SYSREMIC LUPUS ERYTHROMATOUS PATIENT WITH MULTIORGAN INVOLVEMENT

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ABSTRACT

It's unusual for systemic lupus erythematosus (SLE) to present with diffuse alveolar hemorrhage (DAH) as the earliest presentation. Diffuse alveolar hemorrhage (DAH) refers to the effusion of blood into the alveoli due to damaged pulmonary microvasculature. It's a rare but severe complication of systemic lupus associated with a high mortality rate. It occurs in three different overlapping phenotypes, which are acute capillaritis, bland pulmonary hemorrhage, and diffuse alveolar damage. The illness develops over hours to multiple days.

Systemic lupus erythematosus (SLE) is an autoimmune systemic disease with many organ involvements with high morbidity and mortality percentage. Central and Peripheral nervous system complications generally develop during the course of the illness and actually uncommonly from the beginning of the illness. Guillain-Barré syndrome (GBS) is a rare autoimmune polyneuropathy usually occurring post-viral, post vaccination, or surgery. Systemic lupus erythematosus (SLE) has been associated with several neuropsychiatric manifestations and development of GBS. GBS as the first presentation of SLE is exceedingly rare. Here, we present the case of a patient with diffuse alveolar hemorrhage and Guillain-Barré syndrome as an atypical presentation of systemic lupus erythematosus (SLE) flare.

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease counted by a range of manifestations involving skin rashes, generalized fatigue, arthritis, glomerulonephritis, neurological, cardiovascular involvement, stroke, and influences on the lungs. Several of these manifestations can leads to early death. It affects 20 – 70 individuals per 100,000 people, with an occurrence of 6 – 10 times more often female [1].

Diffuse alveolar hemorrhage was first described in 1904 by Dr William Osler and is one of the most destructive complications of systemic lupus erythematosus [2]. DAH is a severe and potentially fateful complication, although with reduced mortality over recent generations, reported rates are still between 0 – 92% (with an average of 50%), factors like the development of acute hemoptysis, requirement of mechanical ventilation, sepsis and thrombocytopenia are associated with increased risk of mortality [3].

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, relapsing, autoimmune disease with multisystemic involvement and different clinical presentations. Neurologic complications are common and frequent in SLE. Central nervous system (CNS) involvement is one of the most common complications that can happen at any stage of SLE. Peripheral nervous system involvement in SLE is uncommon, but presents with distal symmetric axonal polyneuropathy and multiple mononeuropathies [4]. Acute inflammatory demyelinating polyneuropathy (AIDP) or the classic type of Guillain- barre syndrome (GBS) is very rare.

Our case report describes severe diffuse alveolar hemorrhage and Guillain- Barré syndrome as the presenting manifestation of SLE in a 20-year-old female who developed severe hypoxemia leading to mechanical ventilation. The patient successfully responded with the combined use of APRV mechanical ventilation mode, Intravenous Immunoglobulin, Cyclophosphamide and pulse therapy of methylprednisolone.

CASE PRESENTATION

A 20-year-old female medically free, presented to our emergency department complaining of fever, vomiting 10 times with coffee ground, diarrhea for 4 attacks and green in color, no melena. History of dysuria with lower abdominal pain, headache, ear pain, oral ulcer (lower lip), generalized weakness, and one episode of epistaxis.

On presentation, the patient arrived to Intensive critical care hypoxic on High-flow oxygen. She was hypotensive, and immediately intubated and connected to mechanical ventilation. Was started on low dose Noradrenaline infusion. Chest x-ray showed bilateral pulmonary infiltrates

chest x-ray: [figure 1]

Laboratory investigation revealed Hemoglobin 6.39 gm, Platelet 1140000, WBC 15800. ANA and anti-ds DNA were positive with 1:1280 titer. 24 hours Urine protein showed total protein 17778 mg/day with a urine protein/creatinine ratio of 7365. Urine creatinine was 13900 umol/l. C3 level was < 40 and C4 < 8. C-reactive protein 96 mg/dl with all cultures negative.

Echocardiography showed left ventricular ejection fraction around 52 %, septal hypokinesia with mild tricuspid regurgitation, right ventricular systolic pressure 24 mmHg.

Patient underwent esophagogastroduodenoscopy which revealed hyperemic gastric mucosa more in the fundus with a hemorrhagic spot. No features of vasculitis or Helicobacter pylori organisms seen in the submitted biopsy. After 3 days of intubation, the patient was extubated and was conscious oriented. After the patient became stable, she underwent high-resolution computed tomography (HRCT) which showed: bilateral

diffuse alveolar hemorrhagic infiltration, as shown in figure [2].

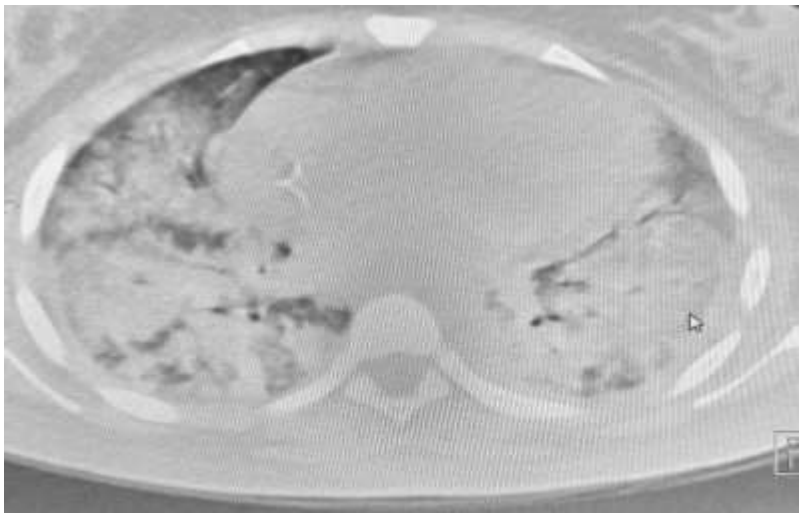

Figure [2].

We performed chest computerized tomography with contrast which didn't reveal any radiological evidence of pulmonary embolism. Hence, we repeated the echocardiograph which revealed tachycardia, ejection fraction 53% with septal mid-hypokinesia, mild mitral regurgitation suggestive of lupus myocarditis. Ultrasound abdomen was normal. We couldn't perform Bronchoscopy since her oxygen requirement was around 15 litre/min. We decided to start Pulse methylprednisolone 1 gram daily for 5 days. Since the response was weak the decision of plasma exchange 6 sessions every other day, intravenous immune globulin (IVIG) 0.4gram/kg/day with total of 5 doses with intravenous cyclophosphamide 500 mg every two weeks for 6 doses & extended pulse therapy for 7 days was taken. After one session of plasma exchange, the further sessions were stopped due to the effect of plasma exchange on cyclophosphamide. The patient had lower limb weakness and nerve conduction study was performed which revealed marked reduced motor amp of all tested nerve, positive temporal dispersion and absent f wave of right ulnar, preserved sensory nerves with evidence of acute motor axonal neuropathy (AMAN) type of Guillain-Barré syndrome (GBS). The treatment plan was revised to cyclophosphamide EURO-LUPUS 500 mg every two weeks for 6 doses, intravenous immune globulin (IVIG) for 5 days, and trimethoprim + sulfamethoxazole 960 mg orally 3 times weekly. Patient after 15 days in ICU showed dramatic improvement and was shifted to the ward conscious, oriented. She was vitally

stable on 2L oxygen nasal cannula. In the ward the patient performed second high-resolution computed tomography (HRCT) to rule out the progression of alveolar hemorrhage and it showed an interval decrease in the amount and shape of previous alveolar hemorrhage, as shown in figure [3].

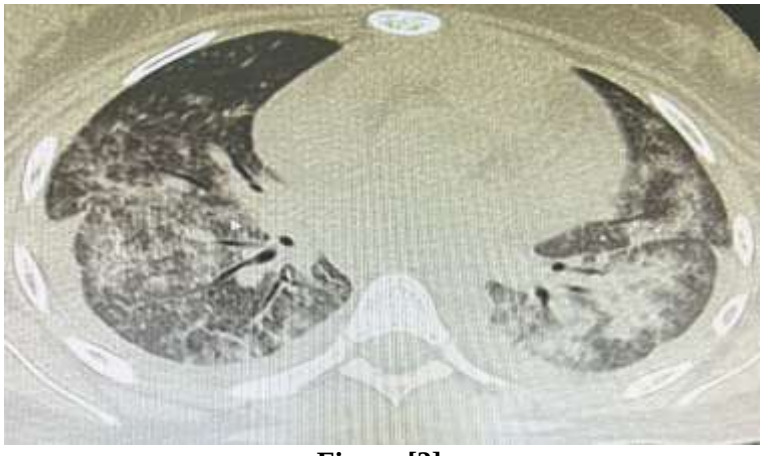

Figure [3].

She was discharged from the hospital on room air with no weakness. She continued to follow up with nephrology and rheumatology OPD to complete the last two doses of cyclophosphamide in day care unit. Current laboratory investigation showed urine protein/creatinine of 176 with urine creatinine 1015 umol/L. The urine protein random was 179 mg/L. We also repeated C3 level which improved to 104.6 mg/dl, c-reactive protein 0.16 mg/dL. She will continue to receive cyclophosphamide (one dose remaining).

DISCUSSION

Diffuse alveolar hemorrhage (DAH) is a rare complication of systemic lupus erythematosus (SLE). It's exceedingly uncommon as the presenting manifestation of SLE [5]. DAH in SLE is considered life-threatening with mortality rates about 50% [5]. The exact reason of DAH pathology is unknown but the overall view is pulmonary capillaritis or bland hemorrhage leading to damage of the basement membranes and leakage of erythrocytes into the alveolar space [3] The most commonly associated organ involvement in SLE cases with DAH is nephritis (about 70% of cases). Anti-dsDNA was elevated in 75% of cases and low complement in 86% of cases [6]. There's a lack of randomized clinical trials to better treat cases with SLE associated with DAH and management remains individualized across different medical centers [7]. The most considerably used therapies are methylprednisolone, cyclophosphamide, and plasmapheresis [8]. One study analyzing 140 cases (172 episodes) found that corticosteroids were most frequently used (98%) followed by cyclophosphamide (54%), plasmapheresis (31%), azathioprine (7%), intravenous immunoglobulin (IVIG, 5%), mycophenolate (3%), the B cell-targeting therapy rituximab (RTX, 6%), and stem cell transplantation (2%) [6]. The combination of methylprednisolone and cyclophosphamide is associated with an increased survival rate [9]. Cyclophosphamide treatment is associated with better survival rates than other treatment options like plasmapheresis [6]. Different forms of lupus-related polyneuropathy have been reported in 10 – 20% of cases with SLE [10]. Still, GBS which is a demyelinating polyneuropathy and a rare complication in lupus [11]. The frequency of SLE with GBS has been reported to be between 0.6% and 1.7% [12]. GBS as a presenting manifestation of SLE remains rare, with the first case registered in 1964 [13]. the diagnosis of our case with Guillain- Barre syndrome was based on limb symmetry, flaccid paralysis, and electromyography showing demyelinating polyneuropathy AMAN type. In our case, the diagnosis of SLE was made with renal involvement (nephritis), anemia, positive ANA, and positive ds- DNA antibodies, meeting the minimum 4 of 11 criteria of SLE diagnosis by the American college of rheumatology.

The pathogenesis of GBS in SLE is not very clear. Gao Z et al. reported multiple factors responsible like vascular occlusion of small vessels, cytokines (interferon- α and interleukin- 6), and various autoantibodies involving anti-cardiolipin antibodies and lupus anticoagulant that damage myelin components [14].

Neuropsychiatric systemic lupus erythematosus (NPSLE), involves the central nervous system, the peripheral nervous system, and the autonomic nervous system, which is fatal and lead to death in SLE patients [15]. The previous literature suggested four treatment options that have been used in GBS with SLE, including corticosteroids, cyclophosphamide, plasmapheresis, and immunoglobulin. Although clinical trials have proved that corticosteroid treatment had no beneficial effect on GBS during the past decades [16].

Regarding the treatment, we treat our patient with Pulse Therapy Methylprednisolone 1000 mg IV Once Daily For 7 days, Cyclophosphamide Euro-Lupus 500 Mg Every Two Weeks For 6 Doses, Intravenous immune globulin (IVIG) 0.4gram/kg per day for total of 5 Days and Trimethoprim + Sulfamethoxazole 960 mg orally 3 times weekly. This treatment was effective and her condition improved significantly with power grade 5 in all limbs during her follow-up visit.

CONCLUSIONS

DAH and GBS are rare presenting manifestations and deadly complications of SLE. It is important to keep SLE in the differential of patients presenting with DAH and GBS because of its high mortality. Early and aggressive therapy should be implemented to improve outcomes. The use of pulse dose steroids, cyclophosphamide, and IVIG resulted in an improvement in our patient's status.

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