Adenocarcinoma hepatoide de pulmón: a propósito de un caso raro

Hepatoid adenocarcinoma of the lung: a rare case report

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ABSTRACT

Background: Hepatoid adenocarcinoma of the lung (HAL) is a rare type of carcinoma that histologically resembles a primary hepatocellular carcinoma (HCC), leading to a potential misdiagnosis.

Clinical case: A 72-year-old man with a history of heavy tobacco smoking and recent ischemic stroke, was admitted due to hemoptysis (less than 100 ml/hour), dyspnea, and pleuritic chest pain from the last month. The CT scan revealed a left hilar mediastinal lesion (<10 cm), and multiple hepatic lesions. A bronchoscopy showed diffuse mucosal infiltration of the left main bronchus without active bleeding. Hepatotropic virus serology and alpha-fetoprotein were normal, and initial histology data reassembled HCC. The differential diagnosis dilemma was to determine whether it was an HCC with lung metastasis or primary lung cancer with liver metastases; however, considering the clinical setting and the histology features, a HAL diagnosis was made. Unfortunately, one week later after discharge, the patient had massive hemoptysis and died.

Discussion: HAL is a rare type of lung cancer associated with a poor prognosis and no specific oncological treatment. Histological features resemble an HCC; hence, the diagnosis required special attention to clinical, epidemiological, imaging, and pathology data for a correct diagnosis.

Keywords: Cancer, hepatocellular carcinoma, hepatoid adenocarcinoma of the lung, pathology.

RESUMEN

Antecedentes: El adenocarcinoma hepatoide de pulmón (HAL) es un tipo raro de carcinoma que histológicamente se asemeja a un carcinoma hepatocelular (CHC) primario, lo que lleva a un potencial diagnóstico erróneo.

Caso clínico: Un varón de 72 años, con antecedentes de fuerte tabaquismo y accidente cerebrovascular isquémico reciente, ingresó por hemoptisis (menos de 100 ml/hora), disnea y dolor torácico pleurítico desde hacía un mes. La TC reveló una lesión mediastínica hiliar izquierda (<10 cm) y múltiples lesiones hepáticas. Una broncoscopia mostró infiltración mucosa difusa del bronquio principal izquierdo sin hemorragia activa. La serología del virus hepatotropo y la alfa-fetoproteína fueron normales, y los datos histológicos iniciales reafirmaron un CHC. El dilema del diagnóstico diferencial era determinar si se trataba de un CHC con metástasis pulmonares o de un cáncer de pulmón primario con metástasis hepáticas; sin embargo, teniendo en cuenta el contexto clínico y las características histológicas, se hizo un diagnóstico de HAL. Lamentablemente, una semana después del alta, el paciente sufrió una hemoptisis masiva y falleció.

Discusión: El HAL es un tipo raro de cáncer de pulmón asociado a un mal pronóstico y sin tratamiento oncológico específico. Las características histológicas se asemejan a las de un CHC; por lo tanto, el diagnóstico requirió especial atención a los datos clínicos, epidemiológicos, de imagen y patológicos para un diagnóstico correcto.

Palabras clave: Cáncer, carcinoma hepatocelular, adenocarcinoma hepatoide de pulmón, patología.

BACKGROUND

Lung cancer remains the leading cause of cancer death worldwide despite efforts in prevention, diagnosis, and treatment. It is classified into two main groups, small-cell carcinoma (SCLC), which can reach up to 15% of the cases, and non-small-cell carcinoma (NSCLC), which represents the majority up to 85%; within NSCLC classification there are different subtypes: adenocarcinoma, squamous cell carcinoma, and large-cell lung carcinoma[1]. Hepatoid adenocarcinoma of the lung (HAL) is a rare type of carcinoma that histologically resembles a primary hepatocellular carcinoma (HCC). HAL presents an aggressive course with lower survival rates compared to other NSCLCs, while its diagnosis remains a challenge for clinicians and pathologists because it can easily be confused with HCC especially when liver metastases are present.[2]

We aimed to describe a rare type of lung cancer that histologically resembles a primary hepatocellular carcinoma leading to a potential misdiagnosis and highlight the importance of proper bidirectional communication between clinicians and pathologists.

CLINICAL PRESENTATION

A 72-year-old-man with a previous history of heavy tobacco smoking and ischemic stroke two months before admission in treatment with clopidogrel 75 mg qd, was hospitalized due to hemoptysis (less than 100 ml/hour), dyspnea, and pleuritic chest pain from the last month. Laboratory tests showed hemoglobin 16.4 g/dL, platelets 248,000/µL, leukocytes 8,900/µL, alanine aminotransferase 50 U/L, bilirubin 0.7 mg/dL, gamma-glutamyl transferase 214 U/L, creatinine 0.70 mg/dL with no electrolyte imbalance, and C-reactive protein 4.5 mg/dL. The thoracoabdominopelvic CT scan evinced a left hilar mediastinal lesion (<10 cm), and multiple hepatic lesions suggestive of malignan-

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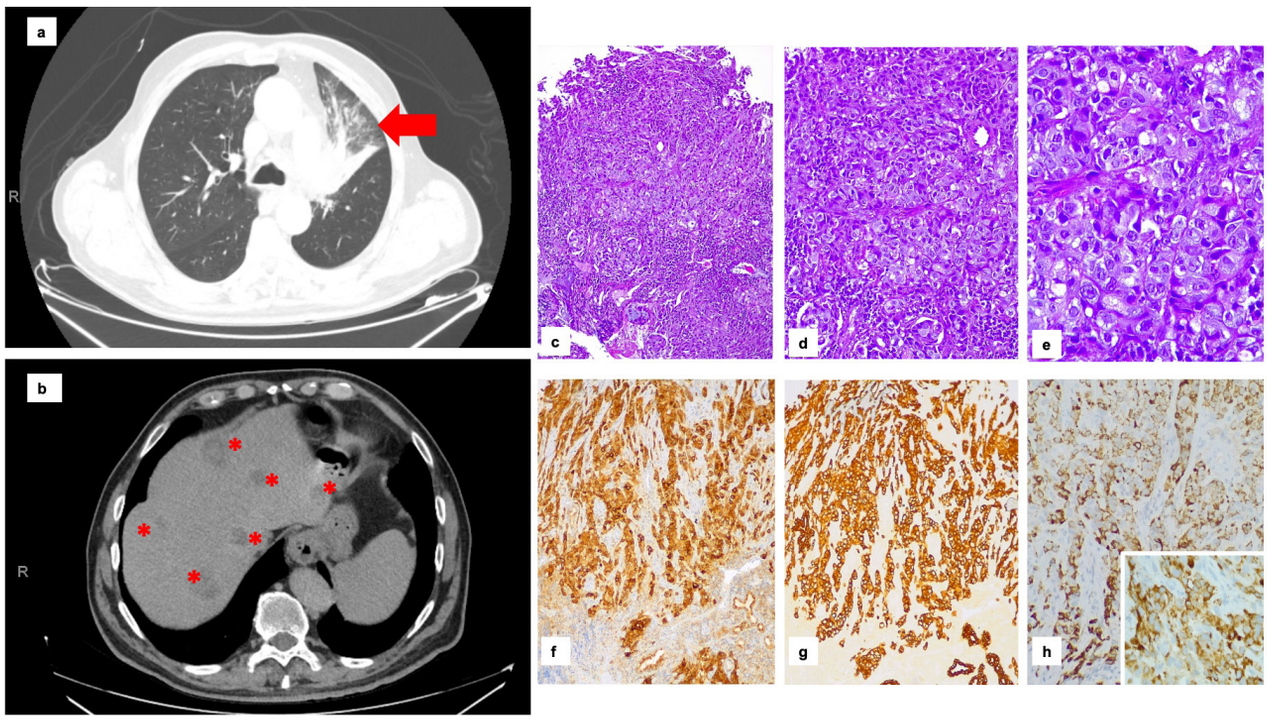
Figure 1. Left hilar mediastinal lesion (red arrow; panel a), and multiple hepatic lesions (red stars; panel b) suggestive of malignancy in thoracoabdominopelvic CT scan. Biopsy histological and immunohistochemical features are shown in panels c to h. Bronchial mucosa infiltrated by an epithelial neoplasm with nested and trabecular growth patterns (c-d); and polygonal cells with abundant eosinophilic, fine granulate cytoplasm, and atypical nuclei with prominent nucleoli, resembling liver cells (e), stained by hematoxylin-eosin (HE 10X, 20X, and 40X, respectively). Immunohistochemical tumor expression: epithelial membrane antigen (f), cytokeratin-7 (g), and hepatocyte antigen (inset with higher magnification, panel h).



cy (Figure 1 a-b). A bronchoscopy was performed showing diffuse mucosal infiltration of the left main bronchus with a decreased lumen and traces of bleeding without active bleeding, and a lung biopsy was taken. Hepatotropic virus serology was negative, and serum biomarkers showed alpha-fetoprotein 3.4 µg/L (0.89 - 8.78) and CYFRA 21-1 46.9 µg/L (0.1 - 2.08). Unexpectedly, the histology study resembles HCC (Figure 1 c-e); and the immunochemistry was positive for cytokeratin (CK) 7, epithelial membrane antigen, and hepatocyte antigen stains and negative for CK-20, CDX-2, TTF-1, p40, p63, C-kit, SALL-4, and glypican-3 stains (Figure 1 f-h). Based on these findings, the differential diagnosis dilemma was to determine whether it was an HCC with lung metastasis or primary lung cancer with liver metastases. A multidisciplinary team met to reassess the clinical case considering the clinical setting and the histology features, leading to the diagnosis of HAL with liver metastasis. During hospitalization, clopidogrel was stopped and hemoptysis was controlled with oral tranexamic acid 500 mg bid with no further episodes. Unfortunately, one week later after hospital discharge, the patient was readmitted to the intensive care unit due to massive hemoptysis and finally died.

DISCUSSION

Hepatoid adenocarcinoma by large is a rare type of extrahepatic carcinoma with histological features resembling those of HCC. Most cases are located in the stomach, where it was first described in 1985. Since then, it has been described as affecting other organs including the gallbladder, uterus, lung, and urinary bladder, and less frequently in the esophagus, colon, ovary, and ureter[3]. Among the few cases reported of HAL in the literature, there seems to be a predominance of males with a mean age of 60 years, being more frequent among heavy tobacco smokers. A solitary bulky-type mass is often seen in the upper lobes, associated with liver metastasis. Typical symptoms are chest pain, dyspnea, and hemoptysis[2,3]. Thus, it is important to keep a high clinical suspicion in the differential diagnosis of HAL since the most frequent extrahepatic metastasis of HCC is in the lung; however, HCC is associated with alcohol consumption, hepatitis B and C viruses, chronic liver disease, others[4]. Histological diagnosis might be challenging. Some immunohistochemical markers for differential diagnosis have been proposed, such as the arginase-1 which is a sensitive and specific marker of benign and malignant hepatocytes; however, this marker has not been evaluated specifically in HAL cells[5]. Table 1 compares our case with others previously published in the literature.

CONCLUSION

HAL is a rare type of lung cancer associated with a poor prognosis and no specific oncological treatment. Histological features resemble an HCC; hence, the diagnosis required special attention to clinical, epidemiological, imaging, and pathology data for a correct diagnosis.

FUNDING
None.

CONFLICT OF INTEREST
No conflict of interest is declared.

ETHICAL ASPECTS
Written informed consent was obtained from the patient before submission.

Table 1. Clinical characteristics of previous cases* of HAL compared with our case.

	PREVIOUS CASES (N=28)	OUR CASE
Age at diagnosis	60 (mean)	72
Ratio male-female	27/28 : 1/28	Male
Ratio upper-lower lobes	22/28 : 6/28	Upper/hilum mediastinum
History of heavy smoker	14/15	Yes
Clinical presentation	Cough, dyspnea, hemoptysis, Fatigue, weight loss	Hemoptysis, dyspnea, chest pain
Bulky mass	10/27	No
Metastatic disease at diagnosis	13/28	Yes
Elevated serum AFP at diagnosis	19/20	No
Immunohistochemical stains	CK7, CK19, HEA 125, MOC31, EpCAM	CK7; EMA; hepatocyte antigen

HAL: hepatoid adenocarcinoma of the lung; AFP: alpha-fetoprotein; CK: cytokeratin; EMA: epithelial membrane antigen.
* Adapted from Grossman K, *et al*. 2016.

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