An interesting Case of Diffuse Alveolar Hemorrhage with an Elusive Etiology

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Background

Diffuse alveolar hemorrhage (DAH) is a life threatening condition, typically characterized by hemoptysis, anemia, and alveolar opacities on imaging, resulting in acute respiratory failure. It is often diagnosed based on findings of hemosiderin laden macrophages on cytology of the bronchoalveolar lavage (BAL) or on progressively bloodier aliquots of BAL fluid. There are four general categories in the etiology of DAH, including pulmonary capillaritis, bland hemorrhage, and diffuse alveolar damage (DAD), and miscellaneous. Treatment for DAH is largely determined by the underlying etiology but oftentimes includes steroid therapy and stopping the offending agent if discovered. We report a case of a patient who presented to the emergency department with worsening hemoptysis for the past 36 hours with associated shortness of breath, oxygen desaturation and fatigue, who was diagnosed with DAH due to hydralazine associated antineutrophil cytoplasmic antibodies (ANCA) vasculitis.

Case Description

Patient is a 78-year-old female with hypertension, diabetes mellitus and emphysema who presented for two weeks worsening nonproductive cough with associated generalized fatigue. She stated that approximately a day and half prior to admission, the hemoptysis started and progressively worsened, without associated rhonchi or wheezing. Initially she reported blood tinged sputum production which turned into bloody streaks with a few clots. She was placed on 3 liters nasal cannula due to desaturation to 88-90% on room air. She denied any new medications, anticoagulation, antiplatelet medication, or nonsteroidal anti-inflammatory drugs. She denied any previous such episodes, recent travel, or sick contacts. She denied eye, skin, or joint symptoms. Family history was significant for liver cirrhosis amongst her siblings but no history of lung cancers or autoimmune conditions. Physical exam was relatively unrevealing except for a small amount of blood in the corner of her mouth.

Her workup included laboratory workup with initial hemoglobin (HgB) of 7.5 grams/deciliter (g/dl) with normal white blood cell count and platelet count of 98 units/microliters. Coagulation panel, complete metabolic panel, lactic acid, lactate dehydrogenase were all unremarkable. Urine analysis showed elevated protein and blood. Chest computed tomography (CT) with contrast was performed and ruled out pulmonary embolism but illustrated extensive bilateral ground glass opacities throughout the lungs. (Figure 1) The autoimmune panel was pending at the time of the bronchoscopy during which serial aliquots from BAL were taken and had shown progressive bloody samples. (Figure 2) Cytology results confirmed the diagnosis of DAH, with findings of hemosiderin laden macrophages. (Figure 3)

Patient was empirically started on methylprednisolone 250 mg every 12 hours for 5 days, while work up for the etiology was underway. Antinuclear antibody (ANA) was positive along with anti-histone antibodies (AHA) of 1.6 units. She was preliminarily diagnosed with drug induced vasculitis causing DAH from home hydralazine medication, which was stopped. Patient improved with the pulse dose steroids and removal of offending hydralazine over the next couple of days. Patient's cough became dry again and became less frequent. In the following days the rest of the autoimmune panel resulted, indicating significant values for perinuclear-ANCA (P-ANCA) of 1:640, anti-Myeloperoxidase antibody > 8.0 units, anti-cardiolipin IgM antibody level of 36 units/ml (u/ml), low complete C3 level of 65 milligram/deciliter (mg/dl), low complement C4 of 4 mg/dl, and low total complement level of 40 u/ml, as well as negative rheumatoid factor (RF), cyclic citrulline peptide (CCP), cytoplasmic-ANCA (C-ANCA), anti-proteinase 3 antibody, sjogren syndrome-related antigen-A (SSA/Ro) and sjogren syndrome-related antigen-B (SS-B/La antibody), double stranded deoxyribonucleic acid (DS-DNA) antibody. At this time the patient was diagnosed with Hydralazine associated ANCA vasculitis which caused the DAH and initially started on pulse steroids and discharged on the immunosuppressant rituximab with outpatient rheumatology follow up.

Figures

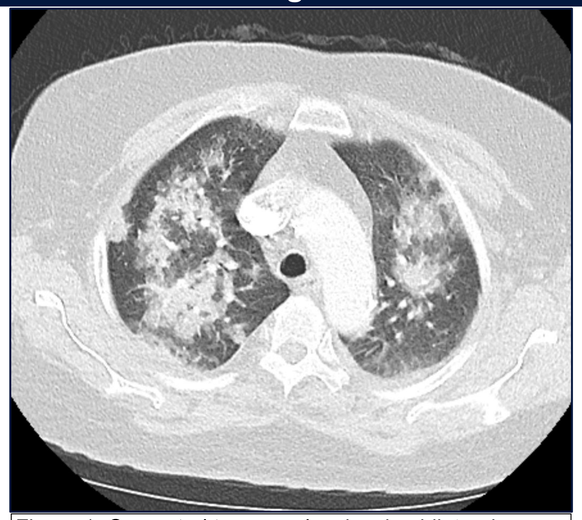

Figure 1: Computed tomography showing bilateral ground glass opacities

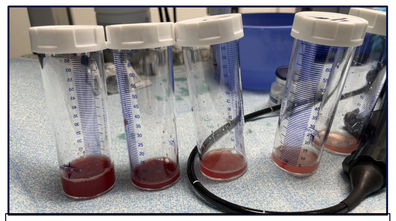

Figure 2: Bronchoalveolar lavage Alioquits

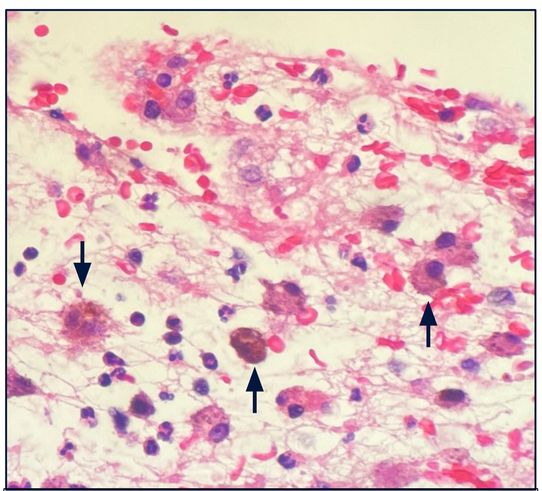

Figure 3: Cytology illustrating hemosiderian laden macrophages

Discussion

While hydralazine is known to cause drug induced lupus, the known potential to cause diffuse alveolar hemorrhage is not very well documented. In a small study by Almroth et al., looked at 17 cases of hydralazine-associated vasculitis, a few of the patients reported pulmonary symptoms including hemoptysis in which autoimmune was performed and found to show positivity for ANA, P-ANCA, MPO antibody, and Anti-Histone Antibody as well as negative anti-DS-DNA negative [1]. The case report goes on to discuss how the hydralazine-associated vasculitis has been found with autoimmune work up showing Anti-MPO antibodies, P-ANCA, anti-Histone antibodies, ANA. Multiple other case reports have shown varied autoimmune markers responses with different doses and durations of hydralazine use prior to diagnosis [1,5]. Typical treatment for hydralazine associated ANCA vasculitis includes cessation of hydralazine and induction therapy with steroids [2,3,]. If the pulmonary symptoms are severe upon presentations, additional immunosuppressants like cyclophosphamide and rituximab anD even plasmapheresis should be considered

Conclusion

DAH can be a life threatening medical emergency potentially requiring intubation. Prompt diagnosis and autoimmune, rheumatologic, infectious, malignant workup to uncover the etiology is of utmost importance. Medication reconciliation is a crucial part of the workup as this could reveal underlying etiology as well as partially responsible for worsening. Drug associated ANCA vasculitis treatment starts with stopping the offending agent with induction supportive therapy with steroids and other steroid sparing agents.

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