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Therapeutic plasma exchange in paediatric SLE: a case series from India

P Prasun Giri[1], R Sinha[1,2], P Pal[1] and B Sarkar[2]
[1]Institute of Child Health, Kolkata, India; and [2]AMRI Hospitals, Kolkata, India

Therapeutic plasma exchange (TPE) has been reported to be a useful adjunct in severe systemic lupus erythematosus (SLE) but paediatric literature continues to be scanty. We hereby present three cases of refractory paediatric SLE (pSLE) with thrombotic thrombocytopenic purpura (TTP), diffuse alveolar haemorrhage (DAH) and crescentic glomerulonephritis which were treated with TPE as an adjunctive therapy. TPE was carried out in haemodialysis units using the membrane filtration technique. Demonstrable benefit of TPE was seen in all three cases. In refractory pSLE, TPE may be a useful tool and should be considered. The report additionally highlights the feasibility of undertaking TPE in haemodialysis units, which is important as haemodialysis units are more readily available than dedicated apheresis units in developing countries. *Lupus* (2015) **0,** 1–3.

Key words: Nephritis; systemic lupus erythematosus; lupus anticoagulant

Introduction

Systemic lupus erythematosus (SLE) is associated with multi-system involvement and can sometimes be refractory to conventional immunosuppressants wherein adjunct therapy with therapeutic plasma exchange (TPE) has been tried with variable effects.[1] Documented experience of TPE in paediatric SLE (pSLE) is limited and is particularly scanty owing to resource-constrained set-up.[2,3] We hereby report the outcome of three cases of refractory pSLE from India wherein TPE was performed.

Case reports

Case 1

A 14-year-old boy was admitted with seizures and oliguria. There was history of fever and on admission he was oedematous with low Glasgow Coma Score (6/15), bilateral papilloedema and sluggish respiratory efforts necessitating intubation and ventilation. Investigation revealed significant anaemia (haemoglobin (Hb) 6.6 g/dl), thrombocytopenia (platelets 52,000/dl) and elevated reticulocyte count with presence of fragmented red blood cells (RBCs) in the peripheral smear. His infective parameters (C-reactive protein and total leucocyte count (TLC)), liver function (LFT) as well as coagulation profile were normal but his renal profile was altered (urea 63 mg/dl, creatinine (Cr) 1.5 mg/dl and urinalysis 3+ proteinuria with plenty of RBCs). Further investigations showed elevated lactate dehydrogenase (LDH), low complements, positive antinuclear antibody (ANA), negative double-stranded DNA (dsDNA) antibody and positive anti-Smith antibody. Thrombotic thrombocytopenic purpura (TTP) secondary to SLE was diagnosed but he did not respond to pulse methylprednisolone and cyclophosphamide. TPE was initiated on Day 3 (D3) with significant response as shown by the LDH trend (Figure 1). In total, eight cycles were given over 10 days and as a result of overall improvement he was extubated by D6. Subsequent renal biopsy confirmed grade 4 SLE nephritis and he was discharged on oral prednisolone, mycophenolate mofetil and hydroxychloroquine. On follow-up at eight weeks he had Cr 0.9 mg/dl, urine 1+ proteinuria and normal complements level.

Correspondence to: Rajiv Sinha, 37G Bondel Road, Kolkata – 700019, India.
Email: rajivsinha_in@yahoo.com
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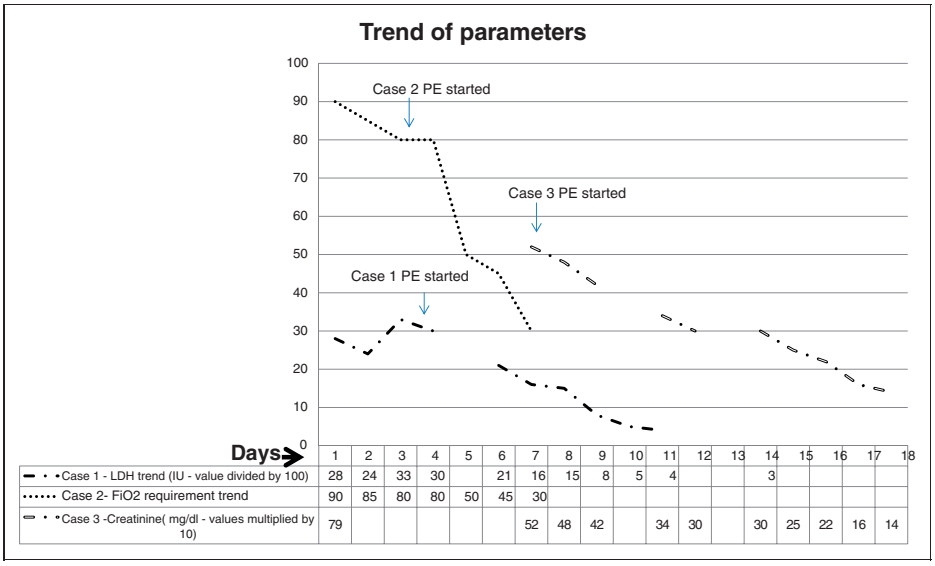

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Case 1 - LDH trend (IU - value divided by 100)	28	24	33	30		21	16	15	8	5	4			3				
Case 2- FiO2 requirement trend	90	85	80	80	50	45	30											
Case 3 -Creatinine(mg/dl - values multiplied by 10)	79						52	48	42		34	30		30	25	22	16	14

Figure 1 Trend of important parameters in the three cases post-initiation of plasmapheresis.
PE: plasma exchange; LDH: lactate dehydrogenase; FiO2: fraction of inspired oxygen.

Case 2

A 12-year-old girl was admitted with a history of arthritis for one month along with fever, pallor, rash and palatal ulcer. Investigation revealed neutropenia (TLC 4×10^9/l, 44% neutrophils), thrombocytopenia (platelet 1.1×10^6/l) and anaemia (Hb 6.2 g/dl). Infective parameters, LFT, coagulation and renal profiles were normal. Chest X-ray (CXR) showed clear lung fields and echocardiography was normal except for mild pericardial effusion. Diagnosis of SLE was supported by positive ANA, dsDNA and low complements. She was transfused (post-transfusion Hb 10.4 g/dl) and commenced on pulse methylprednisolone but on D3 developed severe respiratory distress. Echocardiography was unchanged but CXR showed a bilateral white-out lung field. She had to be ventilated and following intubation almost 500 ml of fresh blood was aspirated from the endotracheal tube, suggesting diffuse alveolar haemorrhage (DAH). Hb dropped to 7.2 g/dl but there were no other bleeding manifestations and her coagulation remained normal. Cyclophosphamide was added but pulmonary haemorrhage persisted with a high oxygen requirement. Daily TPE was commenced on D4 with marked improvement in her oxygen requirement (Figure 1). She was extubated by D8 subsequent to which TPE was stopped. Unfortunately she developed fulminate pseudomonas sepsis on D18 and died on D20 but her pulmonary haemorrhage never recurred.

Case 3

A 13-year-old girl was admitted with oliguria, anasarca and hypertension (blood pressure (BP) 160/110 mmHg). Investigations revealed grossly deranged renal parameters (urea 140 mg/dl, Cr 7.9 mg/dl, Na 128 MEq/dl, K 6.8 MEeq/dl, Alb 2.1 mg/dl, and urine 3+ for protein as well as blood) along with neutropenia (TLC 4.5×10^9/l, 56% neutrophils), anaemia (Hb 9.6 g/dl) and reduced platelets (1.3×10^9/l). She also had low complements, and positive ANA and dsDNA. In view of her severe renal dysfunction, haemodialysis was initiated concurrent with pulse methylprednisolone and cyclophosphamide. Renal biopsy was performed on D5 which revealed 90% cellular crescents on a background of Class IV lupus nephritis. In light of her biopsy finding and persistent dialysis dependency, TPE was initiated on D7 wherein a sustained response was obtained (Figure 1). She received a total of nine cycles and was discharged on D27 on hydroxychloroquine, steroids and monthly cyclophosphamide. At six-month follow-up her renal profile had normalized (Cr 0.8 mg/dl and urine 1+ for proteinuria and haematuria) and so had the complement levels.

In all three cases TPE was carried out in the haemodialysis unit by the membrane filtration technique using a polysulfone membrane filter (surface area 0.6 m^2). Standard protocols were followed[4] and no major complications were noted. A minor complication included hypotension, a couple of which required saline bolus and a couple of

events of chills and rigour which were managed conservatively.

Discussion

TPE has been tried in refractory SLE on the presumption that it evokes immediate immunosuppressive response by removing circulating immune complexes and autoantibodies.[1,5] Adult reports are variable and evidence in pSLE is limited to a few case reports/series with hardly any reports from resource-limited set-up.[3] As pSLE is felt to be more severe and quite different from adult-onset SLE,[6] more literature is needed regarding the utility of TPE in it. We hereby reported our experience of TPE in three cases of pSLE with severe systemic involvement.

The American Society for Apheresis (ASFA) has categorized the evidence for TPE in SLE.[4,7] SLE with TTP has been recognized as a category 1 indication, i.e. first-line therapy. As DAH in SLE is rare, there are primarily case series[8,9] and hence despite favourable case reports ASFA has categorized TPE for DAH at level II indication, i.e. second-line therapy. The jury is still out for TPE in immune complex glomerulonephritis (which includes SLE nephritis) with crescents. The ASFA has categorized it as level III and suggested that decisions should be individualized. In the present case series Cases 1 and 3 responded very well to TPE and even in Case 2, DAH resolved. Although Case 2 developed fulminate pseudomonas sepsis, it happened almost a week after TPE was stopped. Case 3 fell under the category III recommendation but similar to ours there are other favourable reports of TPE in SLE nephritis, particularly in dialysis-dependent scenarios.[6] In fact renal was the commonest cause for initiation of TPE in pSLE in the largest review published to date, with 75% favourable response.[2]

Registry data have continued to report a steady number of TPE (2–3% annually) being carried out for severe SLE.[1] Additionally, retrospective paediatric reviews have also shown significant benefit.[2] The rarity of these cases in paediatric age groups makes clinical trials difficult and case reports remain important in our quest to understand the role of TPE in pSLE.

In conclusion, TPE seems to have scope as adjunctive therapy in refractory pSLE. All TPEs were performed in a haemodialysis unit, which underscores its feasibility even in resource-limited set-up, as haemodialysis facilities are more readily available than dedicated apheresis facilities. This report should encourage further exploration of the use of TPE in life-threatening pSLE.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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