CASE REPORT

Oral and gastrointestinal symptomatic metastases as initial presentation of lung cancer

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SUMMARY

Metastasis to the tongue, duodenum or pancreas from primary lung cancer is uncommon. Primary lung cancer presenting with symptoms related to metastases at these sites, at initial presentation is extremely rare. We report a 45-year-old man with disseminated lung malignancy who presented with dyspepsia, melena, symptoms due to anaemia and swelling in the tongue. Oral examination revealed a hard submucosal anterior tongue lesion. Biopsies from the tongue lesion and the duodenal ulcer seen on upper gastrointestinal endoscopy were suggestive of metastasis from lung primary. CT revealed lung primary with disseminated metastasis to lung, liver, adrenals, kidneys, head and body of pancreas, duodenum and intra-abdominal lymph nodes. The patient was treated with palliative chemotherapy. The unusual presentation and diagnostic details are discussed.

BACKGROUND

Distant metastasis from lung cancer is common; however the tongue, duodenum or pancreas are relatively rare sites. Often such metastases are found months after initial diagnosis or at autopsy. Symptoms from the tongue, duodenal or pancreatic metastasis at the initial presentation is extremely rare. About 1% of lesions in the oral cavity are due to metastasis from other primary sites.¹ Like with primary tongue cancer, metastatic tongue lesions could be ulcerative to polypoid.¹ The prevalence of small bowel metastases from lung cancer ranges between 2.6 and 10.7%.² There are reports of duodenal metastasis from lung primary resulting in complications like massive upper gastrointestinal haemorrhage, perforation and obstruction.^{3–6}

Metastasis to the pancreas from lung cancer is seen in about 3%.⁷ Autopsy studies show that lung is one of common primary sites with pancreatic metastasis.⁸ Metastases to the pancreas are found with squamous, small cell and adenocarcinoma of lung.^{9–11} We report a patient with disseminated lung malignancy whose initial symptoms were related to tongue and duodenal metastases.

CASE PRESENTATION

A 45-year-old man, a smoker, presented with 2-month history of melena, dyspepsia and loss of weight. He had symptoms due to anaemia; fatigue, breathlessness on exertion and required blood transfusions. The Eastern Cooperative Oncology Group (ECOG) performance status was 1. He had a swelling in the left side of tongue, with difficulty articulating, eating and hoarseness of voice. He had

non-insulin-dependent diabetes mellitus. On examination he was pale. There was a hard submucosal swelling with no ulceration, involving the left anterior two-third of tongue, ~2 cm from the tip, not crossing the midline, with no regional neck nodes.

INVESTIGATIONS

He had anaemia with haemoglobin 8.8 g/dL. Upper gastrointestinal endoscopy revealed an ulceroproliferative fragile growth in the proximal duodenum with 50% circumferential involvement. Histopathology from duodenal mucosal biopsy, revealed poorly differentiated adenocarcinoma with mucosal infiltration by tumour arranged in sheets, clusters and singly dispersed polygonal cells displaying moderately pleomorphic hyperchromatic to vesicular nuclei; there were few with distinct nucleoli and moderate to abundant amounts of cytoplasm. The intervening stroma showed desmoplasia and secondary infiltrates of lymphocytes, neutrophils, eosinophils and plasma cells. The tumour cells were diffusely positive for pan cytokeratin, thyroid transcription factor (TTF-1) and was negative for chromogranin, synaptophysin and leukocyte common antigen (LCA) (figure 1). In view of the diffuse TTF-1 positivity, the possibility of metastasis from the lung was considered. The tumour cells were negative for ALK D5F3 and no mutations were seen in all four exons of the epidermal growth factor receptor gene (exons 18, 19, 20 and 21).

Biopsy of the tongue lesion showed poorly differentiated adenocarcinoma, tumour cells displayed moderate to markedly pleomorphic, vesicular, mitotically active nuclei, prominent nucleoli and abundant amounts of eosinophilic cytoplasm with no definite lymphovascular or perineural invasion. The tumour cells were diffusely positive for TTF1, focally positive for CK7 and Napsin A and negative for P63. The immunoprofile was suggestive of lung primary (figure 2).

Contrast-enhanced CT of the thorax and abdomen revealed a left upper lobe lung mass (2.1×4.2 cm) with lower left paratracheal nodal mass (4×3.2 cm; figure 3). There were smaller nodes in the subcarinal, paraoesophageal and hilar region. There were ill-defined hypodense lesions one in the proximal body of pancreas (1.4×1.7 cm) and another in the head of pancreas (1.9×1.8 cm) with peripancreatic and periportal lymphadenopathy (figure 4). There were other metastases to both lungs, liver, bilateral adrenal and kidney. The

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Figure 1 Duodenal mucosal biopsy showing infiltration by tumour composed of sheets, clusters and singly dispersed polygonal cells displaying moderately pleomorphic hyperchromatic to vesicular nuclei, few with distinct nucleoli and moderate to abundant amounts of cytoplasm (H&E $\times 100$ and H&E $\times 400$).

mass in the duodenum at the junction of first and second part was also seen.

DIFFERENTIAL DIAGNOSIS

An initial diagnosis of duodenal or pancreatic malignancy with duodenal infiltration was considered, in view of melena, anaemia and the gastroscopy findings, with a synchronous tongue malignancy. However, the histopathology and immunoprofile from both these sites were suggestive of a lung primary with duodenal and tongue metastasis, which was further confirmed on radiological imaging.

TREATMENT

In view of the disseminated metastatic lung cancer, the patient was treated with palliative doublet chemotherapy with carboplatin and pemetrexed. The disease progressed following two cycles of chemotherapy with worsening of performance status. Chemotherapy was stopped and supportive care was continued.

Figure 2 Biopsy from tongue showing infiltration by tumour composed of islands and nests of polygonal cells with moderately pleomorphic vesicular nuclei, prominent nucleoli and abundant amounts of cytoplasm (H&E $\times 100$ and H&E $\times 400$).

Figure 3 Contrast-enhanced CT of the thorax showing a left upper lobe lung mass (2.1 $\times$ 4.2 cm).

Anaemia was treated with blood transfusions and oral haematinics.

OUTCOME AND FOLLOW-UP

The patient returned home after chemotherapy at our institution and was lost follow-up. Attempts to contact the patient through telephone were not successful.

DISCUSSION

The brain, liver, adrenals and bone are the common sites of metastases from primary lung cancer. Metastasis to the tongue, duodenum and pancreas as with this patient can occur with disseminated metastases, but are not usually symptomatic or diagnosed before death, and very rarely are part of the initial presentation.¹ The initial presentation of this patient was unusual, as his symptoms were related to anaemia, gastrointestinal and oral symptoms than the primary lung cancer.

Primary cancers spread through systemic, venous or lymphatic circulation. Metastasis to tongue, duodenum and pancreas in

Figure 4 Contrast-enhanced CT of the abdomen showing hypodense lesion in the proximal body of pancreas (1.4 $\times$ 1.7 cm) and another hypodense lesion in the head of pancreas (1.9 $\times$ 1.8 cm).

our patient could have occurred more commonly through systemic or venous circulation and less likely through lymphatics as this patient had widespread metastases. This patient had diabetes, and it has been earlier proposed that diabetes could impede the immune system and its surveillance of cancer cells and contribute to unusual metastases.¹

There are reports of tongue metastasis from squamous, large cell lung carcinoma and adenocarcinoma as in our patient.^{1 12}

Metastases to the small bowel from lung primary are usually asymptomatic; however there are some reports of small bowel perforation secondary to the metastases.^{13 14} Perforation secondary to small bowel metastasis has been reported most commonly with adenocarcinoma in 23.7%, followed by squamous cell carcinoma (22.7%), large cell carcinoma (20.6%) and small cell carcinoma (19.6%).¹³

Haemorrhage from small bowel metastases is uncommon, as in our patient; however, there are a few reports of duodenal metastasis from primary lung cancer with melena.^{3 4} There are other reports of gastrointestinal bleeding from duodenal metastasis later on after the diagnosis of lung cancer. There is a recent report of a patient who presented with iron deficiency anaemia and reduced effort tolerance without melena, who on evaluation was found to have lung cancer with duodenal metastasis.¹⁵ The most common site of small bowel metastasis is the jejunum followed by the ileum.¹³ Results from a cohort of 733 patients with non-small cell lung cancer, with 218 autopsies revealed small bowel metastasis in 4.6%, all being adenocarcinoma. Interestingly all these patients had concurrent metastasis in other sites: adrenals, mediastinal nodes, liver, pleura, contralateral lung, bones and brain.¹⁶

Metastasis to the pancreas from lung cancer is most common with small cell lung cancer (10.5%) followed by adenocarcinoma (2.3%) with solitary nodule at the head being the most common pattern.⁷

The patient we report also had extensive metastasis at different sites including, both lungs, liver, bilateral adrenal, kidney, head and body of pancreas, mediastinal and intra-abdominal lymph nodes and tongue. Such extensive metastasis may be linked to the activation of different molecular pathways enabling

epithelial mesenchymal transition, cell migration and invasion.¹⁷ The median survival of patients with intestinal metastasis is 2.3 months, with old age, extraintestinal metastasis and intestinal perforation being risk factors for poor prognosis.² Palliative chemotherapy or radiotherapy to alleviate symptoms can be considered as appropriate. Considering the disseminated systemic disease, this patient received palliative chemotherapy.

Isolated metastasis to the tongue, duodenum or pancreas from lung cancer is uncommon, but has been reported. This report is unique as this patient had metastases involving three unusual sites, with symptoms relating to duodenal metastasis and tongue metastases at initial presentation. Metastases to unusual sites should be considered if symptoms relating to those sites are present in patients with disseminated lung cancer.

Contributors JJ, GI and AS were involved in patient care. JJ and SB wrote the manuscript. GI and AS reviewed the manuscript. GI contributed the pathology photomicrograph.

Competing interests None declared.

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Learning points

- ▶ Metastasis of lung cancer to three unusual sites like tongue, duodenum and pancreas at initial presentation is rare.
- ▶ Symptomatic duodenal metastasis especially bleeding at presentation is extremely rare.
- ▶ Immunohistochemistry performed on biopsy specimens from metastatic site can help in establishing correct diagnosis.
- ▶ In disseminated lung cancer, metastasis should be considered in patients with upper gastrointestinal symptoms (dyspepsia, melena) or oral lesions.
- ▶ The prognosis of patients with disseminated metastasis, especially in unusual sites is poor.

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