# A case report of diffuse alveolar hemorrhage: A rare and fatal complication of systemic lupus erythematosus

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## ABSTRACT

Diffuse alveolar hemorrhage (DAH) is a rare but potentially catastrophic complication of Systemic lupus Erythematosus (SLE), known to complicate about 2–5% of SLE cases. Here, we describe the case of a 9-year-old girl who presented DAH with at the initial diagnosis of SLE. A high index of suspicion is needed for prompt diagnosis in such cases and they require aggressive management at the initial diagnosis to avoid the associated high mortality.

**Key words:** Diffuse alveolar hemorrhage, Pulmonary complication, Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by multisystem inflammation and the presence of circulating autoantibodies directed against self-antigens [1]. It is more prevalent among females (female to male ratio: 2–5:1 before puberty and 9:1 during the reproductive age group). Childhood SLE is rare before 5 years of age and is usually diagnosed in adolescence (median age at diagnosis: 11–12 years) [2]. Pleuropulmonary manifestations such as pleuritis, acute lupus pneumonitis, chronic interstitial pneumonitis, pulmonary hypertension, and diffuse alveolar hemorrhage (DAH) are present in 5–67% of pediatric SLE patients [3,4].

DAH is a rare but a potentially catastrophic complication, described in about 2–5% of patients with SLE and can also present as the initial manifestation [1]. It carries a mortality rate of 50–80% [1,4,5]. The pathophysiology of DAH is postulated to be due to an immune-mediated alveolar capillary endothelial damage and inflammation, with neutrophilic capillaritis and associated destruction of alveolar septae, resulting in local or diffuse bleeding from those capillaries [6,7].

## CASE REPORT

A 9-year-old girl presented with complaints of fever, cough, and joint pain for 1 week and easy fatiguability, breathlessness, and palpitations for 3 days. She had joint pain predominantly involving bilateral wrist, metacarpophalangeal, knee and ankle joints, and it was not associated with swelling or redness around the joint. She had palpitations and breathlessness initially on exertion, which had progressed to be present even at rest at the time of presentation, and would aggravate on lying down. She had no significant past history, family history, or birth history. She was immunized up to date and developmentally appropriate for her age. Her diet was appropriate for her age, containing adequate calories, proteins, and micronutrients.

On examination, she had pallor, tachycardia with bounding peripheral pulses, tachypnea with markedly increased work of breathing with a saturation of 89% at room air and elevated blood pressure. She had a hyperdynamic apical impulse associated with a hemic murmur, and decreased air entry in right mammary, infra-axillary and infrascapular areas, with hepatosplenomegaly.

Her initial blood investigations revealed anemia (hemoglobin- 4.4 g/dl), a normal total leukocyte count (TLC - 5140 cells/µL), thrombocytopenia (platelet count - 1.36 lakh/µL), markedly elevated ESR (110 mm/h), and raised serum ferritin levels (240 ng/ml). Direct coombs test was negative and reticulocyte count was 13.6% (with a corrected reticulocyte count of 4.2%). Peripheral smear showed a microcytic hypochromic picture with no other significant findings. Urine routine and microscopy showed proteinuria (urine albumin of 2+) and hematuria (6–8 red blood cells [RBCs]/hpf). Her renal and liver function tests, prothrombin time and INR were normal and the C-Reactive protein and antistreptolysin O titers were negative.

Chest X-ray showed non-homogenous opacities involving the right middle and lower lung zones with cardiomegaly

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(cardiothoracic ratio: 0.68) suggestive of pericardial effusion, as depicted in Fig. 1. Echocardiography showed moderate pericardial effusion with mildly thickened pericardium. Her Antinuclear Antibody profile was positive for Anti-dsDNA, Anti-smith antibody, Anti-histone antibody, Anti-ro antibody, Anti-ribosomal P protein, and Anti-SSB antibody. Both C3 and C4 levels were low and blood and urine cultures showed no growth.

She was diagnosed as a case of SLE with cardiac, pulmonary, and renal manifestations. Rheumatologist and nephrologist were involved in the management of the case and on day 3 of admission, intravenous methylprednisolone pulse therapy was started and continued for three days under antibiotic cover, with other supportive measures (packed RBC transfusion, medications for management of heart failure, and hypertension) to which she responded very well. By day 5 of admission, she was hemodynamically stable, oral prednisolone was continued, and hydroxychloroquine was added. Renal biopsy was planned.

During the course of her hospital stay, the child improved clinically. Two weeks later she developed sudden onset of breathlessness with massive hemoptysis, associated with a sudden fall in her hemoglobin and hematocrit levels. She had developed diffuse pulmonary alveolar hemorrhage and succumbed to death within next 3 h. As the child deteriorated very rapidly, other immunosuppressive agents like cyclophosphamide could not be administered to the child. A postmortem lung biopsy and histopathology would have further substantiated the diagnosis and given us more histopathological information on the subject. However, it could not be done as the parents refused to give consent.

## DISCUSSION

DAH is a rare but a potentially lethal complication of SLE and can be the initial manifestation of SLE [1]. DAH can be acute (developing over hours) or subacute (developing over several days) [1]. It is typically defined by the presence of three major components: (1) Symptoms (dyspnea, cough, and hemoptysis) and signs (bronchoscopy with bloody return), (2) a sudden new drop in hemoglobin (typically 1.5–2 g/dL), and (3) new, diffuse infiltrates on chest imaging [7,8]. Most studies have shown that dyspnea (74–100%) is a more common presenting symptom than hemoptysis (approximately 25%), especially in pediatric age group [9]. Studies focused on DAH risk factors in SLE reported the association of lupus nephritis, hypocomplementemia, thrombocytopenia, and anti-ds DNA positivity/enhanced levels from baseline as independent risk factors [7,8]. All the above risk factors were present in our patient.

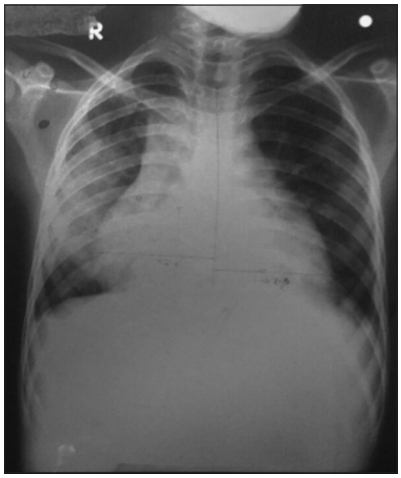


**Figure 1: The chest radiograph shows non homogenous opacities involving the right middle and lower lung zones with cardiomegaly (cardiothoracic ratio: 0.68) suggestive of pericardial effusion**

Many treatment modalities have been suggested and used for the treatment of DAH. However, there are not many recent large randomized controlled trials 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, with improved outcomes when immunosuppressive therapy is used concurrently in the acute setting. Cyclophosphamide is the most commonly studied drug that showed improved outcomes when used in combination with intravenous corticosteroid pulse therapy [7,8,10]. Martínez-Martínez and Abud-Mendoza [8] found that cyclophosphamide use was associated with less mortality compared to other immunosuppressive agents although it was not found to be statistically significant.

Kazzaz *et al*. [7] studied 22 cases of SLE with DAH, where all patients were treated with increased immunosuppression, including various combinations of corticosteroids, plasmapheresis, cyclophosphamide, rituximab, and mycophenolate mofetil. All patients in their cohort survived their initial episode of DAH. While their patients with DAH did well in the short-term, their long-term survival was significantly worse than controls. Singla *et al*. [10] reviewed seven cases of DAH in children with SLE, where all patients had received corticosteroids and additional immunomodulation to achieve disease control. Outcomes at their center were favorable, with 14% mortality. This was in direct contrast to reported fatalities of 69% and 33% in SLE patients with DAH from studies by Araujo *et al.* [11] and Martínez-Martínez and Abud-Mendoza [8].

Araujo *et al.* compared the outcomes of DAH in juvenile (JSLE) and adult onset SLE and found that DAH in JSLE has a worse outcome most likely related to respiratory failure and also DAH onset in JSLE already treated with high-dose steroids raises the concern of inadequate response to this treatment and reinforces the recommendation of early aggressive alternative therapies in this group of patients [11]. Other alternative therapies including plasmapheresis, rituximab, IV immunoglobulins, mycophenolate mofetil, recombinant activated factor VII, and mesenchymal stem cell therapy have been tried; however, no strong evidence could be obtained [12]).

## CONCLUSION

DAH should be considered in any child with SLE who develops hemoptysis with respiratory insufficiency, with a falling hematocrit

and radiographic evidence of pulmonary infiltrates. Mortality associated with DAH typically exceeds 50–80% with recurrences reported even after the survival of initial bleed. Hence, DAH in SLE needs to be managed aggressively at initial presentation.

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