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Case report

A fatal case of diffuse alveolar hemorrhage as the initial presentation of systemic lupus erythematosus: A case report and literature review

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A B S T R A C T

Diffuse alveolar hemorrhage (DAH) is a rare fatal pulmonary complication of systemic lupus erythematosus (SLE). The clinical syndrome is characterized by hemoptysis, acute fall in hematocrit, hypoxemic respiratory failure, and diffuses pulmonary infiltrates. We describe a case of 23-year-old female who presented with Ludwig's angina that was complicated by diffuse alveolar hemorrhage as the initial presentation of undiagnosed systemic lupus erythematosus. A high index of suspicion is need for prompt diagnosis and treatment in order to avoid the high mortality associated with such cases.

1. Case description

The patient has past medical history significant for remote pulmonary embolism and alcohol use disorder. She presented with a sore throat associated with left side facial and neck pain for the last couple of weeks prior to her admission. The patient noted dyspnea and dry cough associated with fever, chills, and dysphagia mainly to solid food. She denied any prior history of allergy, sick contact or smoking.

On presentation, the patient noted to have a temperature (T) of 101.5, pulse rate (PR) of 125, respiratory rate (RR) of 18 and oxygen saturation of 92% on room air. The physical exam was significant for erythema of the pharynx and cervical lymphadenopathy mainly on the Left side. There was no evidence of cranial nerves palsy or focal neurological deficit. The cardiac exam revealed trace bilateral pedal pitting edema and normal vesicular breathing on chest evaluation.

Laboratory workup revealed elevated white blood cells (WBC) count of 14.6, hemoglobin (HGB) of 10.3, hematocrit (HCT) of 33.7 without previous history of chronic anemia or recent blood loss, platelets (Plt) of 224, blood urea nitrogen (BUN) of 30 and creatinine (Cr) of 1.0. The rest of her laboratory investigations were consistent with normal levels of her electrolytes and no evidence of liver injury.

Computed chromatography (CT) scan of chest and neck revealed a retropharyngeal fluid collection of 1.1 × 1.3 × 8.5 cm with extensive parapharyngeal soft tissue edema more worse on the left side suspicious for Ludwig's angina. In addition to bilateral pleural effusion more pronounced on the left side.

Blood cultures were obtained, and the patient was started on empiric antibiotic therapy with Ampicillin and Sulbactam. Ear-Nose-Throat (ENT) surgeon was consulted, recommended operative evaluation due to concern for Ludwig's angina and threatened airway. The patient had an incision and drainage of a small abscess with placement of tracheostomy tube.

On the following days, the patient developed worsening respiratory function requiring intubation and mechanical ventilation. Chest x-ray showed new bilateral infiltrates with her labs significant for worsening kidney functions and elevated inflammatory markers. Flexible bronchoscopy revealed diffuse alveolar hemorrhage. Autoimmune workup came back positive for antinuclear antibodies (1:10240), anti-double-stranded DNA (dsDNA) antibodies (1:1280), anti-smith (Sm) antibodies, low complement levels (both C3 and C4), with negative serology for antiphospholipid syndrome.

The patient was managed with high dose intravenous corticosteroids (1 g a day) inform of pulse therapy for several days with an improvement of her condition. She then developed recurrent episodes of DAH despite the addition of immunosuppressive therapy inform of cyclophosphamide and plasmapheresis. Her condition continued to worsen with a complete shutdown of her kidneys. Family elected to proceed with palliative and comfort measures after repeated trials of steroids, cyclophosphamide, and plasmapheresis.

2. Introduction

Diffuse alveolar hemorrhage is a rare but life-threatening complication of systemic lupus erythematosus. It is usually seen in patients with established diagnosis of SLE but can be seen as the initial presentation in some patients. [1,2]. Although there are no well-established guidelines for management due lack of large clinical trials, DAH has been classically treated with high dose intravenous corticosteroids

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therapy, in addition to cyclophosphamide and plasmapheresis. [3].

3. Discussion

Systemic lupus erythematosus is an autoimmune disease that globally affects mucosal surfaces. It mainly affects females with a female to male ratio of 9:1. It is commonly seen in young females of reproductive age with an average age of onset of 15–45 years. Pulmonary complications are commonly described in 50–70% of patients with SLE. The range of such complications includes pleuritis, pneumonitis, interstitial lung disease, pulmonary hypertension, and alveolar hemorrhage.[4 5] Diffuse alveolar hemorrhage is a rare but fatal condition that is described in 2–5% of patient with SLE. It usually presents early in the course of the disease but can present as the initial manifestation of SLE in 11–20%. It carries a high rate of mortality ranging anywhere from 50 to 80%. [1–6].

The pathophysiology of DAH is not well understood, suggested theories postulate immune-mediated alveolar capillary endothelial damage and inflammation that would result in local or diffuse bleeding from those capillaries. [7,8]. Most patients with DAH present with respiratory symptoms, including dyspnea, chest pain, and cough that are usually associated with renal involvement. Hemoptysis, acute drop in hemoglobin and new infiltrates on chest x-ray constitute the classic triad of DAH. Less common findings include fever, acute severe respiratory distress, tachycardia, and bronchial breath sounds. [1,9,10].

Diagnostic workup usually involves serology such as anti-double-stranded antibodies (dsDNA), complements levels, in addition to assessment for any associated renal injury and other autoimmune conditions such as antiphospholipid syndrome. Prior studies showed that thrombocytopenia (count < 50000), low complement (C3) level and active lupus nephritis to be independent risk factors for DAH in patients with SLE. [1,6,9].

Imaging studies are commonly consistent with unexplained new infiltrates, usually diffuse but can be seen in the peri-hilar regions, while apices are spared. Pulmonary functions evaluation usually reveals increase diffusion capacity to carbon monoxide, that can correlate with disease activity and active bleeding. Fibro-optic bronchoscopy confirms alveolar hemorrhage as the source of hemoptysis and bleeding. [1,6,11,12].

Various treatment modalities have been suggested and used for the treatment of DAH. No recent large randomized controlled trials were conducted to compare efficacy between available therapies. The mainstay of treatment is high dose intravenous corticosteroids, in form of pulse therapy. Most patients respond to steroids treatment, with improved survival outcomes when immunosuppressive therapy is used concurrently in the acute setting. Cyclophosphamide is the most commonly utilized drug with observed survival benefits. Plasmapheresis can be used to treat DAH in patients with SLE, with no significant improvement in outcomes. Better outcomes are observed when plasmapheresis is used for management of DAH due to small vessel vasculitis rather than SLE, hence the current role of plasmapheresis is controversial. [1,9,13].

Other alternative therapy is rituximab (RTX), a specific anti-CD20 antigen B-cell antibody, that has been described in several case studies with reported favorable outcomes. Rituximab was used as initial therapy in some of those reports or in addition to the traditional management, for both short and long-term purposes, with successful treatment of some recurrent cases of DAH. B-cell depletion index was used as a marker to evaluate response to RTX therapy by checking levels of CD19 cells count few weeks after initiation of therapy, with favorable outcomes in patients with minimal to undetectable levels after treatment. [14–16].

Local administration of recombinant activated factor VII through intrapulmonary route has been reported to be effective in symptomatic patients with DAH. It induces hemostasis by direct activation of tissue factor receptors from the alveolar side. Even though successful treatment attempts were reported by various case reports and case series, large controlled trials are needed to assess the safety profile of both local and systemic administration of such therapy. [17–20].

Mortality related to DAH in patients with SLE remains high despite the increase in number of available therapies with rates ranging from 50 to 80%. Several factors were found to directly affect mortality in different studies. Infections seem to be more common in patients with DAH and are associated with higher rate of mortality. [1,21,22]. Sick patients who require mechanical ventilation are reported to have worse outcomes when compare to other patients. [1,21–23]. Other risk factors include renal failure and thrombocytopenia. [22,23].

4. Conclusion

DAH is a rare catastrophic complication of SLE with poor outcomes and high mortality despite the increase in modern available therapies. It usually presents in patients with established diagnosis even on medical therapy but can be the initial manifestation of undiagnosed SLE in a small number of patients. It should be suspected in young female patients with worsening respiratory status and new infiltrates on chest imaging. Aggressive management is warranted to improve the outcomes and quality of life of affect patients.

Disclosures

No financial disclosures or conflicts of interest.

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