Case Report

The role of plasma exchange for fulminant lupus with multiorgan involvement

Meghena Mathew[1], Srilekha Sairam[2], Nagarajan Ramakrishnan[3], Ashwin K Mani[4]

From [1]Consultant, [4]Senior Consultant, Department of Critical Care medicine, [2]Consultant, Department of Rhematology, Apollo First Med Hospital, [3]Director and Senior Consultant, Department of Critical Care Medicine, Apollo Hospitals, Chennai, Tamil Nadu, India

ABSTRACT

Fulminant lupus is a fatal presentation of systemic lupus erythematosus (SLE) and immunosuppression is the key treatment modality. However, there can be conditions that preclude their use. We present the case report of a 21-years-old female with SLE with multiorgan involvement where plasma exchange resulted in good recovery of all the affected vital organs. She presented with fever and generalized lymphadenopathy and then developed cardiac, pulmonary, and neurologic involvement of lupus. She was started on plasma exchange. Her blood culture grew *Streptococcus pneumoniae*. While on plasma exchange, she was found to have bilateral ptosis. Acetylcholine receptor antibody was positive confirming Myasthenia gravis. She showed good recovery of all organs following plasma exchange. This case report highlights the positive role of plasma exchange in a patient with fulminant lupus and concomitant sepsis. We see that this is the second such case reported where plasma exchange had a positive outcome.

Key words: Diffuse alveolar hemorrhage, Lupus encephalopathy, Lupus myocarditis, Plasma exchange, Sepsis

Systemic lupus erythematosus (SLE) is an autoimmune disease with a diverse range of manifestations due to the production of antibodies. Both cellular and humoral immunity take part in organ injury. In cases where extensive and overwhelming antibody production turns catastrophic, therapeutic plasma exchange has shown promising outcomes with the rapid removal of a large amount of antibodies. Plasma exchange is a technique that involves the removal of plasma with replacement with colloid/crystalloid solution. This technique has an added advantage in that it replaces plasma without causing volume overload. There is no data on the prevalence of severe lupus. The data on the prevalence of individual organ involvement in severe lupus is also equally unclear. However, there are few studies that mention the mortality rate in patients with myocarditis and cardiogenic shock is 20% [1].

In this case report, we look at the outcome of plasma exchange when performed in a patient with sepsis. Aggressive immunosuppression is the key mode for the management of severe lupus. This can potentially be risky in patients with sepsis. In the case report-mentioned below, we could not initiate immunosuppression as our patient also had concurrent *Streptococcus pneumoniae* bacteremia. Plasma exchange was a safe and effective option. Our review of the literature could find only one such case of severe lupus, and myocarditis and sepsis successfully treated [2].

Access this article online	
Received - 12 October 2020 Initial Review - 31 October 2020 Accepted - 20 November 2020	Quick Response code
DOI: 10.32677/IJCR.2020.v06.i11.015	

CASE REPORT

A 21-year-old female was admitted with complaints of worsening joint pains and fever (99–101°F) for 1 month. Joints pain was involving both large and small joints with no specific diurnal variations and no aggravating or relieving factors. She was diagnosed with mixed connective tissue disease/SLE and on treatment with steroids for 4 months and subsequently, on alternative medicines.

General examination revealed bilateral pedal edema. Vitals were normal at the time of examination with a heart rate of 80/min and blood pressure of 100/60 mm Hg. Auscultation revealed bilateral basal crackles and all other systemic examination was normal. She had stopped steroids 4 weeks before the admission to our hospital.

Positron Emission Tomography and not Positive scan showed generalized lymphadenopathy, splenomegaly with bilateral lung parenchyma showing ground-glass infiltrates, and interstitial thickening. Her autoimmune panel was positive for the anti-nuclear antibody, Sm D1, SS-A, SS-B, ds DNA, and anti-nucleosome antibody. She was admitted for axillary lymph node biopsy. The lymph node biopsy was planned as she had a fever for 4 weeks and a possibility of underlying tuberculosis was considered.

Post-operatively on day 1, she became dyspneic. She was hypoxic and hypotensive. She was shifted to intensive care unit (ICU) and started on non-invasive ventilation, steroids (methylprednisolone 40 mg intravenous twice daily), broad-spectrum antibiotics (meropenem 1 g 3 times a day and

Correspondence to: Ashwin K Mani, Department of Critical Care Medicine, Apollo First Med Hospital, Chennai, Tamil Nadu, India. E-mail: ashwin.mani@gmail.com

teicoplanin 400 mg intravenous twice daily), and vasopressors for hypotension. On day 2 of ICU stay, she developed recurrent episodes of ventricular tachycardia and was started on amiodarone infusion (900 mg over 24 h).

Electrocardiography showed ST elevation in all the precordial leads. Echocardiogram showed moderate left ventricular dysfunction with an ejection fraction of 40% and elevated troponin I >50. She was intubated for hemodynamic instability and worsening respiratory failure. She received a loading dose of antiplatelets and heparin and was placed on norepinephrine (0.2 mcg/kg/min). On day 3, she developed hemorrhagic endotracheal secretions and a concomitant drop in hemoglobin level with severe hypoxemia of PaO_2/FiO_2 <100 on positive end-expiratory pressure >10. With the background of mixed connective disease and SLE, a possibility of diffuse alveolar hemorrhage was considered.

The antiplatelets and heparin were stopped. She continued to have bleeding from the endotracheal tube with worsening hypoxemia and a drop in hemoglobin. Bronchoalveolar lavage could not be done as she had severe hypoxemia. Chest X-ray showed bilateral diffuse infiltrates consistent with a diagnosis of acute respiratory distress syndrome (Fig. 1). She received a pulse dose of Methylprednisolone 1 g once daily for 3 days with lung-protective ventilation, including prone ventilation and sedation. As she continued to remain hypoxic with myocardial dysfunction, it was decided to start her on plasma exchange. Based on her clinical presentation, imaging, and blood investigations, a provisional diagnosis of cardiogenic shock and pulmonary edema was confirmed.

She underwent plasma exchange, the details of which are mentioned in Table 1. Her blood investigations revealed leukocytosis and blood culture grew *S. pneumoniae* and antibiotics were de-escalated to crystalline penicillin (5 lakh units every 6 h). After a period of 24 h in a prone position, she was made supine. She had shown improvement in oxygenation. Sedation and neuromuscular agents were gradually weaned, but she continued to remain unresponsive with diffuse areflexic weakness of all four limbs.

Magnetic resonance imaging brain showed a diffuse area of mild diffusion restriction and T2-weighted hyperintensity seen in bilateral cerebral white matter, corpus callosum splenium part, bilateral cerebellar tonsil, and cervical spinal cord with discrete oval foci of FLAIR hyperintensity seen in the bilateral cerebral hemisphere and multiple tiny scattered micro bleed seen in bilateral cerebral-hemisphere along with diffuse mild cerebral edema with no midline shift suggestive of SLE-related diffuse vasculitis, lupus plaques, and metabolic leukoencephalopathy changes. Nerve conduction study showed motor polyradiculoneuropathy (predominantly demyelinating). Antiphospholipid antibody and anti-cardiolipin antibody were negative. Her clinical presentation and serology suggested a diagnosis of fulminant lupus with myocarditis and alveolar hemorrhage and lupus encephalitis.

Steroids were continued along with plasma exchange to prevent the rebound antibody phenomenon. She underwent seven cycles of plasma exchange (Fresenius Dialysis Machine). Neurological symptoms gradually started to improve. She was awake and oriented but continued to have limb weakness and tracheostomy was done anticipating prolonged ventilator support. While on plasma exchange, she developed ptosis and bilateral ophthalmoplegia. Creatine phosphokinase was normal, but acetylcholine receptor antibody was positive. She was started on pyridostigmine for concomitant myasthenia gravis (MG). Her weakness slowly improved and she was gradually weaned off from the ventilator support. Repeat two dimensional echocardiogram showed improved left ventricular function. Following plasma exchange, cyclophosphamide (500 mg intravenous once daily for 1 day) was started with a tapering dose of steroids. She was mobilized to the ward after 20 days of ICU stay, and rehabilitation and supportive care were continued in the ward. The lymph node biopsy showed cortical and paracortical reactive hyperplasia. She underwent successful de-cannulation of tracheostomy 2 weeks after discharge.

Table 1: Plasma exchange details

Day	Products used	Volume of exchange
D 1	Pooled plasma	2 L
D 2	Pooled plasma	2 L
D 3	7 units of plasma+100 ml of 20% albumin	2 L
D 4	7 units of plasma+100 ml of 20% albumin	2 L
D 5	10 unit of fresh frozen plasma and+100 ml of 20% albumin	2 L
D 6	10 unit of fresh frozen plasma and+100 ml of 20% albumin	2 L
D 7	10 unit of fresh frozen plasma and+100 ml of 20% albumin	2 L

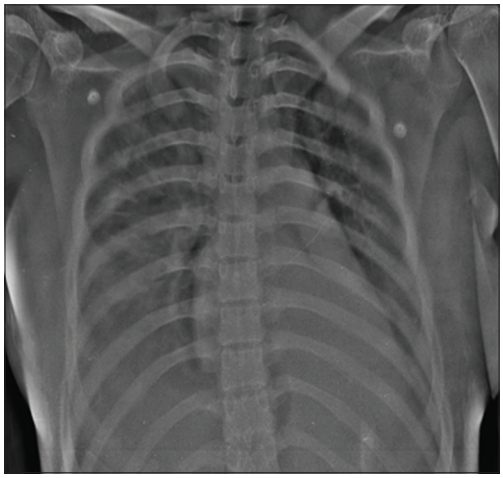

Figure 1: Chest X-ray showing bilateral infiltrates

DISCUSSION

SLE is an autoimmune disease with a varied range of manifestations due to the production of antibodies affecting multiple organs. Immune complexes, autoantibodies such as ds DNA and complement, and cytokines have been implicated in the pathogenesis of SLE. Acute flare and complications are common during the course of illness, but these generally respond to pulsed

steroids and immunosuppressants.

Plasma exchange is considered in patients with poor response to steroids and in anticipation of a rapid response. In life-threatening conditions where there is a rapid surge of these antibodies, it is essential to reduce the levels of these antibodies and immune complexes which can be well achieved with interventions like plasma exchange. It is an effective treatment when a rapid reduction of antibodies is desired. Some of the other autoimmune conditions with varied manifestations and where therapeutic plasma exchange has helped include antiphospholipid syndrome, ANCA-positive vasculitis, autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, and systemic sclerosis (scleroderma). It remains the last modality of treatment in patients with SLE with life-threatening conditions where immunosuppression has failed.

Plasma exchange removes high molecular weight substances, including pathogenic autoantibodies, immune complexes, cryoglobulins, myeloma light chains, endotoxins, and lipoproteins that contain cholesterol. It holds a category IV recommendation for lupus nephritis and a category II indication for pulmonary alveolar hemorrhage as per the American Society of Apheresis (ASFA) guidelines [3-5]. Approximately 50% of patients with SLE will have antiphospholipid antibodies, and about 1% of them can present with catastrophic antiphospholipid antibody syndrome which has a mortality rate of 48%. SLE is one of the most common indications for plasma exchange in India and worldwide [6]. A combination of steroids, anticoagulation, and plasma exchange has shown good outcomes.

One of the concerns with plasma exchange is antibody rebound post-cessation of therapy. Hence, plasma exchange has to be followed with steroids and immunosuppressants like cyclophosphamide just like in our patient. The role of plasma exchange in sepsis is of unclear benefit. Probably, early intervention in septic shock might have some beneficial role, where it removes both pro- and anti-inflammatory cytokines and is replenished with healthy plasma [7]. It may have a role as rescue therapy in sepsis.

SLE and fatal organ involvement have been described below in detail. The discussion also has looked at the role of plasma exchange in individual organ involvement in SLE. The development of symptomatic myocarditis is quite rare in SLE. Cardiac manifestation is more common if the patient also has anti-Ro and antinuclear ribonucleoprotein antibodies. Endomyocardial biopsy is the gold standard for diagnosis.

The treatment of choice is steroids. There are case reports where the patients have responded to plasma exchange and immunoglobulins [8,9]. Even though 70% of patients have a good prognosis with the resolution of left ventricular failure over days, nearly 4–10% can succumb due to refractory cardiogenic shock or malignant arrhythmias. Extracorporeal support devices can be considered in case of refractory shock until the time immunosuppression agents start showing an effect. Our patient also had myocarditis with elevated troponin but with post-plasma exchange and immune-suppressive therapy, her left ventricular function gradually improved. An endomyocardial biopsy could not be done as she was too unstable to undergo an invasive procedure.

Alveolar hemorrhage accounts for <4% of hospital admissions due to SLE and is associated with a high mortality rate of 53–86% [10]. Plasma exchange holds category II indication for pulmonary alveolar hemorrhage as per the ASFA guidelines. The other common presentation in SLE is that of neuropsychiatric complications and plasma exchange has been used in severe cases [11]. Neuropsychiatric presentations include confusion, anxiety, cognitive decline, mood disorders, seizures, aseptic meningitis, cerebrovascular disease, demyelination, headaches, movement disorders, and muscle and myoneural junction problems.

Pathogenesis includes immune complexes and antibodies damaging the neuronal tissue and myoneural junction. Severe manifestations may be refractory to high dose steroids and plasma exchange has to be performed early. Neuropsychiatric manifestations are associated with high mortality and with a very poor response to immunosuppressive therapy and plasma exchange is probably a safe and effective option [11].

As per the ASFA, plasma exchange is a Class II indication in lupus encephalopathy [12]. It may warrant a total of 3–6 exchanges. However, there are case reports which have shown patients with severe lupus encephalopathy responding to high-dose steroids and cyclophosphamide. To summarize, there is a lack of randomized controlled trials yet to support plasma exchange in varied presentations of SLE. The treating physician has to understand the pros and cons and consider multiple factors before recommending this treatment.

The interesting feature in our patient who had severe multi-system involvement including encephalopathy, myocarditis, and alveolar hemorrhage in the background of pneumococcal sepsis is that plasma exchange played a pivotal role in the recovery of all the organs. Our review of the literature did not reveal any case reports where a patient who had severe multiorgan involvement in lupus with pneumococcal bacteremia treated with plasma exchange and had a good outcome. Our patient also developed demyelinating polyneuropathy with acetylcholine receptor antibody-positive suggestive of MG. Plasma exchange is a proven therapy for myasthenic crisis as well, but our patient developed neuromuscular weakness while already on plasma exchange. It is a possibility that she already had neuromuscular weakness and infection had precipitated the Myasthenic crisis. She responded well to plasma exchange and pyridostigmine. Steroids were continued and she was started on cyclophosphamide.

CONCLUSION

Our case report signifies the importance of plasma exchange in SLE flare with multiorgan involvement. In rapidly deteriorating patients who did not respond to a pulse dose of steroids, plasma exchange can be considered for rapid removal of circulating antibodies. Plasma exchange may be a better option in patients with concomitant sepsis, where high-dose immunosuppression may carry a very high risk.

REFERENCES

1. Tanwani J, Tselios K, Gladman DD, Su J, Urowitz MB. Lupus myocarditis: A single center experience and a comparative analysis of observational cohort studies. Lupus 2018;27:1296-302.
2. Xing ZX, Yu K, Yang H, Liu GY, Chen N, Wang Y, *et al*. Successful use of plasma exchange in fulminant lupus myocarditis coexisting with pneumonia: A case report. World J Clin Cases 2020;8:2056-65.
3. Szczepiorkowski ZM, Winters JL, Bandarenko N, Kim HC, Linenberger ML, Marques MB, *et al*. Guidelines on the use of therapeutic apheresis in clinical practice--evidence-based approach from the Apheresis Applications Committee of the American Society for Apheresis. J Clin Apher 2010;25:83-177.
4. Hoshi K, Matsuda M, Ishikawa M, Mitsuhashi S, Gono T, Hashimoto T, *et al*. Successful treatment of fulminant pulmonary hemorrhage associated with systemic lupus erythematosus. Clin Rheumatol 2004;23:252-5.
5. Huang DF, Tsai ST, Wang SR. Recovery of both acute massive pulmonary hemorrhage and acute renal failure in a systemic lupus erythematosus patient with lupus anticoagulant by the combined therapy of plasmapheresis plus cyclophosphamide. Transfus Sci 1994;15:283-8.
6. Ranganathan L, Menon R, Ramakrishnan N, Venkatraman R, Ramachandran P. Therapeutic plasma exchange practices in intensive care unit. Indian J Crit Care Med 2019;23:336-8.
7. Knaup H, Stahl K, Schmidt BM, Idowu TO, Busch M, Wiesner O, *et al*. Early therapeutic plasma exchange in septic shock: A prospective open-label nonrandomized pilot study focusing on safety, hemodynamics, vascular barrier function, and biologic markers. Crit Care 2018;22:285.
8. Sherer Y, Levy Y, Shoenfeld Y. Marked improvement of severe cardiac dysfunction after one course of intravenous immunoglobulin in a patient with systemic lupus erythematosus. Clin Rheumatol 1999;18:238-40.
9. Tamburino C, Fiore CE, Foti R, Salomone E, Di Paola R, Grimaldi DR, *et al*. Endomyocardial biopsy in diagnosis and management of cardiovascular manifestations of systemic lupus erythematosus (SLE). Clin Rheumatol 1989;8:108-12.
10. Zamora MR, Warner ML, Tuder R, Schwarz MI. Diffuse alveolar hemorrhage and systemic lupus erythematosus. Clinical presentation, histology, survival, and outcome. Medicine (Baltimore) 1997;76:192-202.
11. Pagnoux C. Plasma exchange for systemic lupus erythematosus. Transfus Apher Sci 2007;36:187-93.
12. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, *et al*. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the writing committee of the American society for apheresis: The seventh special issue. J Clin Apher 2016;31:149-62.

Funding: None; Conflicts of Interest: None Stated.

How to cite this article: Mathew M, Sairam S, Ramakrishnan N, Mani AK. The role of plasma exchange for fulminant lupus with multiorgan involvement. Indian J Case Reports. 2020;6(11):652-655.