

Idiopathic pulmonary hemosiderosis presenting in an adult: A case report and review of the literature

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ABSTRACT

Diffuse alveolar hemorrhage (DAH) is characterized by the presence of hemoptysis, anemia, and the presence of diffuse parenchymal infiltrates on imaging studies. Idiopathic pulmonary hemosiderosis (IPH) is an uncommon cause of diffuse alveolar hemorrhage (DAH) and is classically known to present in childhood. Adult-onset IPH is extremely rare. We report the case of a 48-year-old female patient who presented with hemoptysis and acute hypoxic respiratory failure, requiring intubation and mechanical ventilation. Imaging studies showed diffuse bilateral patchy infiltrates. Bronchoalveolar lavage (BAL) confirmed the diagnosis of DAH. Extensive workup including video-assisted thoracoscopic surgical lung biopsy (VATS) failed to reveal any vasculitis, infectious, immunological or connective tissue disorder, as the underlying cause for DAH. The patient was successfully treated with high-dose steroid therapy.

KEY WORDS: Adult-onset, diffuse alveolar hemorrhage, glucocorticoid therapy, idiopathic pulmonary hemosiderosis

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INTRODUCTION

Idiopathic pulmonary hemosiderosis (IPH) is a rare cause of diffuse alveolar hemorrhage (DAH), with an estimated reported incidence of 0.24 to 1.23 cases per million in selected populations.^[1] IPH classically presents in childhood, with most cases diagnosed before the age of 10 years.^[2,3] Adult-onset IPH accounts for only 20% of the cases, most of which are diagnosed before the age of 30 years, with a male to female ratio of 2:1.^[4] IPH is a diagnosis of exclusion, therefore, the known causes of pulmonary hemosiderosis should be ruled out prior to establishing the diagnosis of IPH.^[5] Given the potential lethality of the disease, IPH should be suspected in patients with recurrent/massive hemoptysis, anemia, and patchy opacities on radiological investigations, when other common causes of alveolar hemorrhage are ruled out. We report the case of a 48-year-old female who was

newly diagnosed with IPH after excluding other causes of alveolar hemorrhage.

CASE REPORT

A 48-year-old woman, a non-smoker, presented with a five-day history of progressively worsening dyspnea and intermittent hemoptysis, which consisted of 5 to 10 ml of bright red blood, which occurred up to 10 times a day. She denied any fever, weight loss, night sweats, skin rash, joint pain or loss of appetite. She denied having any pets, recent sick contacts, occupational or environmental exposures, and failed to recall any medication or dietary supplement use. She worked as a physician assistant. She denied any illicit drug use and had no risk factors for human immunodeficiency virus (HIV). The patient experienced increased respiratory distress on the day of presentation and came to the hospital for further evaluation. She was found to be hypoxic, tachypneic, and tachycardic requiring intubation for acute respiratory failure.

On examination, the patient was orally intubated. Vital signs were – Blood pressure - 118/74 mmHg, Pulse - 104/minute, Respiratory Rate -24/minute, Temperature - 97°F, and saturation - 98% on FiO 100%. There was no palpable lymphadenopathy. Respiratory

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examination revealed bilaterally scattered crepitations without any wheezing. Cardiac, abdominal, and extremity examinations were normal.

Initial laboratory results showed anemia (hemoglobin - 9.4 mg/dl, hematocrit 28%) with normal leukocyte and platelet counts. Renal function, electrolytes, liver function, and Pro-BNP tests were normal. Her serum ethanol level was undetectable with negative urine toxicology for cocaine, opiates, phencyclidine, and cannabinoids. Arterial blood gas was 7.32/52/310 on FiO₂ of 100%. Her electrocardiogram showed sinus tachycardia at 104 beats/minute, with a normal axis and no ST-T changes. Her chest radiograph showed bilateral patchy opacities with no effusion or pneumothorax [Figure 1]. The chest computed tomography (CT) scan showed bilateral scattered ground glass opacities with septal thickening [Figure 2] and no lymphadenopathy.

An HIV test, urine Legionella, and streptococcal antigen were negative. The patient continued to have persistent bloody secretions after intubation. Bronchoscopy was performed on the day of admission. Bronchoalveolar lavage (BAL) showed pinkish fluid that was not clearing with repeated lavage. On cytological examination, the BAL fluid showed hemosiderin-laden macrophages [Figure 3]. To establish a definite diagnosis it was decided to proceed with video-assisted thoracoscopic lung biopsy. A histopathological examination of the lung biopsy revealed pneumocytic hyperplasia, intra-alveolar red blood cells (RBCs), and abundant hemosiderin-laden macrophages, with no evidence of capillaritis or increased hyaline deposits [Figure 4].

Blood, sputum, and BAL cultures failed to identify any infectious etiology. A transthoracic echocardiogram showed a normal left ventricular contractility without any evidence of valvular abnormalities. Workup for vasculitis, immunological, and connective tissue disorders was negative. This included negative ANA, ds-DNA, ANCA antibodies, immunoglobulin levels, antiphospholipid antibodies, rheumatoid factor, anti-GBM antibodies, anti-Smith antibodies, anti-RNP antibodies, Scl antibodies, hepatitis panel, cryoglobulin levels, and celiac antibodies.

The patient was started on intravenous high dose (125 mg twice a day) hydrocortisone therapy. The patient showed clinical improvement over the next three days, with improvement in her oxygenation and resolution of hemoptysis. She was successfully extubated on the seventh day of admission. The patient was discharged home on prednisone therapy (15 mg/day). She continues to be on prednisone therapy and has shown no evidence of recurrence at the 18-month follow-up.

DISCUSSION

The approach to a patient presenting with DAH should

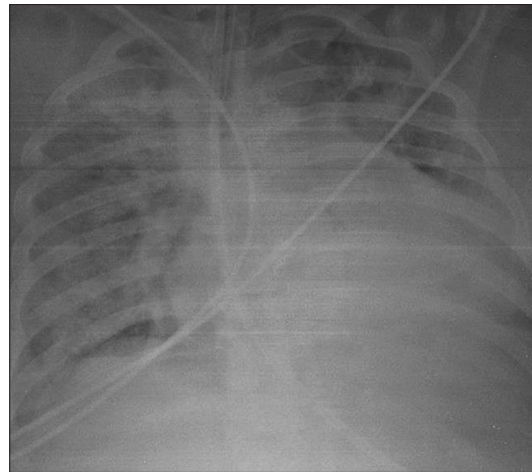


Figure 1: Chest radiograph showing bilateral patchy opacities without any effusion or pneumothorax

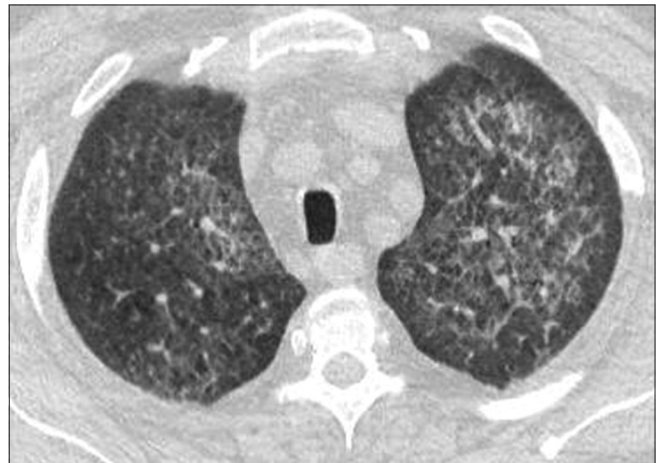


Figure 2: CT chest showing bilateral scattered ground-glass opacities with septal thickening

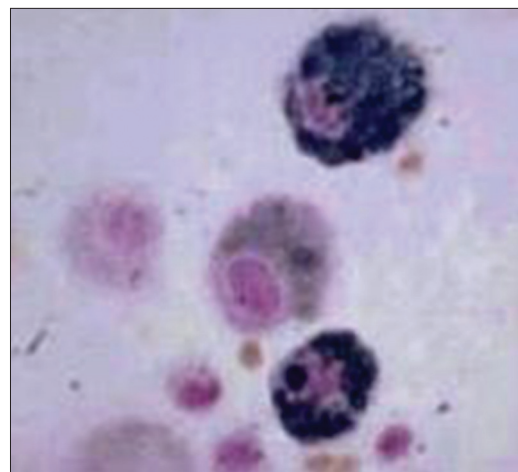


Figure 3: Cytological examination of the BAL fluid showing hemosiderin-laden macrophages

include extensive history, physical examination, and laboratory tests, to rule out exposure to possible offending drugs, coagulopathies, conditions associated with acute

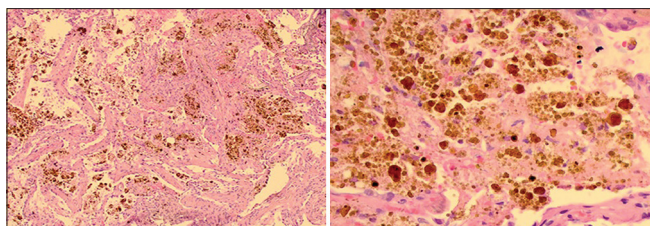


Figure 4: Histopathological examination of the lung biopsy showing abundant hemosiderin-laden macrophages, with no evidence of capillaritis or increased hyaline deposits

respiratory distress syndrome (ARDS), including infections, systemic vasculitis (granulomatosis with polyangitis, IgA nephropathy, cryoglobulinemia), immunological disorders, connective tissue diseases (Goodpasture's syndrome, systemic lupus erythematosus (SLE), systemic sclerosis, rheumatoid arthritis, antiphospholipid antibody syndrome, polymyositis) and mitral valve disease. A diagnosis of IPH could only be made after exclusion of other known causes of DAH and should be confirmed with a lung biopsy.^[6]

The exact pathogenesis of IPH remains unclear. However, an autoimmune mechanism has been proposed. Several infectious and mycotoxigenic mechanisms have also been postulated. Adult patients with acute, fulminant form of IPH might present with massive hemoptysis and acute hypoxic respiratory failure. Those with subacute form of IPH might present with cough, dyspnea, fatigue, intermittent hemoptysis and varying degrees of anemia. Radiologically, an acute form is characterized by the presence of alveolar infiltrates, with multiple ground-glass opacities seen on a computed tomography (CT) scan. Patients with the subacute form might develop pulmonary fibrosis characterized by the presence of interstitial reticulomicronodular densities on the CT scan. It is important to remember that patients might experience fulminant as well as subacute forms of IPH during the clinical course of the disease.

Many different therapeutic approaches have been tried for the treatment of IPH. Due to an extremely low incidence rate, there have been no randomized control trials to estimate the efficacy of therapy with immunomodulatory and/or anti-inflammatory agents. Thereby, the treatment recommendations are based solely on the data from few case series and case reports. Corticosteroids have been shown to reduce the morbidity and mortality during acute episodes of alveolar hemorrhage and slow the progression to fibrosis.^[7] The therapeutic dose of glucocorticoids ranges from 0.5 mg/kg/day to 2 mg/kg/day during the acute bleeding episode.^[1,5] IPH is known to recur immediately after the cessation of steroid therapy. Thereby, most patients are treated with prednisone for about two years after the resolution of the acute phase, at a maintenance dose of 10 to 15 mg/day. In a disease

that is refractory to corticosteroids, hydroxychloroquine and azathioprine have been used with favorable results in some patients.^[8]

Although these treatment options have been seen to be beneficial in patients, approximately 14 – 29% of them die from acute or chronic respiratory failure. Those that do survive, generally have chronic anemia and eventual pulmonary fibrosis secondary to recurrent intrapulmonary bleeding. Overall, adults seem to have a more prolonged survival, as compared to children with IPH.^[1]

Key learning points from this case include:

1. DAH commonly presents with hemoptysis, anemia and diffuse bilateral infiltrates on the imaging studies
2. Adult-onset IPH is an extremely rare, but a potentially lethal cause of DAH
3. IPH is a diagnosis of exclusion with lung biopsy being the gold-standard for establishing the diagnosis
4. High-dose glucocorticoid therapy (0.5 mg/kg/day to 2 mg/kg/day) is recommended for the treatment of acute, fulminant form of IPH, and is known to be associated with favorable outcomes
5. Therapy with immunomodulator drugs should be reserved for patients not responding to glucocorticoid therapy.

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