Cerebral Thrombosis in Systemic Lupus Erythematosus with The Antibody Antiphospholipid Syndrome


ABSTRACT

Systemic lupus erythematosus (SLE) has numerous manifestations. Haematology is the common system influenced by the disease. The antibody antiphospholipid syndrome, secondary hematoloy disorder in SLE, is related to high incidence of thrombosis. The thrombosis events like myocardial infarction and stroke are high in mortality. We reported a 36-year old woman treated for lung tuberculosis (TB) with secondary infection, nephritis lupus, and pancytopenia. The general condition has improved and the patient was planned to discharge while she suddenly fell down, unconscious and had seizure. The CT-scan showed an area of hypodensity on the left thalamus. Haematology results showed high level of fibrinogen and D-dimer as the signs of thrombosis. The anticardiolipin antibody was intermediately positive for IgG and IgM, but lupus anticoagulan was weakly positive. The serial test within 2 months still showed positive IgG. The patient received supportive treatment, heparinization, neurotropic drugs and anticonvulsant. She was discharged in good condition while continuing oral anticoagulant to prevent recurrent seizure.

Key words: cerebral thrombosis, systemic lupus erythematosus, antibody antiphospholipid syndrome.

INTRODUCTION

Antiphospholipid antibodies are the family of autoantibodies that present a broad range of target specificities and affinities, all recognizing various combinations of phospholipids, phospholipids binding protein or both. The term “antiphospholipid syndrome” was first coined to denote the clinical association between antiphospholipid antibodies and syndrome of hypercoagulability in which venous or arterial thrombosis, or both, may occur. Systemic lupus erythematosus (SLE) is the most common disease related to the secondary antiphospholipid syndrome (APS). Current diagnosis criteria for antiphospholipid syndrome are using a consensus statement, provide simplified criteria for diagnosis of the APS.1-5

There are several mechanisms that have been acknowledged in the pathogenesis of thrombosis in APS. Inhibition of natural anticoagulant, platelet activation, disorder of fibrinolytic and coagulation activation, have played an important part in hypercoagulation condition. Lupus anticoagulant (LA) is a stronger risk factor for thrombosis than anticardiolipin antibodies (ACA) in APS.1, 5-7

Systemic lupus erythematosis is a complex disorder that may affect multiple organs or systems. Most of the cases found in women, usually of childbearing age. Prevalence of SLE varies, depends on race and genetic inheritance. In white women the prevalence is 1:1000.8-11

Among patients with SLE antiphospholipid antibodies are reported in 20–55% of cases. The Manifestation of APS in SLE varies in different conditions. Stroke related to APS is one of the central nervous system complications. The estimation of cerebrovascular accident was 10 times higher in 18 to 44 years old women with SLE compared to those without SLE.1, 12-15

CASE ILLUSTRATION

Mrs. R, 36 years old, presented to RSCM with shortness of breath since 4 days prior to admission. She had been admitted to another hospital 2 days before, where the diagnosis of tuberculosis and suspected lupus were established. The patient was presently on anti TB drug therapy. She had 1-month history of cough, sometimes with green coloured sputum. She also had a fluctuating fever, night sweats, loss of appetite, weight loss, and
nausea. Since one year ago, she had had recurrent ulcers in the mouth, hair loss and flushing on the face due to sunlight exposure. No other significant history.

On physical examination, the patient looked severely ill and fully alert. Blood pressure (BP) was 130/80 mmHg, regular pulse rate at 88x/min, temperature was 36.6°C, respiratory rate (RR) 24x/min. The height was 158 cm and body weight (BW) was estimated 40 kg. The conjunctivas were pale, sclera were not icteric, there was a sign of Malar rash and stomatitis, no palpable lymph nodes. Vesicular breath sound with rales in both lungs. The rest of the physical examination were normal.

On laboratory examination, Hb 9.2 g/dl, Ht 27%, leukocyte 2100/uL, platelet count 73000/uL, diff count 0/0/0/0/91/7/2 and positive coomb’s test. Urinalysis leukocyte 2-3, erythrocyte 20-25, protein 2+, blood 2+, BJ 1.030 and the others were normal. Ureum 92 mg/dl, creatinin 2.6 mg/dl, estimated GFR by Cockcroft and Gaul was 23.6 ml/min, random blood glucose 155 mg/dl, AST 45 U/L, ALT 40 U/L, albumin 1.9 g/dl, globulin 2.8 g/dl, Na 143 meq/L and K 3.6 meq/L. The results of blood gas analysis (BGA) was pH 7.5, pO$_2$ 78, pCO$_2$ 22, HCO$_3$ 17.5 and O$_2$ sat. 96.8 %.

Normal ECG with tachycardia (QRS rate 100x/min). CXR showed infiltrate in both lungs dominantly on the right.

Based on all data, the problems of this patient were (1) lung TB with secondary infection, (2) lupus nephritis, (3) pancytopenia caused by SLE, (4) SLE. Lung TB with secondary infection was differentiated with lupus pneumonitis based on history of cough, with green coloured sputum, fluctuating fever, night sweats, loss of appetite, loss of weight and nausea. Rales in both lungs and CXR showed infiltrate in both lungs especially on the right. We planned to check ESR, AFB smear 3x, MOR, Gram and consulted to the Pulmonary division. We continued the anti TB drugs R/H/Z/E 450/300/1000/750, vitamin B6 3 x 10 mg and we added Ceftriaxone 1 x 2gr for secondary infection. As for supportive treatment, we administered the normosaline fluid/12-h and oxygenation 3lt/min.

Lupus nephritis was based on blood ureum 92 mg/dl, creatinin 2.6 mg/dl, estimated GFR 23.6 ml/min and urinalysis leukocyte 2-3, erythrocyte 20-25, protein 2+, blood 2+ and because she suffered from SLE. We planned to perform measured GFR, 24-h quantitative protein urine and renal biopsy. The treatments were restricted protein (32 gram) diet with normal calories intake; steroid (prednisone) 1.5 mg/kgBW. The later was switched to methylprednisolon with converting dose (3 x 4 tab) due to slightly increased level of liver function test. We assumed it was caused by anti TB drugs, proved by previous data of normal liver function. We planned to perform serial liver function test.

Pancytopenia caused by SLE was based on decreasing Hb, leukocyte, platelet count and positive direct Coomb’s test. SLE was based on a sign of malar rash, stomatitis, photosensitivity, haematologic disorders and renal abnormality. For confirmation we examined ANA, anti Ds-DNA and C3/C4. We treated the patient with methylprednisolon 3 x 4 tab and ranitidine 2 x 1amp as gastric protector.

On the 4th day of hospitalization, the general condition was improved, she looked moderately ill, RR was 20x/min and other vital signs were within normal limit. On laboratory finding, creatinin level returned to normal (0.9 mg/dl), measured GFR 71.9 ml/min, 24-h protein urine 3780 mg, Hb 8 g/dl, leukocyte 7400/uL, Ht 28.3%, and platelet count 83000. Due to the increasing level of liver function test and by the advice from the Pulmonary division, we stopped giving Pyrazinamide temporarily and performed liver function monitoring. Due to financial reasons, renal biopsy and other tests could not be completed. By significant improvement of general condition, clinically and laboratory, the Nephrology Division suggested to discharge the patient and evaluate in polyclinic. We added Captopril 2 x 12.5 mg and liver protector. On the day-12, urinalysis finding showed proteinuria 1+ and the other was normal. The
decision to discharge the patient was also agreed by Pulmonary and Rheumatology Division.

On the 13th day, early in the morning, the patient fell down in the bathroom, unconscious and had repeating convulsions. She was somnolent, BP 160/80 mmHg, RR 28x/min, temperature 40°C and pulse 100x/min. Random blood glucose 134 mg/dl, electrolyte and blood gas analysis were within normal limit. The Neurology Department suspected an intracerebral hemorrhages and suggested to perform brain CT. The brain CT yielded a subacute infarction on the left thalamus. We diagnosed the unconsciousness caused by cerebral infarction with other problems of lung TB with secondary infection with suspected sepsis, lupus nephritis, pancytopenia caused by SLE and SLE. We planned to check haemostatic and blood culture. We performed also supportive treatment such insertion of nasogastric tube with liquid diet 6 x 250cc, catheter urine and oxygenation. We switched Ceftriaxone to Ceftazidim 2 x 1 gr and oral to injection Methylprednisolon 2 x 250 mg. The neurologist suggested to give Fenitoin 3 x 100 mg and intravenous Citicholine 2 x 500 mg.

On day-14, haemostatic signs were PT 13.6’ (control 13.2’), APTT 30.3’(control 31.2’), fibrinogen 670 mg/dl and D-dimer 700 ng/dl. Haematology division agreed to start heparinization with target of APTT 1.5–2.5x control. After 3 days, there was significant improvement on general condition, the patient looked fully alert, vital signs were normal. We put off the nasogastric tube, overlapped heparin with simarc, switched steroids into oral and Pulmonary division suggested to switch Ceftazidim to Levofoxacin drip 1x500 mg. The laboratory findings were ACA positive of both IgG and IgM, lupus anticoagulant positive and C3/C4 within normal limit (75 mg/dl and 15 mg/dl, consecutively).

On the 21st day, general condition was good, she was able to mobilize. As the AST and ALT returned to normal, we started again the pyrazynamide and added Aspirin. Albumin level increased to 2.77 g/dl, but INR level did not yet attain the target (1.4), so we increased the dosage of simarc. On the 23rd day, she was discharged in good condition.

DISCUSSION

Pulmonary infection in this case, as mentioned in the litterature, is one of the co-morbid manifestation in systemic lupus erythematosus, because of immuno compromise status. The involvement of multi organ disorders in SLE gives a severe clinical condition. The disease is characterized by periods of relative quiescences and periods of exacerbations, which may involve any organ or system in various combination. The uncontrolled SLE activity put a coincidence of active SLE and the acute infection became serious complications. As we know the infection is still the most common cause of death in SLE.

The target organs involved in this patient were kidney, hematosis system, skin and musculoskeletal. Positive results of ACA and LA were common in SLE with haematology manifestation and related with the disease itself.

On the beginning, we analyzed the cause of unconsciousness and repeated convulsion were intracerebral hemorrhage due to head trauma or cranial injury. That was because she had a history of fall down and the status of on-steroid therapy would decrease the possibility of having cerebral lupus.

The latest data of brain CT and hemostatic supported the evidents of cerebral thrombosis as the cause of this condition. Our treatment included supportive therapy, adequate antimicrobial drug to eliminate infection, neurotropic drugs and anticoagulant with heparinization. Decision to start heparinization was consulted and approved by Haematology and Oncology division with target of APTT 1.5 – 2.5x control. As we know, the management of SLE includes glucocorticoids, antimalarial agents and immunosuppressant drugs. SLE patients with APS should also receive antiplatelet and anticoagulant. After aggressive treatment and intensive monitoring, the condition was improved.

Antiphospholipid antibody syndrome was secondary in systemic lupus erythematosus condition. From the laboratory results we found positive lupus anticoagulant antibodies and anticardiolipin antibodies of both IgG
and IgM. Those positive results had correlation with increasing risk and incidence of thrombo-embolic events. Criteria for antiphospholipid antibody syndrome in this patient were supported by the incidence of thromboembolic event (cerebral thrombosis) with positive results of both antiphospholipid antibodies. Persistence of positive ACA (IgG) after 2 months has fulfilled the criteria of APS.

As there was evidence of thrombosis, the patient required an oral anticoagulant (Warfarin) as maintenance treatment. The target of INR for arterial thrombosis should be at least 2.5, but it varies in the literature. The Haematology and Oncology division recommended to maintain INR level between 1.5 – 2.5, and continued the evaluation in the next few days in polyclinic.

**CONCLUSION**

Eventhough infection is the most dangerous complication related to death in SLE, multi organ involvement has made consideration of any other possibility of complication and manifestation. Similar to APS, the complication associated with SLE, which found in many organs or systems such as venous thrombosis, cardiac event and central nervous system. Venous thrombosis is the most common clinical manifestation of antiphospholipid antibody syndrome. This complication could also have serious consequences, if not managed seriously.1, 3, 12-15

**REFERENCES**