# Diffuse alveolar hemorrhage in a young woman with systemic lupus erythematosus: Case report and literature review

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## Abstract

Diffuse Alveolar Hemorrhage (DAH) is rarely reported complication of Systemic Lupus Erythematosus (SLE).

A young woman diagnosed SLE, with a previously normal plain chest radiograph, developed acute onset cough, dyspnoea and hemoptysis. The repeat urgent chest radiograph revealed alveolar opacities. The triad of acute onset respiratory symptoms on a background of SLE and previously normal chest radiography raised the suspicion of DAH in her. She made satisfactory clinical response to high dose corticosteroid and pulse intravenous cyclophosphamide.

We conclude that high index of suspicion is required for recognition of DAH. Prompt diagnosis and management are keys to successful outcome.

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

## Introduction

Diffuse Alveolar Hemorrhage (DAH) is an acute, life threatening event and is defined as a clinical syndrome resulting from injury to the alveolar arterioles, capillaries and venules leading to red blood cell accumulation in the distal air spaces characterized by the clinical triad of hemoptysis, anemia, and progressive hypoxemia. Diffuse alveolar hemorrhage can complicate a large number of clinical conditions. It may present in different ways and may be life-threatening[1]. It poses an important challenge for the clinician[1].

It is also known as intrapulmonary hemorrhage, diffuse pulmonary hemorrhage, pulmonary alveolar hemorrhage, pulmonary capillary hemorrhage, alveolar bleeding, or microvascular pulmonary hemorrhage. DAH is a rarely reported condition. At onset up to 11% of systemic lupus erythematosus patients have DAH[2]. It is more commonly seen in SLE than any other connective disease[2]. Although no prospective study has yet identified which cause is the most common, in a series of 34 cases, Wegener granulomatosis accounted for 11 cases, Goodpasture syndrome four cases, Idiopathic pulmonary hemosiderosis four, Collagen vascular disease four, and Microscopic polyangiitis three[2]. DAH has protean clinical presentation and this frequently reflect either alveolar bleeding alone or features of the underlying cause (e.g. arthritis in systemic lupus erythematosus). Hence, its recognition requires a high degree of suspicion. Reported prognosis is poor; with in-hospital mortality ranging from 20% to 100%[4]. Early identification of prognostic factors may be useful in the initiation of appropriate treatment. Hence this case report has been written to create awareness among physicians and refresh our knowledge of rare complication of systemic lupus erythematosus.

## Case report

Miss A.M. was a 22 year old lady referred from Federal Medical Centre Abakaliki Ebonyi State Nigeria. She presented to our Rheumatology clinic of University of Nigeria Teaching Hospital Enugu on 22nd March 2010 and was subsequently admitted into the female medical ward. She was suspected to be a case of systemic lupus erythematosus based on American College of Rheumatology classification few weeks to presentation to us. She presented with recurrent fever and polyarthralgia of one year duration. There was also history of paraesthesiae over the feet, recurrent mouth sores, skin rashes over the cheeks and also exposed areas of the body that is worse with exposure to sunlight, hair loss, facial puffiness and leg swelling, progressive weight loss, anorexia, fatigue and an episode of precordial chest pain suggestive of pericarditis. There was no history of reduction in urine output, excessively frothy urine, raynaunds phenomenon, sicca symptoms, skin tightening, proximal muscle weakness and reflux symptoms. She had no history of cough, drenching sweats, abdominal swelling, diarrhea, polyuria, polydipsia, palpitations, heat intolerance, headaches, seizures and no tremors. Her symptoms were not

controlled hence her referral for further evaluation and appropriate management. Her accompanying laboratory results revealed proteinuria and active urinary sediment suggestive of glomerulonephritis, markedly raised ESR and the plain chest radiograph taken on the 15th of March 2010 was normal.

Examination revealed chronically ill-looking young woman that was not in respiratory distress, pallor, patchy alopecia, and bilateral pitting leg oedema. She was febrile with a temperature of $37.8^0$ C. There was no jaundice, peripheral lymphadenopathy and dehydration. Examination of her skin revealed malar rash, photosensitive fixed erythematosus patches on the arms and legs. The digestive system examination revealed palate mucosal erythema and erosions and ascites demonstrable by shifting dullness. The central and peripheral nervous system examination revealed only hypoaesthesiae in a glove and stocking distribution. She was Stein-Broker's classification S3 functionally impaired. The cardiovascular and chest examinations were normal. The provisional diagnosis was systemic lupus erythematosus. She was admitted and commenced on oral hematinics. The following investigations were requested: Full Blood Count, reticulocyte count, ESR, urinalysis and urine microscopy, culture and sensitivity, Serum electrolytes urea and creatinine (SEUCR), HIV, anti-HCV, HBsAg, liver function test, Prothrombin time, Activated Partial Prothrombin Time, serum protein and albumin, stool microscopy, fasting blood glucose, mantoux test and abdominopelvic ultrasound scan (Table 1).

**Table 1**: Investigation results

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| Full Blood Count: Hb 8.7g/dl, WBC total count 3.6 x $10^9$/L , N56 L42 E2 Platelet 120 x $10^9$/L (23/3/2010) Repeat hemoglobin: 6.9g/dl (29/3/2010) |
| Reticulocyte count: 2.4% ESR: 113mm first Hour (Westergren) (17/03/2010) |
| Prothrombin Time: test (23/03/2010) 9.41sec; control: 11.1 sec International Normalised Ratio 1.1 |
| Blood culture: no growth (29/03/2010) Urinalysis and urine M/C/S: proteinuria 2+; no growth |
| SEUCr: (23/03/2010) Na 134 K 3.9 Cl 102 HCO 22 mmol/l urea 2.3mmol/l creatinine 120umol/L |
| HIV: negative for antibodies to HIV 1 &2 (24/03/2010) Anti-HCV: negative HBsAg: negative |
| Liver function and Serum protein and albumin test: normal: |
| Fasting blood glucose: 78mmol/l Mantoux test: (26/03/2010)< 2mm induration after 72 hours |
| Abdominopelvic ultrasound scan: (25/03/2010) normal examination |

She had a comprehensive eye evaluation which revealed only refractive error necessitating only corrective lens. With no contraindication, she was commenced on oral hydroxychloroquine 200mg BD for SLE. Her clinical state remained apparently same till the 7th day in admission when she developed sudden onset shortness of breath, cough and transient haemoptysis. A repeat of the plain chest radiograph was requested. This showed widespread new alveolar opacities in both lung fields (Figure 1).

**Figure 1:** Shows PA view chest radiograph of Miss A.M taken on 30th March 2010. Note the apparent cardiomegaly. This is due to mal-rotation of the patient at the time of the investigation. Her previous chest radiograph that was taken 2 weeks earlier showed normal cardiothoracic ratio. The radiograph also showed widespread alveolar opacities both lung fields.

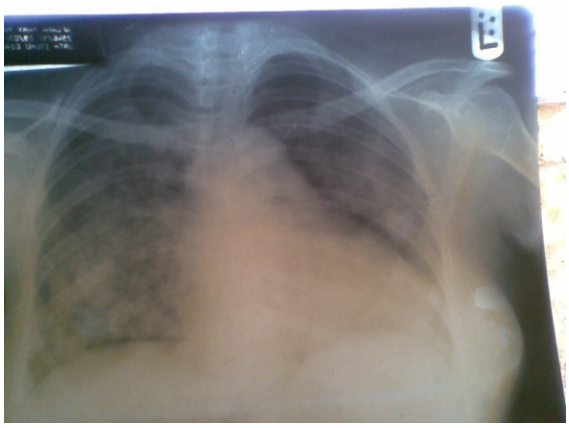
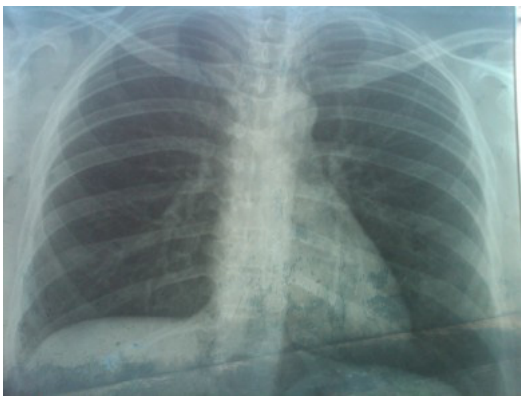


**Figure 2:** Shows the PA view chest radiograph of Miss A.M. taken on the 15th March 2011. The examination report was normal.



The repeat hemoglobin also showed a downward trend. The diagnosis was modified to SLE complicated by diffuse alveolar hemorrhage. She was started on pulse IV cyclophosphamide 500mg twice weekly for six doses, pulse methylprednisolone 1000mg daily x 3 days then oral prednisolone 30mg daily and oxygen therapy. She subsequently made steady and progressive improvement in the affected systems. The SOB and hemoptysis resolved over the next one week and she was discharged home, a week later, on the following medications: oral prednisolone 25mg daily, hydroxychloroquine

200mg BD, oral hematinics and to complete her IV cyclophosphamide as out patient. She completed her IV cyclophosphamide and was started on maintenance oral hydoxychloroquine 200mg daily, azathioprine 50mg daily and low dose prednisolone 5mg daily till date. She has remained in remission and her last clinic attendance was on 18th October 2012.

## Discussion

Dyspnea, cough, and fever are the common initial symptoms of DAH and are most often acute. The fever is usually due to the underlying cause, such as lupus. Hemoptysis may be absent at the time of presentation in up to a third of patients because the total alveolar volume is large and can absorb large amounts of blood, without extending more proximally into the airways. The physical findings are nonspecific and may reflect the underlying systemic vasculitis or collagen vascular disorder. Widespread crepitations may be heard in chest. Our patient with classification of SLE based on ACR classification criteria developed while in the ward on the 7th of admission sudden onset shortness of breath, cough and transient haemoptysis. This triad of acute symptoms on a background of SLE and previously normal chest radiography raised the suspicion of DAH in her. Generally speaking, dyspnea, cough, haemoptysis, and new alveolar infiltrates in conjunction with bloody bronchoalveolar lavage specimens (with numerous erythrocytes and siderophages) establish the diagnosis of diffuse alveolar hemorrhage. The chest radiograph usually provides further support for the diagnosis of DPH, but the draw back is its non-specificity. It most commonly shows the sudden appearance of a diffuse alveolar filling pattern that is often perihilar or basilar and is indistinguishable from pulmonary edema or diffuse infection such as viral or pneumocystis pneumonia[5]. The radiograph is abnormal in 80% of cases and most commonly shows diffuse bilateral patchy consolidation in the mid and lower zones with sparing of apices and costophrenic angles[6]. Resolution, often with a reticular pattern, is rapid and the radiograph may revert to normal in less than two weeks[5]. However, accentuated vascular markings tend to persist after repeated episodes of bleeding due to presence of siderophages in the interstitium and if the bleeding continued over a sufficiently long period, permanent reticulonodular infiltrates develop, resembling the presence of idiopathic pulmonary hemosiderosis[7].

The radiographic abnormalities found in DAH patients are never specific for DAH. This is explained by the fact that a diffuse alveolar filling pattern can be caused by any substance filling the alveoli, which may be edema fluid (pulmonary edema) or inflammatory exudates (pneumonia). The lack of cardiomegaly and pulmonary vascular congestion point away from cardiac pulmonary edema[3]. Our patient had chest radiograph that showed diffuse bilateral alveolar opacities with no evidence of vascular congestion nor pleural effusion. These features resolved and were not evident in the subsequent radiograph taken one year later. It is of note that the radiograph she had done one week to presentation was normal and showed no cardiomegaly. Computed tomography may show areas of consolidation interspersed with areas of ground-glass attenuation and preserved, normal areas. The Diffusing Capacity for Carbon Monoxide (DLCO) may be distinctively increased. Serial increases in the DLCO may indicate progressive alveolar hemorrhage. However, it is worthy of note that the clinical instability of these patients experiencing active alveolar bleeding contraindicates immediate or early performance of the DLCO measurement maneuvers. Thus, the DLCO test is relatively impractical in acute DAH. Those with recurrent DAH may give restrictive pattern of lung function studies. Patients with diffuse alveolar hemorrhage hematology profile generally show falling hemoglobin, rising leucocyte count and elevated acute phase reactants. Active urinary sediment and azotemia may be seen in those with underlying systemic autoimmune disorders.

The diagnostic evaluation in diffuse alveolar hemorrhage usually includes bronchoscopic examination[8] which serves two purposes: to document alveolar hemorrhage by bronchoalveolar lavage and to exclude airway sources of bleeding by visual inspection and to exclude an associated infection. The diagnostic yield of bronchoscopy is higher if the procedure is performed within the first 48 hours of symptoms rather than later. Bronchoalveolar lavage specimens should be sent for routine bacterial, mycobacterial, fungal, and viral stains and cultures, as well as for *Pneumocystis carinii* stains. Our patient had a repeat chest radiography which revealed new onset widespread alveolar opacities. Her repeat hemoglobin level also showed a downward trend.

The sputum culture yielded no growth and mantoux skin testing and accompanying chest radiograph were not suggestive of pulmonary tuberculosis. The DLCO test was impractical in her and in a resource poor setting like ours she could not do CT scan of the chest. There were logistics problems with regards to bronchoscopy within the first 48 hours of onset of her symptoms and because we are aware that the diagnostic yield of bronchoscopy is higher if the procedure is performed within the first 48 hours of symptoms rather than later we decided not to do it. With the results of limited confirmatory test and investigations we strongly felt she had DAH. Effort should be made to find if any underlying cause is present or not present. Management is tailored to presence or absence of underlying systemic cause. For those DAH cases with demonstrable primary multi-systemic autoimmune disorder, corticosteroid with or without disease modifying anti-rheumatic drugs such as azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide and etanercept or other immune biologics may be used in diffuse alveolar hemorrhage. Plasmapheresis may be indicated for DAH associated with Goodpasture syndrome or with other vasculitic processes in which the titres of pathogenetic

immunoglobulins and immune complexes are very high. There are other considerable management measures and these include supplemental oxygen, bronchodilators, reversal of any coagulopathy, intubation with bronchial tamponade, protective strategies for the less involved lung, and mechanical ventilation. Our patient's response to conventional therapy putting into consideration available meager funds was quite remarkable.

The prognosis for diffuse alveolar hemorrhage depends on the underlying cause. Our patient had good outcome mainly because the DAH was recognized and nipped at the bud stage. She is yet to record any recurrence since discharge.

## Conclusion

DAH can occur in our patients with multi-systemic autoimmune disorders. High index of suspicion is required for early diagnosis and prompt initiation of appropriate management is strongly recommended. Prognosis is likely to be improved when early diagnosis is made and prompt appropriate management initiated.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