Diffuse Alveolar Hemorrhage Secondary to Human Metapneumovirus Pulmonary Infection

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ABSTRACT

A 67-year-old man presented with a week of flu-like symptoms, hypoxia, and fever. Respiratory viral panel was positive for human metapneumovirus. Initial chest imaging showed left lower lobe opacification, suggesting a bacterial superimposed on viral pneumonia. Despite antibiotics, the patient became tachycardic and increasingly hypoxic, requiring 40 L high-flow nasal cannula. Repeat imaging demonstrated worsening of a left lower lobe process. Elective bronchoscopy with bronchoalveolar lavage revealed hemorrhage. Subsequent autoimmune, bacterial, and fungal workup was negative. The patient was diagnosed with diffuse alveolar hemorrhage (DAH) secondary to human metapneumovirus pneumonia.

DAH is defined as bleeding into the alveolar spaces of the lungs, a process which carries high rates of morbidity and mortality.[1] While dramatic in name and often associated with hemoptysis, DAH may only present with clinically subtle and nonspecific features with a variety of alternative etiologies to consider. We present this case of DAH secondary to human metapneumovirus (hMPV) to promote discussion of etiologies of DAH aside from systemic vasculitis.

KEYWORDS: diffuse alveolar hemorrhage, metapneumovirus, anemia

INTRODUCTION

Diffuse alveolar hemorrhage (DAH) can originate from any irritant injuring the alveolar microcirculation. It can manifest with a multitude of clinical findings including progressive anemia, hemoptysis, and acute hypoxic respiratory failure.[1] While often associated with systemic vasculitis, there are several other etiologies of DAH which should be considered. There are few literature reports associating hMPV with this life-threatening complication.[2,3]

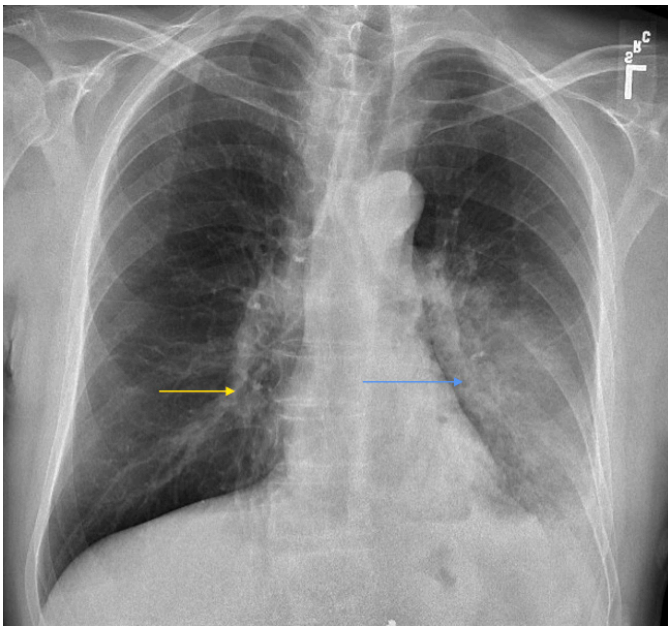
CASE

A 67-year-old man with a history of spinal chordoma status post-surgical excision, chronic kidney disease, and neurogenic bladder presented to the Emergency Department with a fever and a home pulse oximeter (SpO2) reading of 84%.

The patient began feeling ill one week prior to admission. Symptoms included drenching night sweats, chills, cough, left upper quadrant abdominal pain, poor appetite, and headaches. He reported progressive worsening of symptoms until presentation. He worked as an engraver and had a sick contact with an individual who had traveled to Florida within two weeks. He denied tobacco or substance use but endorsed consuming one alcoholic beverage daily.

In the Emergency Department, the patient was febrile to 101F, had a blood pressure of 145/70 mmHg, was tachycardic to 110 BPM, and required 6L of supplemental oxygen to maintain SpO2 at 90%. The patient's exam was significant for mildly diminished lung sounds in the lower left lung field, mild tenderness noted in the left upper quadrant of his abdomen, and pale appearing skin tone. Labs were notable for hyponatremia (129 meq/L), hypokalemia (3.6 meq/L), elevated creatinine (3.6 mg/dl), mild anemia (hgb 11.6x10^3 per hpf), and leukopenia (1.6 x10^3 per hpf). Respiratory viral PCR panel was positive for human metapneumovirus. Chest radiograph (**Figure 1**) on hospital day 1 showed left

Figure 1. Chest X-ray obtained hospital day one demonstrating opacification of the left lower lobe and blunting of the left costophrenic angle (indicated by the blue arrow), and prominence of the right lobe vasculature (indicated by the yellow arrow).



lower lobe airspace opacification suspicious for pneumonia. The patient was started on broad spectrum antibiotics and bronchodilators.

On hospital day 2 the patient's fever and tachycardia persisted. Repeat chest radiograph (**Figure 2**) and CT chest angiogram (**Figure 3**) revealed bilateral dependent consolidation involving both the right and left lobes. There was no evidence of pulmonary embolism. The patient's supplemental oxygen requirement increased to 40L. He was continued to be treated as bacterial superimposed on viral pneumonia with antibiotics and supportive care.

Figure 2. Chest X-ray obtained hospital day 2 demonstrating increased opacification of the left lower lobe lung field (indicated by the blue arrow) and increased opacification of the right lower lung field (indicated by the yellow arrow).

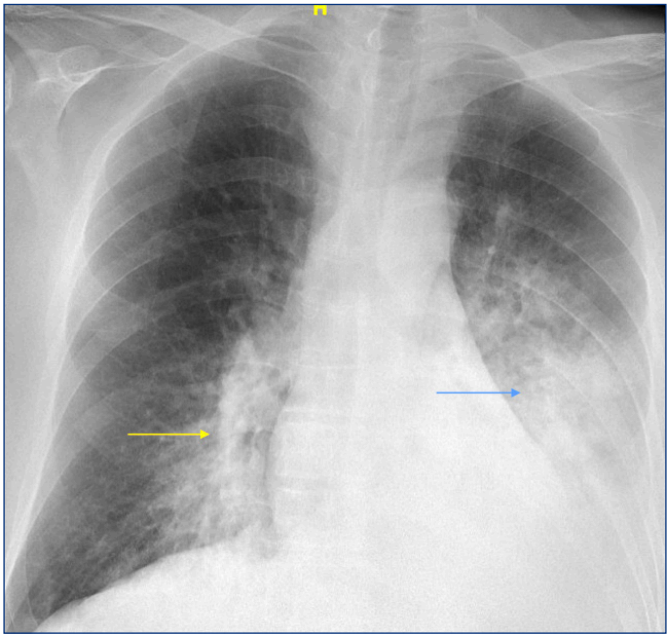
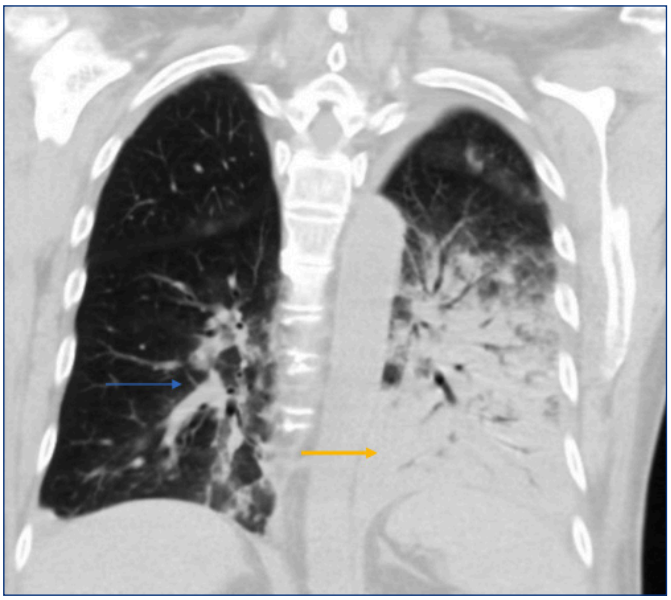


Figure 3. CT chest angiogram obtained on hospital day 2 demonstrating significant opacification in the left lung field (yellow arrow) and additional involvement of the right lower lobe (blue arrow).



The patient's hemoglobin trended down over four days to 6.8 g/dL There were no laboratory signs of hemolysis, sequestration, marrow or cell line failure, or nutritional deficits. The patient did not have hemoptysis or gastrointestinal bleeding. The patient underwent elective intubation and bronchoscopy. Bronchoalveolar lavage (BAL) demonstrated incrementally concentrated blood on sequential washes, diagnostic for diffuse alveolar hemorrhage (DAH). Laboratory and pathology studies were performed. Vasculitis, coagulopathy, and autoimmune causes of DAH were excluded. A fungal or bacterial source of infection was not identified. Sputum culture and lavage showed normal respiratory flora. Supportive respiratory measures and broad-spectrum antibiotics were continued. Pulse steroids were also added. By hospital day 14, the patient had improved and was discharged to a rehab facility on 1-2 L of oxygen. Diagnosis on discharge was DAH secondary to hMPV infection.

DISCUSSION

HMPV is an enveloped, single-stranded, RNA virus first identified in 2001.[3] It spreads via respiratory droplets within a six-ft. radius of an infected individual without proper personal protective gear.[4] It is a seasonal virus with the highest rate of infection occurring in winter months.[1,3] Although predominantly affecting children, elderly, and immunocompromised individuals, studies have demonstrated cases of severe hMPV in immunocompetent adults.[4,5] A retrospective study revealed that severe respiratory hMPV led to 1.7% of ICU admission in a hospital located in Spain. The same study also demonstrated increased incidence of hMPV pneumonia in immunocompetent individuals over the last two years of this 10-year longitudinal study (2016–2017).[4]

A typical presentation of hMPV includes fever, cough, pharyngitis, and myalgias. Few case reports of hMPV demonstrate severe pulmonary complications such as DAH.[3] Typically DAH is associated with fungal or bacterial infections rather than viral ones. Treatment is supportive care and management of symptoms when hMPV is the cause.

Most DAH cases are caused by pulmonary capillaritis, occurring when neutrophils invade lung interstitium and necrose the capillaries. This type of DAH is often caused by systemic vasculitis.[2] The two other types of DAH are known as diffuse alveolar damage (DAD), often occurring in acute respiratory distress syndrome (ARDS), and bland pulmonary hemorrhage from alveolar edema. Definitive diagnosis of the DAH subtypes requires a biopsy of lung tissue to determine histopathology.[1] CT chest imaging can further aid in diagnosis (**Figure 3**). Bronchoscopy with bronchoalveolar lavage

with a rising red blood cell count in sequential aliquots from the same anatomical location is the diagnostic standard.[1] Aliquots should be sent for cell counts, gram stain, fungal, bacterial, and viral culture. Once DAH is identified, workup should be tailored to the patient's presentation and clinical course. As they are often implicated, typical workup of systemic vasculitis includes ANCA, MPO, PR3, anti-GBM, ANA.[2] Although viral respiratory infection is rarely associated with DAH in an immunocompetent host, it is possible as evidenced by the patient presented in this case and should be considered given the implications in guiding treatment.[5]

Clinical determination of virally mediated DAH significantly affects treatment selection. As DAH is commonly inflammatory, corticosteroids and immunosuppressive therapies are standard of care. These are typically initiated upon diagnosis due to high disease mortality.[1] It is of utmost importance to rule out all other explanations for a patient's DAH, especially bacterial or fungal infection, when starting these immunosuppressive medications as they could worsen outcomes.[1] There is currently no antiviral treatment against hMPV, although ribavirin and immunoglobulin G are being explored.[1] The current recommended therapy is supportive;[6] therefore, early identification is crucial to avoid rapidly progressive complications.

A similar case has been reported by Rodriguez et al;[2] both patients presented with tachycardia, hypoxia, and mild anemia with progressively higher oxygen requirements without hemoptysis. Additionally, both patients had a negative autoimmune, vasculitis, and infectious workup other than hMPV. Imaging was also similar, CT angiography demonstrated bilateral multifocal patchy opacities. Our patient's DAH was discovered relatively early and therefore we were able to intervene before he further decompensated. Unfortunately, the DAH patients described by Rodriguez et al had comparably advanced disease given the reported chest imaging and did not survive the hospitalization.

In summary, this case report demonstrates that while rare, DAH can result from a human metapneumovirus infection. If a patient demonstrates worsening hypoxia, tachycardia, or anemia without evidence of hemoptysis, repeat imaging should still be considered to determine if a bronchoscopy is indicated. It is essential to rule out other causes of DAH such as vasculitis, other autoimmune etiologies, and infections prior to labeling hMPV to determine appropriate treatment. It is our hope this case raises awareness of DAH as a sequalae of hMPV to reduce morbidity and mortality.

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