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CASE REPORT

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Recurrent thrombotic thrombocytopenic purpura in a patient with systemic lupus erythematosus

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Abstract We encountered a 39-year-old female patient with systemic lupus erythematosus (SLE) in whom thrombotic thrombocytopenic purpura (TTP) recurred. The patient was successfully treated with corticosteroid in combination with immunosuppressive agents. Because TTP complicating SLE is more resistant to treatment than idiopathic TTP, prompt diagnosis and efficacious initial treatment are critical.

Key words ADAMTS13 · SLE · TTP

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disorder characterized by thrombocytopenia, microangiopathic hemolytic anemia, fever, and neurological or renal manifestations. TTP is known to occur in association with malignancies, infections, pregnancy, various connective tissue diseases such as systemic lupus erythematosus (SLE), and pharmacological agents.[1]

The pathogenesis of the condition is unclear; however, autoimmunity or vasculopathy with endothelial damage and resultant platelet aggregation are considered to play important roles in the condition.[1] Here, we describe a female patient with SLE in whom TTP recurred. The patient was successfully treated with corticosteroid in combination with immunosuppressive agents. Notably, serum level of a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13 (ADAMTS13) fluctuated in accordance with the activity of TTP.

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Case

A 39-year-old female patient with SLE was admitted to the hospital because of general fatigue, anemia, and rapidly progressive thrombocytopenia. The patient was diagnosed as having SLE for the past 8 years, and was treated with immunosuppressants and plasma pheresis, rendering the disease in remission. Although *Pneumocystis* pneumonia had developed 4 years earlier, it was cured by administration of sulfamethoxazole and trimethoprim. She was in stable condition thereafter.

Laboratory values on admission included white blood cell (WBC) 6400 μl^{-1} with normal differentiation; platelet, 5000 μl^{-1}; hemoglobin 10.3 g/dl; serum lactic dehydrogenase, 957 U/l; total bilirubin 2.1 mg/dl; direct bilirubin 0.3 mg/dl. Haptoglobin was not detected. Prothrombin time, activated partial prothrombin time, and fibrinogen levels were within the normal limits. Urinary test and renal function revealed normal. Direct Coombs' test was positive. Although antinuclear antibody and was positive, anti-DNA antibody, anticardiolipin antibody, and lupus anti-coagulant were negative. Serum complement level (C3 and C4) was normal. Preceding viral infections such as cytomegalovirus and human immunodeficiency virus were excluded. Drugs which can induce TTP, such as antineoplastic, cyclosporin, tacrolimus, interferon, and anti-aggregating drugs were not used in advance.

The patient suddenly lost consciousness, and hemoglobin plummeted to 5.4 mg/dl on the fifth day. A smear of peripheral blood revealed schistocytes and helmet cells among erythrocytes. A result of brain computed tomography and magnetic resonance image was not particular. On the basis of these findings the patient was diagnosed as having TTP. She was treated with plasma exchange and intravenous administration of corticosteroid and gamma globulin. After these treatments the patient recovered consciousness and the laboratory values were normalized (platelet 180 000 μl^{-1}; hemoglobin 14.3 g/dl on the 14th day from admission).

The patient was discharged from the hospital with oral corticosteroid, which was gradually tapered, cyclosporin A and prostacyclin.

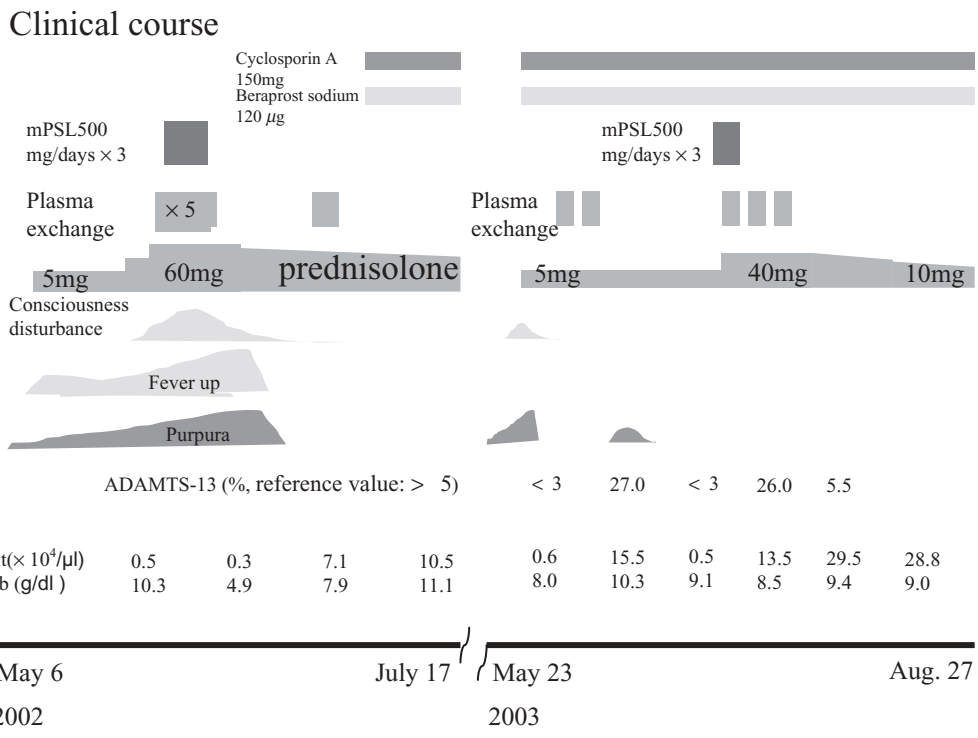

Fig. 1. Clinical course of the patient. Symptoms, therapies, and laboratory indices are indicated

One year after discharge the patient was readmitted to the hospital with similar symptoms and laboratory values. Her condition improved temporarily with the treatment of plasma exchange twice without increasing steroid, and that required adding a high dosage of corticosteroid for recurrence. ADAMTS-13 activity, as monitored in the latter part of the clinical course, tended to fluctuate with the activity of TTP (the course is indicated in Fig. 1).

Discussion

Thrombotic thrombocytopenic purpura affects small vessels and causes platelet aggregates formation in arterioles and capillaries, leading to functional failures in multiple organs.[1] The pathogenesis of the condition is unclear; however, recent studies suggest that a deficiency of ADAMTS13, which cleaves von Willebrand factor, is a possible cause of TTP.[2,3] At the time of the relapse of TTP, our patient was initially treated solely with plasma exchange twice, although TTP recurred and the ADAMTS13 level declined. Induction of steroid pulse therapy and adding a dosage of oral corticosteroid brought beneficial effects in the course of TTP and the value of ADAMTS13. Because the ADAMTS13 level correlated with the activity of TTP in this patient, currently ADAMTS13 is suggested as one of the plausible pathogeneses of TTP in the present case.

On the other hand, ADAMTS13 is not implicated in a part of TTP, such as the ones accompanying lymphoma or exposure to toxins.[1,2] In general, the prognosis of TTP associated with ADAMTS13 seems to be better in comparison with TTP which is not associated with ADAMTS13.[4]

Among the autoimmune diseases, SLE is known to complicate TTP. Reportedly, in 0.5%–4% of patients, SLE complicates TTP.[5,6] Furthermore, pathological findings suggestive of TTP were noted in 28% of a series of autopsied cases of SLE.[7]

Systemic lupus erythematosus may cause endothelial damage and platelet aggregation by itself. In this context, SLE and TTP share clinical manifestations, such as renal dysfunction, thrombocytopenia, and anemia, and even underlying pathophysiology. TTP accompanying SLE tends to present more diverse clinical pictures and to be more resistant to treatment in comparison with idiopathic TTP.[4,8] In patients with SLE complicating TTP, the onset of TTP precedes, concurs, or follows the onset of SLE in 12%, 21%, and 67% of cases, respectively. Importantly, a fatal outcome occurs in 30% of those patients even while SLE is in a stable condition.[8]

There are few reports of cases of SLE with TTP referring to the value of ADAMTS13.

Starck et al. reported two patients with SLE complicated by TTP concurrently measured ADAMTS13 activity.[9] ADAMTS13 value fluctuated according to the activity of TTP. They insisted that applying additional immunosuppressive treatment would be preferable for controlling the inhibitor effect of ADAMTS13 that was thought to be implicated as an autoimmune mechanism. Also Rick et al.[10] reported an SLE patient with TTP who underwent plasma exchanges with steroid several times . The patient improved with those treatments and ADAMTS13 values were improved according to clinical response although no

additional immunosuppressive agent was needed afterward. Both reports showed a favorable outcome although one Japanese case had a fatal outcome with declining ADAMTS13.[11]

Owing to a shortage of reports and because conditions vary, how the existence of ADAMTS13 affects the prognosis of SLE complicating TTP is undetermined. Factors other than ADAMTS13 might be implicated. Accumulating more cases of SLE-complicated TTP is mandatory in order to characterize the pathophysiology of such cases and the relationship with ADAMTS13, so that effective diagnostic and therapeutic strategies can be devised.

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