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(CASE REPORT)

Diffuse Alveolar Hemorrhage as the Initial Presentation of Hepatic Adenocarcinoma: A Case Report

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Abstract

Diffuse alveolar hemorrhage (DAH) is a life-threatening condition resulting from bleeding into the alveolar spaces. It is typically associated with autoimmune vasculitis, infections, drugs, or cardiac disease. Malignancy-related DAH is rare, and cases linked to hepatic adenocarcinoma are extremely uncommon.

We report the case of a 66-year-old male with progressive respiratory failure, severe hypoxemia, and bilateral diffuse alveolo-interstitial infiltrates. Infectious, autoimmune, and cardiac investigations were non-contributory. Chest CT angiography revealed massive DAH. Incidentally, multiple hepatic nodules were identified, and ultrasound-guided biopsy confirmed hepatic adenocarcinoma. The DAH represented an unusual paraneoplastic or metastatic pulmonary manifestation of the tumor.

Although liver cancer frequently metastasizes to the lungs, DAH as its first clinical manifestation is exceptional. Potential mechanisms include fragile tumor-induced neovascularization, pulmonary tumor emboli causing vascular injury, or paraneoplastic immune-mediated capillaritis. Only isolated cases are reported.

In elderly patients with unexplained DAH, especially when constitutional symptoms or extrapulmonary lesions are present, underlying malignancy including hepatic adenocarcinoma should be considered. Early histological sampling is crucial for diagnosis and management.

Keywords: Diffuse alveolar hemorrhage; Hepatic adenocarcinoma; Liver cancer; Case report

1. Introduction

Diffuse alveolar hemorrhage (DAH) is a severe clinical syndrome characterized by bleeding into the alveolar spaces, leading to rapidly progressive dyspnea, hypoxemia, and diffuse pulmonary infiltrates. Common causes include systemic vasculitis, autoimmune connective tissue diseases, infections, drug toxicity, and coagulopathies.

Malignancy-associated DAH is rare but has been reported with hematologic cancers, metastatic tumors, and exceptionally with solid organ adenocarcinomas. Liver cancer, particularly hepatocellular carcinoma, frequently metastasizes to the lung, but hepatic adenocarcinoma presenting primarily with massive DAH is exceedingly rare.

The following case highlights DAH as the initial manifestation of hepatic adenocarcinoma, illustrating diagnostic challenges and reviewing available literature.

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2. Case presentation

A 66-year-old man with no history of smoking, chronic lung disease, or hepatic pathology presented with rapidly worsening respiratory symptoms. He had experienced mild exertional dyspnea for 10 years (Sadoul stage I), which progressed abruptly to Sadoul stage VI over a two-month period following intense physical exertion. This deterioration was accompanied by orthopnea, chest pain, productive cough with whitish sputum, and episodic mild hemoptysis, without fever. He reported a 20-kg unintentional weight loss over four months. Prior outpatient treatments—including levofloxacin, amoxicillin–clavulanate, and two short corticosteroid courses—failed to relieve symptoms. After transient stabilization in the ICU with non-invasive ventilation and ertapenem, he was admitted to the pulmonology department. Initial examination revealed stable hemodynamic and neurological status, oxygen saturation of 82% on room air, heart rate 77 bpm, and no digital clubbing; bilateral diffuse crackles were present, predominant in the mid-lung fields. Laboratory tests showed leukocytosis (13,170/µL), CRP 50 mg/L, markedly elevated D-dimers (12,220 ng/mL), elevated LDH, and normal renal and hepatic function; HIV testing was negative. Infectious investigations—including GeneXpert, AFB smears, respiratory viral PCR (except for a non-SARS coronavirus), autoimmune serologies (ANA, ANCA, anti-DNA, RF), and SARS-CoV-2 PCR were unremarkable. Chest radiographs across three time points revealed persistent diffuse bilateral alveolo-interstitial opacities with central predominance. CT pulmonary angiography demonstrated diffuse high-density ground-glass opacities compatible with massive diffuse alveolar hemorrhage (DAH), right-heart enlargement with pulmonary hypertension, and multiple hypodense hepatic nodules suspicious for metastasis or primary liver malignancy. Subsequent evaluation included ultrasound-guided hepatic biopsy and whole-body imaging. Histopathology identified adenocarcinoma of hepatic origin, composed of malignant gland-forming epithelial cells positive for hepatobiliary markers and negative for pulmonary lineage markers, consistent with a primary hepatic adenocarcinoma (cholangiocarcinoma-type). Bronchoscopy was planned contingent upon improved oxygenation.

- Based on these findings, the patient's clinical presentation, the imaging results and the pathology results, a diagnosis of liver adenocarcinoma complicated by Diffuse alveolar hemorrhage.
- Further investigations, including an MRI and a PET-Scan were planned to confirm the diagnosis and determine the appropriate staging of the liver adenocarcinoma.
- Tragically, the patient passed away due to acute respiratory distress syndrome (ARDS).

3. Discussion

Diffuse alveolar hemorrhage (DAH) is characterized by bleeding into the alveolar spaces due to injury of the pulmonary microcirculation and typically manifests with new infiltrates, anemia, and hypoxemia; hemoptysis may be absent in up to one-third of patients. In most series, DAH is attributed to autoimmune disorders—particularly ANCA-associated vasculitis, systemic lupus erythematosus, and anti–GBM disease—representing 60–70% of cases. Malignancy-related DAH is markedly less common, generally described only in isolated case reports. Compared with typical vasculitic DAH, malignancy-associated presentations tend to exhibit subacute systemic symptoms, preserved coagulation parameters, absence of autoimmune markers, and radiologic patterns more suggestive of infiltrative or metastatic disease.

Several malignancies have been linked to DAH in the literature, most frequently renal cell carcinoma—well known for its rich vascular supply and propensity for spontaneous hemorrhagic metastases. Case reports have also implicated breast carcinoma, thyroid carcinoma, melanoma, and colorectal adenocarcinoma. Hepatic adenocarcinoma or intrahepatic cholangiocarcinoma causing DAH, however, is exceptionally rare. In published cases (fewer than 5 well-documented reports), pulmonary involvement was typically due to diffuse microscopic metastases infiltrating the alveolar septa, causing fragile neovascularization and capillary disruption. These descriptions closely mirror the pathophysiology suspected in our patient, who exhibited severe DAH without autoimmune or infectious triggers, along with radiologic evidence of diffuse ground-glass opacities and hepatobiliary malignancy.

Radiologically, ground-glass opacities due to hepatic adenocarcinoma metastases have been described but are often misinterpreted as infectious pneumonia or interstitial lung disease, leading to delays in diagnosis. In two published cases of cholangiocarcinoma-related DAH, CT imaging showed diffuse bilateral opacities with right-heart strain findings similar to those observed in our patient. Moreover, rapid respiratory deterioration with weight loss and a lack of response to antibiotics or corticosteroids parallels patterns reported in metastatic hepatic tumors presenting with DAH.

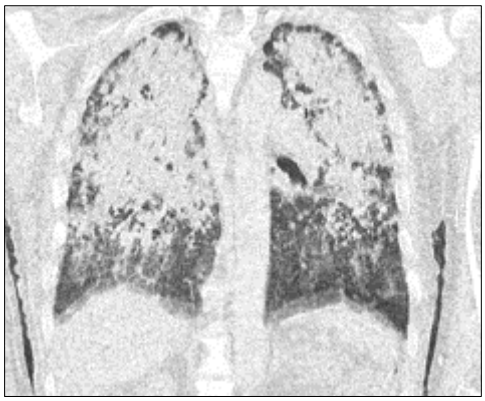
Compared to prior reports, this case is distinctive in the degree of alveolar hemorrhage, the rapidity of respiratory decline from long-standing mild dyspnea to severe hypoxemia, and the presence of multiple hepatic nodules leading to early confirmation of primary hepatic adenocarcinoma via biopsy. The absence of thrombocytopenia or coagulopathy

frequent contributors in malignancy-associated bleeding further emphasizes the role of direct microvascular infiltration rather than systemic hemostatic dysfunction.

Overall, this case highlights key learning points repeatedly emphasized in the literature:

- Malignancy must be considered in unexplained DAH, especially when autoimmune workup is negative and constitutional symptoms (e.g., weight loss) are present.
- Metastatic hepatic adenocarcinoma, although rare, can mimic diffuse interstitial lung disease or acute pulmonary hemorrhage, contributing to delayed diagnosis.
- Early biopsy of extrapulmonary lesions, when feasible, is essential to avoid misdiagnosis and guide timely oncologic management.

This case therefore contributes to the very limited body of published evidence linking primary hepatic adenocarcinoma to life-threatening DAH and reinforces the need for broad diagnostic consideration when facing atypical respiratory presentations in older adults.



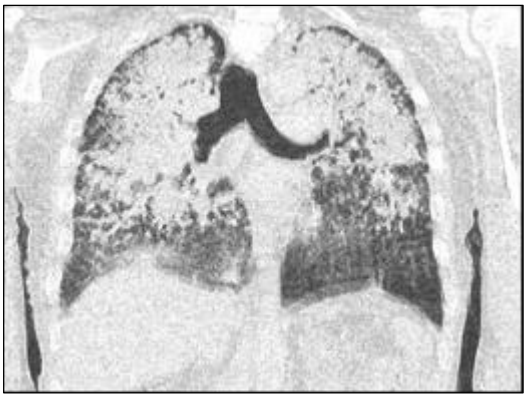
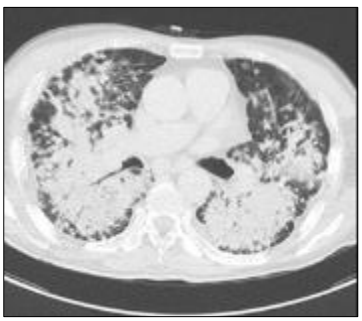
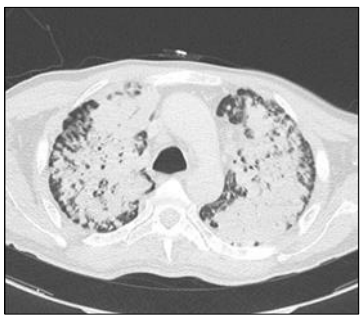


Figure 1 Coronal sections of the parenchymal window from a chest CT scan showing bilateral areas of consolidation





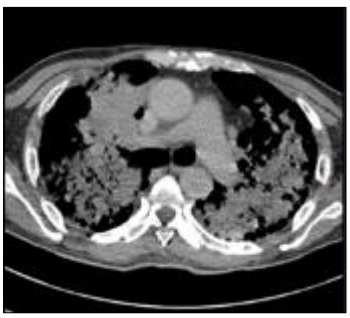


Figure 2 Sagittal sections of the parenchymal and mediastinal windows from a chest CT scan showing bilateral areas of consolidation

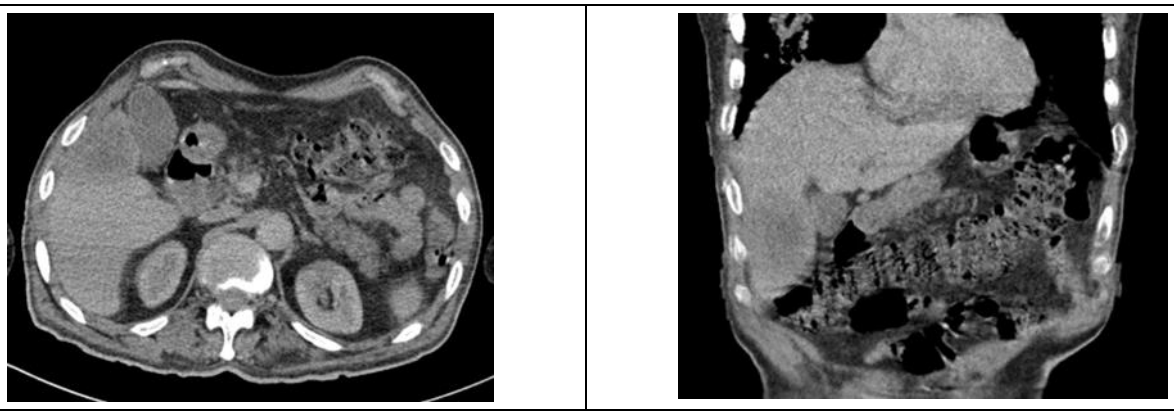


Figure 3 Images from an axial and coronal abdominal CT scan after contrast injection in the portal phase show a rounded, hypodense hepatic mass in segment V with heterogeneous enhancement after contrast injection

4. Conclusion

Unexplained diffuse alveolar hemorrhage, especially in older patients with severe weight loss or abnormal findings outside the lungs, should raise suspicion of an underlying malignancy. Although extremely rare, hepatic adenocarcinoma can present with DAH due to pulmonary metastatic involvement or paraneoplastic vascular injury. Early histopathological confirmation is essential for accurate diagnosis and timely management.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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