Synchronization of plasmapheresis and pulse cyclophosphamide in the treatment of thrombotic thrombocytopenic purpura and SLE associated with pregnancy

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Concurrent thrombotic thrombcytopenic purpura (TTP) and systemic lupus erythematosus (SLE) is a rare condition in pregnancy. Plasmapheresis with steroids improves survival, but these patients still have a high mortality. We describe a patient who simultaneously developed SLE and TTP in the third trimester of pregnancy and recovered after synchronization of plasmapheresis with pulse cyclophosphamide.

A 22-year-old female patient in the 32nd week of pregnancy was admitted for generalized edema, hypertension, and proteinuria. Physical examination revealed pretibial pitting edema and decreased breathing sounds with rales on whole lung field. There was no malar rash, oral ulcer, nor arthritis. Chest radiograph showed bilateral pleural effusion. Results of laboratory tests are listed in Table I. She was diagnosed with pre-eclampsia and the baby was delivered via cesarian section.

Even after the delivery, anemia and thrombocytopenia did not improve and peripheral blood smear showed microangiopathic hemolytic anemia (MAHA) with schistocytosis. Proteinuria persisted and serum creatinine increased. On the basis of MAHA, thromobocytopenia, and proteinuria, she was diagnosed with TTP and daily plasmapheresis started. Subsequent investigation showed positive ANA (homogenous,titer of 1:40) and anti-ds DNA, but negative antiphospholipid antibody and lupus anticoagulant. She was also diagnosed to have SLE with anemia, thrombocytopenia, proteinuria,ANA positivity, anti-DNA positivity, and pleural effusion. After a three-day treatment with steroid pulse therapy, high dose oral steroid was added to the plasmapheresis. On the 25th day of admission, serum creatinine increased to 4.1mg/dL. Hemodialysis was started due to the development of oliguria and dyspnea.

On the 28th day, despite daily plasmapheresis, the clinical picture worsened; the fever persisted and hemoglobin and platelet count did not improve; the patient showed generalized tonic and clonic seizure with aura, but EEG and brain MRI did not show any abnormality. She was treated two times with synchronization of plasmapheresis and pulse cyclophosphamide (1 g) and the prednisone dose was maintained at 90mg/day. Plasmapheresis was decreased in frequency and finally discontinued at a total 38 courses with progressive recovery of neurologic, renal and hematologic involvement. She was discharged in 4 months. She is now taking daily prednisone 12.5 mg and is well.

The incidence of TTP occurring in the setting of SLE has been reported to be as low as 1% (1, 2) and the simultaneous occurrence of the two diseases is thought to be even lower (3, 4). The diagnosis of TTP as a syndrome distinct from SLE is challenging, because many of TTP manifestations can be explained by the clinical manifestations of SLE. However, MAHA, is usually associated with diffuse vasculitis or malignant hypertension, and rarely detected in SLE (5). The presence of thrombocytopenia and MAHA unequivocally defines the diagnosis of TTP.

Plasma exchange remains the treatment of choice for TTP and it can produce remission in about 80% of patients (6). There are no guidelines for the management of TTP in SLE. The different pattern of association of these diseases determines the optimal treatment approach (7). It is suggested that plasmapheresis with steroids can be the initial treatment of cases of TTP in SLE. Nonetheless, Some patients fail to respond to plasmapheresis. Thus, alternative strategies are necessary to treat those. Cyclophosphamide remains the treatment of choice for active life-threatening SLE and it has been used with some success in relapsing TTP (8). Vaidya *et al.* reported two cases of SLE with TTP; one had a good response when cyclophosphamide was given early with plasmapheresis and steroids; the other had a poor outcome in a patient given cyclophosphamide late (5). Our patient deteriorated while she was treated with plasmapheresis and steroids, and she had a slow but steady response after 2 cycles of IV cyclophosphamide synchronized with plasmapheresis (9). In conclusion, we advocate the early use of cyclophosphamide in the treatment of TTP and active SLE that does not respond to plasmapheresis with steroid.

Table I. Laboratory findings of the patient.

	At admission	After 25 days	After 2nd synchronization (55 days)	At discharge (125 days)	2 months after discharge	Normal value
Hb (g/dL)	8.7	7.5	9.6	8.5	10.4	10.7-14.6
WBC (/uL)	4760	9090	3760	5440	10320	3410-9300
Platelet (/uL)	49000	82000	54000	188000	204000	143000-376000
Reticulocyte count	1.8%					0.8-2.6%
Haptoglobulin (mg/dl)	<5.8	<5.8	<5.8	39		27-155
LDH (U/L)	322	443	345	306		100-220
BUN/cr (mg/dL)	18.7/1.1	80.0/4.1	55.9/3.1	48.3/2.3	34.0/2.3	8-25/0.5-1.4
ds-DNA (IU/ml)	>104	28.5			5.0	0-7
C3/C4 (mg/dL)	11/3	22/3	56/11		71/17	65-125/9-37

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References

1. PISTINER M, WALLACE DJ, NESSIM S, METZGER AL, KLINBERG JR: Lupus erythematousus in the 1980's: A survey of 570 patients. *Semin Arthritis Rheum* 1991; 21: 55-64.
2. PORTA C, BOBBIO-PALLAVICINI E, CENTURIONI R, MONTECUCCO CM: Thrombotic thrombocytopenic purpura in systemic lupus erythematous. Italian Co-operative Study Group for TTP (letter). *J Rheumatol* 1993; 20: 1625-6.
3. BRAY VJ, WEST SG, KRISTO DA: Simultaneous presentation of thrombotic throbocytopenic purpura and systemic lupus erythematous. *S Med J* 1994; 87: 827-30.
4. RAPHAEL BS, JAMES AD, JAY G, KENNETH SY, DOBRI DK: Thrombotic throbocytopenic purpura complicating systemic lupus erythematous. Case report and literature review from the plasmapheresis era. *J Rheumatol* 1992; 19: 1469-73.
5. VAIDYA S, ABUL-EZZ S, LIPSMEYER E: Thrombotic throbocytopenic purpura and systemic lupus erythematous. *Scand J Rheumatol* 2001; 30: 308-10
6. ROCK GA, SHUMAK KH, BUSKARD NA *et al.*: Comparision of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. *N Engl J Med* 1991; 325: 393-7.
7. PORTA C, CAPORALI R, MONTECUCCO C: Thrombotic thrombocytopenic purpura and autoimmunity: A tale of shadow and suspects. *Haematologica* 1999; 84: 260-9.
8. BIRD JM, CUMMINS D, MACHIN SJ: Cyclophosphamide for chronic relapsing thrombotic thrombocytopenic purpura. *Lancet* 1990; 336: 565-6.
9. HANS HE, JOHANN OS, PONTUS H, RAINALD AZ, HANS JG: Treatment-free remission in severe systemic lupus erythematosus following synchronization of plasmapheresis with subsequent pulse cyclophosphamide. *Arthritis Rheum* 1994; 37: 1784-93.