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Case report

A patient with diffuse alveolar hemorrhage: A diagnostic dilemma

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ABSTRACT

Diffuse alveolar hemorrhage (DAH) is a usual presentation of pulmonary vasculitis. However, several rare conditions have a similar presentation. We present a 73-year-old man with DAH whose diagnosis only became conclusive near the end of his life. The objective is to discuss the important differential diagnoses in a patient presenting with diffuse alveolar hemorrhage. There are very few case reports on pulmonary angiosarcoma and all of them discussed the rarity of the diagnosis, presentation, and treatment. Here, we would like to bring about the dilemma and challenges we internists face when managing any patient with Diffuse Alveolar Hemorrhage.

Background: Diffuse alveolar hemorrhage (DAH) is a usual presentation of pulmonary vasculitis [1]. However, several rare conditions have a similar presentation. We present a 73-year-old man with DAH whose diagnosis only became conclusive near the end of his life.

Objective: Discuss the important differential diagnoses in a patient presenting with diffuse alveolar hemorrhage.

Case Report: 73-year-old man, former smoker, with a history of repaired abdominal aortic aneurysm (AAA), presented with a 2-week duration of bleeding per rectum. A computed tomography (CT) scan of the abdomen showed sigmoid diverticulosis and associated pericolic hypervascularity. His hemoglobin dropped from 13.5 g/dL to 12.5 g/dL. The esophagogastroduodenoscopy and sigmoidoscopy did not reveal internal bleeding sources. Absence of ongoing blood loss allowed for the patient to discharge with a presumed diagnosis of diverticular bleed.

One month later the patient returned for admission with fatigue, cough, hemoptysis, and shortness of breath. He was pale and had bilateral pedal edema. His hemoglobin decreased to 7 g/dL. Chest X-ray showed bilateral pulmonary infiltrates reported as pulmonary edema. A transthoracic echocardiogram showed an ejection fraction (EF) of 45%. Given the severe anemia, a CT scan of the abdomen was performed which did not reveal any intra-abdominal source of bleeding. A CT of the thorax with contrast ruled out pulmonary embolism but there was alveolar edema with large bilateral pleural effusions (Fig. 1). Bilateral thoracenteses revealed hemothoraces, which necessitated bilateral pleural drain placement. Bronchoscopy revealed diffuse alveolar hemorrhage.

A working diagnosis of vasculitis was made. The patient was started on intravenous steroids, but with no improvement. Plasma exchange (PLEX) therapy was then started. This intervention showed no improvement either. Serologies, including anti-glomerular basement membrane (GBM) antibody, *p*-ANCA, c-ANCA, were all negative. Bacterial cultures from pleural fluid and sputum were negative. Fungal serologies were negative. Viral PCR showed rhinovirus. HIV antibody was negative. Coagulation and thromboelastographic studies were normal. Repeated cytology from pleural fluid was negative. CT scans of chest, abdomen, and pelvis did not show any lesions that could be biopsied. Despite several weeks of hospitalization with multiple empiric therapies, the patient continued to decline clinically. He cumulatively required 22 units of blood, 3 units of platelets, 1 unit of cryoprecipitate, and multiple units of Fresh Frozen Plasma (FFP) with PLEX. A lung biopsy was deemed too high a risk. Kidney biopsy showed normal renal histopathology, ruling out *anti*-GBM pathology. A High-Resolution CT scan of the chest revealed bilateral pulmonary nodules, not seen on previous CTs. A CT guided biopsy of these nodules showed areas of malignant-appearing epithelioid-endothelial cells with adjacent red blood cells. Immunohistochemical staining of the lesion showed malignant cells positive for ERG, CD31, and CD34 features consistent with an angiosarcoma (Fig. 2).

The patient declined chemotherapy. Three days after the definitive diagnosis of metastatic angiosarcoma was made the patient developed sigmoid colonic perforation and died.

Discussion

The initial presentation of this patient was thought to be due to severe anemia and high output congestive heart failure. Even with the

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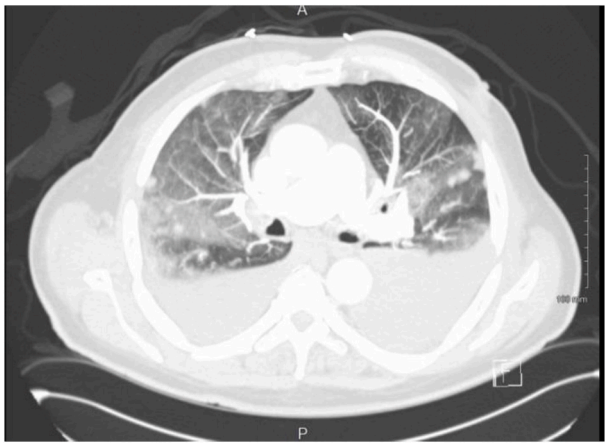

Fig. 1. CT Angiogram of the Thorax shows bilateral airspace disease probably represents alveolar edema with large bilateral pleural effusions.

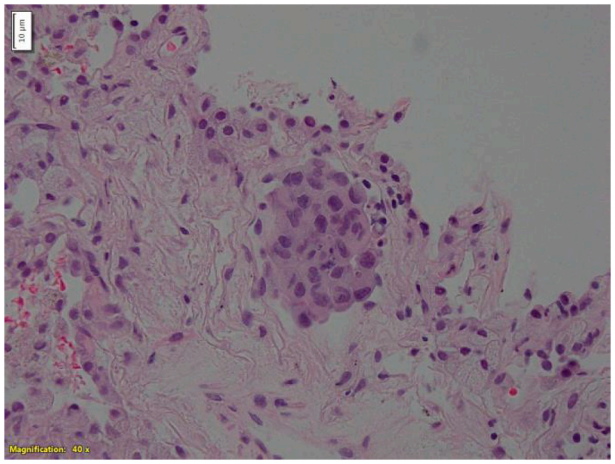

Fig. 2. Biopsy of the Pulmonary Nodule: In the center of the microscopic image is a nested cluster of malignant cells. These cells have atypical, occasionally angulated hyperchromatic nuclei. There is a single central mitotic figure. This cluster of malignant cells is within a vascular space which is lined by atypical cells which are histologically identical to the free-floating tumor cells.

discovery of the patient's diffuse alveolar hemorrhage, the etiology of this remained elusive the majority of the hospital course. The most important cause of diffuse alveolar hemorrhage is vasculitis [1]. Even with negative vasculitis serologies, the patient continued to be managed with immunosuppression, as Isolated Pauciimmune Pulmonary Capillaritis (IPPC)remained high on the differential [2]. IPPC is a lesser-known diagnosis with very few cases published case reports where the diffuse alveolar hemorrhage occurs with underlying pulmonary capillaritis but without any clinical or serological evidence of an underlying systematic disorder [2,6]. PLEX was continued given that 10% of patients with *anti*-GBM disease do not have antibodies [3,7]. Aorto-Bronchial Fistula, another rare diagnosis, was considered given the patient's previous AAA repair but was ruled out with a negative CT angiogram. Coagulopathies and infectious etiologies were considered and ruled out. Malignancy with metastatic disease was contemplated at the onset, but initially, there were no suspicious lesions or biopsy targets identified on imaging.

The eventual diagnosis of angiosarcoma was unexpected in our patients. Angiosarcoma is a blood or lymph vessel cancer that can occur in all parts of the body. It most commonly arises from the skin, head, neck, or breast but can also be from the liver, heart, spleen, bone, or gastrointestinal tract [3]. It has a high likelihood of presenting as metastatic disease [4]. Presentation varies widely depending on the organ of origination and location of metastasis. There is a very small set of case reports of patients who present with angiosarcoma involving the lungs. There are other cases of angiosarcoma that have been reported presenting as diffuse alveolar hemorrhage or pulmonary embolism because there is obstruction and destruction of pulmonary vessels. These cases also have similar high-resolution chest computer tomography findings which often showed multiple bilateral nodules that vary in shape and size along with ground-glass opacities, which was present in this patient [3]. Patients with pulmonary angiosarcoma are often misdiagnosed with tuberculosis or vasculitis [4]. Steroids have been found to make symptoms better which could lead to misdiagnosing the condition as vasculitis which is what happened in our case [3]. Most patients go several months from the time of symptom onset to the time of diagnosis. Many are only diagnosed with autopsy [4,5]. This is a very rare malignancy but should be considered in the differential diagnosis of any patient with DAH, especially if they have associated pneumothorax or hemothorax [4,5].

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