the left frontal lobe), both with associated vasogenic oedema (figure 3C). A whole body bone scan showed tracer uptake in the mid-thoracic vertebrae that correlated with arthritic spurs on the CT of the chest (figure 3D). Finally, PET scan

confirmed extensive metastatic disease with hypermetabolic lesions of the brain, lung, liver, lymph nodes, skeleton and abdominal wall nodule. Of note, chest X-ray and CT of the abdomen and pelvis from 10 months prior to presentation were negative for suspicious lesions.

DIFFERENTIAL DIAGNOSIS

Morphology and immunohistochemistry revealed that these small cells were likely from primary lung cancer given the positive staining for CK7 and TTF-1, and were of the neuroendocrine (NE) origin given the positive staining for chromogranin and synaptophysin. When analysing lung cells of NE origin, there are four major types as classified by the 2004 WHO: typical carcinoid, atypical carcinoid, large cell NE carcinoma and SCLC.⁷ The most common is SCLC which have characteristic features including

Figure 3 CT (A, B, E, F), MRI (C, G) and whole body bone scans (D, H) at presentation (A–D) and following chemoradiation treatment (E–H). Despite therapy, there was an increase in number and/or size of the primary and metastatic small cell lung carcinoma lesions.

small, irregularly shaped round or spindle-shaped cells with finely granular chromatin, nuclear moulding, crush artefact and high mitotic rate.⁷ Typical carcinoid tumours, on the other hand, also appear as small, round cells but are monotonous, with coarsely granular chromatin, very low mitosis, no necrosis and high vascularity.⁷ With respect to immunohistochemistry, small cells have weak reactivity for NE markers, while carcinoid tumours have strong reactivity. Some have also suggested checking Ki-67 proliferation rates to help differentiate the two with rates of less than 25% excluding the diagnosis of SCLC.⁷

Another differential considered was a GI lymphoma. The GI tract is the most common extranodal site involved by lymphomas.⁸ These can generally be easily distinguished from lung cancer on morphology as they are generally smaller cells organised in sheets. On immunohistochemistry, they do not stain for CK7 or CK20, which are epithelial markers, and would instead react positively with B cell or T cell markers.

TREATMENT

Given the multiple rim-enhancing lesions, the patient was immediately managed with steroids and received 3000 cG of whole-brain irradiation divided into 10 fractions. Lung mass biopsy via bronchoscopy was performed, but the pathology was negative for malignancy. He was subsequently started on systemic chemotherapy with carboplatin and etoposide. He was also given allopurinol for tumour lysis prophylaxis and pegfilgrastim for neutropenia. Overall, he completed eight cycles of chemotherapy.

OUTCOME AND FOLLOW-UP

Two months after completing his chemotherapy, he started experiencing multiple falls associated with lightheadedness, back pain, left leg weakness and numbness. Examination demonstrated vertebral body tenderness over the lumbar spine, left psoas motor weakness, decreased sensation to light touch over anterior left thigh and reported paraesthesias over the same region. He was again started on steroids while awaiting MRI of the spine. As suspected, there were epidural tumours at T10 and L3, cord signal abnormality, but no cord compression. He underwent a total of 2000 cG of palliative radiation to T9 to L4 dorso-lumbar spine and was started on zoledronic acid. A follow-up imaging demonstrated enlargement of primary lung lesion, increasing thoracic lymphadenopathy, increase in number and size of hepatic and splenic hypoattenuated lesions, widespread bone lesions and persistence of brain lesions (although the brain MRI study was limited by motion artefact; [figure 3E–H](#)). Topotecan as a second-line chemotherapy was not recommended because of the patient's liver function. He was discharged to home hospice as per the patient and his family wishes and the patient died 11 months after diagnosis of disease.

DISCUSSION

Two-thirds of SCLCs have metastasised by the time of diagnosis.² The incidence of GI metastases from primary lung cancer ranges from less than 0.5% to 14%.^{4–9} Given the proximity to the lungs, the oesophagus is the most common site of GI involvement as a result of direct extension of the malignancy.⁴ By comparison, haematogenous spread is thought to contribute to metastases to the remainder of the GI tract, most commonly to the small intestine, followed by the stomach and large intestine.^{4–9} Clinical presentations of GI metastases include abdominal pain, nausea and vomiting, anaemia, change in bowel habits, weight loss and jaundice. More advanced metastatic disease can present with obstruction, perforation or haemorrhage, which generally portends a poor prognosis.¹⁰

Histologically, some authors argue squamous cell carcinoma to be the most common primary lung cancer to metastasise to the GI tract while others argue it to be adenocarcinoma.⁵ SCLC remains an infrequent source of metastasis to the GI tract.

We describe a rare case of extensive-stage SCLC that was incidentally diagnosed by surveillance colonoscopy in the absence of pulmonary or GI symptoms. In such instances, immunohistochemistry plays an essential role in identifying the primary lesion. GI malignancies can be differentiated from lung cancer on the basis of immunoreactivity to a number of markers. The former are typically immunoreactive for CK20 and homeobox protein CDX2 while the latter stain positively with CK7 and TTF-1.^{2–11} Additional markers for SCLC include keratin, epithelial membrane antigen and NE markers such as chromogranin A, neuron-specific enolase, neural cell adhesion molecule and synaptophysin.² Although this study was limited by lack of histological confirmation of the primary lung lesion as small cell carcinoma, more than 95% of these carcinomas arise in the lung and remains the top differential for metastatic small cell carcinoma of unknown primary site.⁷

Most of the literature on SCLC classify patients on the basis of the Veteran's Administration Lung Study Group's 2-stage classification scheme of limited-stage disease and extensive-stage disease.^{2–12} For patients with extensive-stage disease, median survival rates are 9–11 months, about half that of limited-stage disease.² Given his extensive smoking history, would screening low-dose spiral CT have resulted in earlier diagnosis and, thus, better prognosis for our patient? According to the National Lung Screening Trial (NLST), there is decreased mortality from lung cancer in asymptomatic, high-risk individuals screened with low-dose CT.¹³ However, Cuffe *et al*¹⁴ argue that because SCLC is inherently aggressive and its biology dictates early dissemination, there is limited utility of CT in detecting limited-stage SCLC. On the contrary, increasing use of CT may identify limited-stage disease that can be considered for curative intent surgical resection and/or chemoradiation, improving long-term outcomes.¹⁵

Learning points

- ▶ Gastrointestinal metastases by small cell lung carcinoma (SCLC) are rare but, if undetected, can result in obstruction, perforation or haemorrhage.
- ▶ Immunohistochemistry is essential in identifying malignancies of unknown primary site and, thus, provide targeted therapy.
- ▶ It is yet unclear whether high-risk patients with SCLC benefit from low-dose CT screening on the basis of findings from the National Lung Screening Trial (NLST) trial.

Acknowledgements The authors are grateful to Dr VT Chang for his critical review of the manuscript. Dr VT Chang and Dr S Kasimis were the Oncologists on service. They also thank Dr Shahida Ahmed for providing the histology images.

Contributors AMK helped to manage the patient while admitted, performed the literature search, wrote the article and is the guarantor for the publication. SK and VD helped to manage the patient while admitted and reviewed the article prior to publication. HB provided colonoscopy imaging and reviewed the article prior to publication.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin* 2013;63:11–30.
- 2 Kalemkerian GP, Akerley W, Bogner P, *et al.* Small cell lung cancer. *J Natl Compr Canc Netw* 2013;11:78–98.
- 3 Govindan R, Page N, Morgensztern D, *et al.* Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. *J Clin Oncol* 2006;24:4539–44.
- 4 Antler AS, Ough Y, Pitchumoni CS, *et al.* Gastrointestinal metastases from malignant tumors of the lung. *Cancer* 1982;49:170–2.
- 5 Rossi G, Marchioni A, Romagnani E, *et al.* Primary lung cancer presenting with gastrointestinal tract involvement: clinicopathologic and immunohistochemical features in a series of 18 consecutive cases. *J Thorac Oncol* 2007;2:115–20.
- 6 Sai-Ching JY, Mouhammed AH, Thosani SN. Lung cancer-induced paraneoplastic syndromes. *Curr Opin Pulm Med* 2011;17:260–8.
- 7 Rekhtman N. Neuroendocrine tumors of the lung: an update. *Arch Pathol Lab Med* 2010;134:1628–38.
- 8 Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. *World J Gastroenterol* 2011;17:697–707.
- 9 Kim SY, Ha HK, Park SW, *et al.* Gastrointestinal metastasis from primary lung cancer: CT findings and clinicopathologic features. *Am J Roentgenol* 2009;192: W197–201.
- 10 Garwood RA, Sawyer MD, Ledesma EJ, *et al.* A case and review of bowel perforation secondary to metastatic lung cancer. *Am Surg* 2005;71:110–6.
- 11 Wang NP, Zee S, Zarbo RJ, *et al.* Coordinate expression of cytokeratins 7 and 20 defines unique subsets of carcinomas. *Appl Immunohistochem* 1995;3:99–107.
- 12 Jett JR, Schild SE, Kesler KE, *et al.* Treatment of small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2013;143: e400S–19S.
- 13 Aberle DR, Adams AM, Berg CD, *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;365:395–409.
- 14 Cuffe S, Mous T, Summerfield R, *et al.* Characteristics and outcomes of small cell lung cancer patients diagnosed during two lung cancer computed tomographic screening programs in heavy smokers. *J Thorac Oncol* 2011;6:818–22.
- 15 Koizumi T, Fukushima T, Hamanaka K, *et al.* Surgical outcomes in patients with small cell lung cancer: comparative analysis of computed tomography-detected patients with others. *World J Surg Oncol* 2013;11:61.

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