

Bilateral endobronchial metastases from hepatocellular carcinoma (HCC): A case report with literature review

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Abstract

Hepatocellular carcinoma presenting with endobronchial metastases is extremely rare, with less than 15 cases reported over the last 4 decades. We describe a case of a 62-year-old male who first presented with pulmonary symptoms secondary to bilateral endobronchial metastatic disease from newly diagnosed hepatocellular carcinoma.

KEYWORDS

bronchoscopy, endobronchial, hepatocellular carcinoma, metastases, pathology

INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary tumour of the liver and typically develops in the setting of chronic liver disease. In approximately 15% of cases, extrahepatic metastases are present at the time of diagnosis, and the most frequent site of extrahepatic metastases is in the lungs.^{1,2} However, only a few cases of endobronchial metastases (EBM) have been reported³ and the majority of the secondary deposits are found in the pulmonary parenchyma. We describe a case of HCC presenting with bilateral EBM.

CASE REPORT

A 62-year-old male ex-smoker with a past medical history of asthma and intravenous drug use was admitted for a 6-month history of persistent cough, weight loss, and reduced exercise tolerance. He also recently developed haemoptysis, coughing up blood clots and tubular soft tissue.

Chest radiograph showed bilateral lower zone large nodules. Computed tomography of the thorax showed lobulated soft tissue density masses which extend intraluminally within both lower lobe bronchus giving a finger in glove appearance

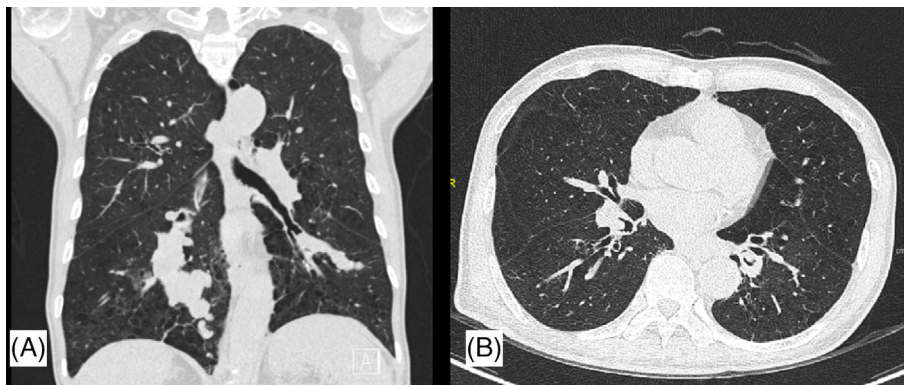


FIGURE 1 Coronal (A) and axial (B) views of contrasted chest computed tomography demonstrate bilateral endobronchial lesions.

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suggesting that these lesions are endobronchial in nature rather than intraparenchymal (Figure 1).

Bronchoscopy showed endobronchial lesions in the basal segments of both bilateral lower lobes (Figure 2). Endobronchial biopsy of the endobronchial lesions revealed multiple

pieces of totally necrotic tissue with a small amount of lymphocytes. No fungal elements were seen. Aerobic culture of the bronchial washings grew *Escherichia coli* and *Enterobacter cloacae*. The patient was treated with 14 days of antibiotics.

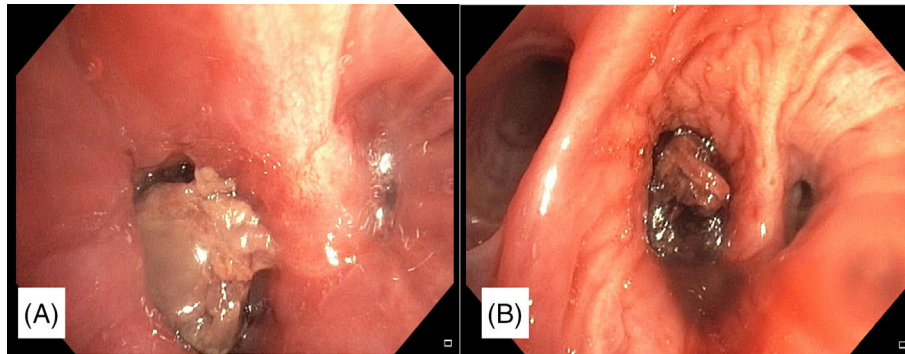


FIGURE 2 (A) Endobronchial lesion seen in entrance to right lower lobe basal segments. (B) Endobronchial lesion seen in entrance to left lower lobe basal segments.

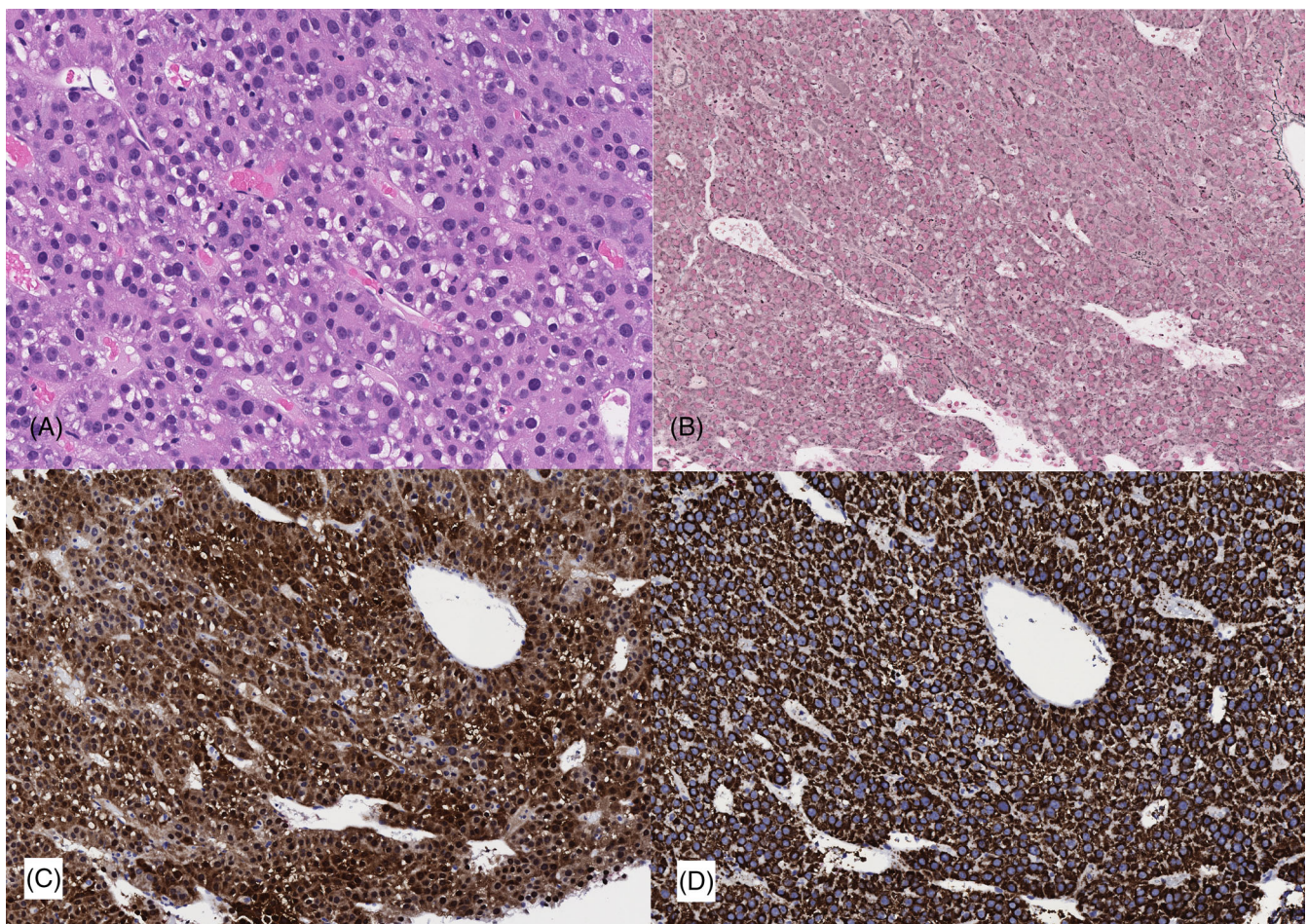


FIGURE 3 (A) High power views of the metastatic hepatocellular carcinoma showing irregular islands and broad trabeculae of polygonal cells separated by sinusoidal spaces. The tumour cells have enlarged rounded nuclei, prominent nucleoli, and granular eosinophilic cytoplasm. H&E $\times 200$. (B) The reticulin stain shows a paucireticulin pattern in the tumour. Reticulin $\times 100$. (C) The immunohistochemical stain for arginase-I is positive in the tumour cells. Arginase-I $\times 100$. (D) The immunohistochemical stain for HepPar1 is positive in the tumour cells. HepPar1 $\times 100$.

TABLE 1 Characteristics of case reports of endobronchial metastases from hepatocellular carcinoma over the last 35 years.

Case No.	Gender	Age	Presentation/ symptoms	Duration of symptoms	Time from HCC diagnosis	HCV status	Bronchus location	Treatment	Author	Year
1	F	66	Pneumonia	*	Synchronous	*	Right upper lobe	Chemotherapy	Camps C ⁹	1988
2	M	61	Cough, haemoptysis	*	9 years	*	Right main bronchus	*	Murayama ¹⁰	1992
3	*	*	*	*	9 months	*	*	*	Salud ¹¹	1996
4	F	61	Cough, haemoptysis	1 month	1 year 4 months	*	Right upper lobe	Lobectomy	Lee ¹²	2003
5	M	80	Haemoptysis	*	2 years	Positive	Left lower lobe	Radiotherapy	Kido ¹³	2005
6	M	65	Haemoptysis	*	8 years	*	Right bronchus intermedius	Pneumonectomy	Purandare ¹⁴	2009
7	F	71	Dyspnoea, respiratory failure	3 months	7 years	Positive	Bilateral	Bronchial Stent	Uchida ¹⁵	2010
8	F	20	Dyspnoea, chest pain	2 months	3 years	Negative	Right upper lobe	Targeted therapy (Sorafenib) + Chemotherapy	Szumera- Cieckiewicz ⁸	2013
9	M	51	Cough	2 months	6 years	*	Left lower lobe	N/A	Dong ¹⁶	2014
10	F	63	Dyspnoea, cough	1 month	1 year	*	Right upper lobe	Supportive Care	El-Badrawy ¹⁷	2018
11	M	62	Cough, haemoptysis	3 months	1 year	*	Bilateral	Bronchoscopy (Nd YAG laser) + Immunotherapy (Pembrolizumab)	Cheung ³	2019
12	M	72	Hemoptysis	4 days	15 years	*	Right upper lobe	*	Cai ¹⁸	2020
13	M	80	*	*	13 years	*	Right upper lobe	Targeted therapy (Sorafenib)	Zhang ¹⁹	2022
14	M	62	Hemoptysis, weight loss	6 months	Synchronous	Positive	Bilateral lower lobes	Targeted therapy (Levatinib)	Current Report	2023

Note: *No data available.

The patient also had deranged liver transaminases, which prompted further investigation. The patient was eventually diagnosed with chronic hepatitis C infection, Child-Pugh class A cirrhosis, and multifocal HCC. The patient underwent Y-90 selective internal radiation therapy.

Despite treatment with targeted sensitivity and susceptibility-guided antibiotic therapy for 14 days, the patient remained febrile and the endobronchial lesions did not resolve or reduce in size. A repeat attempt to obtain a histological diagnosis was made via Computed Tomography-guided Transthoracic Core Biopsy performed on the intraluminal masses, particularly to target the less necrotic areas which could not be reached by endoscopy. The cores of the tissue showed a metastatic HCC consisting of irregular islands and broad trabeculae of polygonal cells separated by sinusoidal spaces. The tumour cells showed enlarged rounded nuclei, prominent nucleoli, and granular eosinophilic cytoplasm (Figure 3). Mitotic activity and areas of necrosis were seen. The reticulin stain showed a paucireticulin pattern. Cytokeratin AE1/3, arginase-I, and Hepatocyte Paraffin 1 were positive in the tumour cells. HCC with EBM was diagnosed.

The patient opted for oral Levatinib as systemic therapy. The patient was also given Sofosbuvir, Velpatasvir, and Ribavirin for hepatitis C treatment. Two months into treatment, patient stopped oral levatinib due to side effects of lower limb edema and instead opted for best supportive care.

A follow-up CT thorax 1 month later showed an increase in size of the lobulated soft tissues within the dilated airways in the bilateral lower lobes associated with the collapse of the left lower lobe as well as partial collapse of the right lower lobe. The patient eventually passed away.

DISCUSSION

Metastatic disease of the lungs from extrathoracic solid tumours is a common occurrence. However, the finding of metastatic tumours manifesting as endobronchial masses is a rare event.⁴ EBM are defined as bronchoscopically visible involvement of the subsegmental or more proximal central bronchus with histologically verified extrathoracic primary malignancy.^{5,6}

EBM were also classified by Kiryu et al. into four groups according to their developmental mode as follows: type I, direct metastasis to the bronchus; type II, bronchial invasion by a parenchymal lesion; type III, bronchial invasion by mediastinal or hilar lymph node metastasis; and in the case of our patient: type IV, peripheral lesions extended along the proximal bronchus.⁵

In 2014, Marchioni and colleagues documented a case series of 174 patients with EBM from extrathoracic solid tumours collected over 18 years.⁴ Extrapulmonary tumours most often resulting in EBM included carcinomas from the breast, colon-rectum, and kidney.^{4,7}

HCC however, only represented 2% of all extrapulmonary malignancies exhibiting metastatic spread to the tracheobronchial tree.⁴ Currently, there are only 13 cases reported to date

(Table 1) found in our literature search. The most common symptoms reported were dyspnoea, cough, and haemoptysis,^{4,6} which was also seen in our literature search. Notably, almost a quarter of the patients did not have respiratory symptoms^{4,6} upon diagnosis.

Although it remains unclear why EBM are more frequently detected in certain carcinomas,⁶ systemic use of chest CT scans and bronchoscopy could be useful for patients presenting with carcinomas from the breast, colon-rectum, and kidney.⁴

Histologically, HCC consists of polygonal cells with atypical nuclei and higher nuclear-to-cytoplasmic ratio commonly arranged in a trabecular pattern. Bile production may be seen. The markers of HCC are arginase-I and hepatocyte paraffin 1, which were positive in our case, and alpha-1-fetoprotein.⁸

The treatment of EBM should be individualized according to patient symptoms, histopathological diagnosis, size and site of metastases, and general condition of the patient. The decision for endobronchial intervention will depend on tumour location, degree of intrinsic obstruction, and local resource availability and expertise.³

In conclusion, EBM from HCC are an exceptionally rare manifestation of advanced-stage disease, which may present with respiratory symptoms. Accurate diagnosis and management require an interdisciplinary and patient-centred approach.

AUTHOR CONTRIBUTIONS

Leping Koay: The conception or design of the work, the acquisition, analysis or interpretation of data for the work. Drafting the work and revising it critically for important intellectual content. **Hwei Yee Lee:** Revising the work critically for important intellectual content. **Huiying Xu:** Revising the work critically for important intellectual content. **Chee Kiang Phua:** Revising the work critically for important intellectual content.

CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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