Original Article

Clinical Characteristics and Outcomes of Thrombotic Thrombocytopenic Purpura with Severe ADAMTS13 Deficiency at the King Chulalongkorn Memorial Hospital

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Abstract

Introduction: *Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal hematologic disorder. Published studies and clinical data of TTP patients in Thailand are still lacking.* ***Objective:*** *The purpose of this study is to review the clinical characteristics, laboratory data, therapeutic interventions and treatment outcomes of patients diagnosed TTP at the King Chulalongkorn Memorial Hospital (KCMH).* ***Patients and Methods:*** *Patients who were diagnosed with TTP and had severe (< 10%) deficiency of ADAMTS13 levels at the KCMH between July 2004 and November 2013 were retrospectively reviewed.* ***Results:*** *Of 16 documented TTP (14 adults and 2 children) with severe ADAMTS13 deficiency, the mean age of patients was 46.1 years. Fourteen were classified as idiopathic (87.5%), while two were HIV-associated TTP (12.5%). Neurologic abnormalities were the most common clinical symptoms, presented in 14 patients (87.5%). Their laboratory results such as hemoglobin levels and platelet counts were comparable with those of patients with severe ADAMTS13 deficiency from other studies. At the time of first diagnosis, all 14 adult patients received plasma exchange therapy but varied in the doses and types of immunosuppressive drugs. The median interval of symptom-to-plasma exchange was 9.5 days. The complete remission (CR) rate and the overall survival of TTP patients were similar at 68.8%, whereas the survival rate in the idiopathic subgroup was 78.6%. The recurrence rate was 45.5% in the first year. Of 5 first relapsed patients, 4 achieved CR with immunosuppressive therapy without plasma exchange.* ***Conclusion:*** *Our study demonstrated comparable clinical and laboratory characteristics of TTP patients to other studies. However, the CR rate and the survival rate were lower. Immunosuppressive drugs play an important role in treating idiopathic TTP in our cohort.*

Keywords : ● *Thrombotic thrombocytopenic purpura* ● *Severe ADAMTS 13 deficiency* ● *Treatment outcomes*

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal hematologic disorder characterized by a pentad of microangiopathic hemolytic anemia, thrombocytopenia, fever, neurologic and renal involvements. TTP results from the deficiency of a disintegrin-like and metalloproteinase with thrombospondin type 1 motif, member 13 (ADAMTS13) enzyme, which normally cleaves large von Willebrand's factor (vWF) multimers into smaller appropriate sizes with reduced vWF activity. Therefore, uncleaved large vWF multimers lead to platelet microthrombi formation and mechanical injury of red cells causing microvascular thrombosis and subsequent organ ischemia, especially in the central nervous system and kidneys.

The diagnosis of TTP is based on clinical features and basic laboratory investigations such as complete blood count and peripheral blood smear. However, the diagnosis of TTP remains challenging as it usually presents without the full classic pentad.[1] Neurologic involvement, renal abnormalities and fever are unremarkable in some cases. As a result, it is recommended that the presence of unexplained microangiopathic hemolytic anemia and thrombocytopenia is sufficient to consider the diagnosis of TTP.[2]

ADAMTS13 activity is the most helpful laboratory test for the diagnosis of TTP. A previous study demonstrated the promising specificity of severe deficiency of ADAMTS13 (< 5-10%) in the diagnosis of TTP as other thrombocytopenic conditions such as disseminated intravascular coagulation (DIC) and heparin-induced thrombocytopenia (HIT) generally have a mild to moderate decrease in ADAMTS13 activity.[3] In addition, severely deficient ADAMTS13 levels were associated with increased relapse in TTP survivors.[4] Nevertheless, the data from many other studies suggested the variability between the clinical outcomes and the severity of ADAMTS13 deficiency. Clinical presentations of patients with severe ADAMTS13 deficiency were not different from those who were less severe.[5,6] Consequently, ADAMTS13 level should not affect a decision to initiate plasma exchange, which was proven to improve survival and had become the standard treatment of TTP for several decades.[7,8]

Until now, there are few studies of this potentially fatal disorder published in Thailand. The purpose of this retrospective study is to review the clinical characteristics, laboratory data, therapeutic intervention and treatment outcomes of patients diagnosed TTP in our institute.

Patients and Methods

Clinical and laboratory data of patients diagnosed with TTP at the King Chulalongkorn Memorial Hospital (KCMH) between July 2004 and November 2013 were retrospectively reviewed. The study was approved by the Ethics Committee of Faculty of Medicine, Chulalongkorn University. The inclusion criteria were patients with TTP who had severe deficiency of ADAMTS13 levels (< 10%). All patients' data including demographic data, underlying diseases, clinical presentations, relevant laboratory profiles, such as complete blood count, peripheral blood smear, ADAMTS13 levels, serum creatinine, serum lactate dehydrogenase (LDH), antinuclear antibodies (ANA), HIV serology, and coagulation studies were extracted from medical records. Treatment details, including the interval between the beginning of symptoms and initiating plasma exchange, immunosuppressive drugs and treatment response were also retrieved from the medical records. All data were analyzed and presented using descriptive statistics.

ADAMTS13 assay

The ADAMTS13 assay was performed using an enzyme immunoassay technique to detect residual vWF collagen binding activity as previously described.[9] Briefly, plasma samples from patients suspected TTP were collected into a sodium citrate tube and was prepared for platelet-poor plasma by double centrifugation. The test plasma was then added into pooled normal human plasma, in which protease activity had been neutralized. vWF were digested by vWF-cleaving protease in the test plasma. The residual vWF was quantified using vWF collagen binding activity. The ADAMTS13 activity of

the test sample was then read from a dose-response curve obtained from the serial dilutions of the reference plasma.[9]

Definitions

Treatment response was defined as an increase in platelet count to the level of ≥ 150 x 10^9/L and a decrease in LDH to a normal level.

Complete remission (CR) was defined as an achievement of treatment response for 30 days or more without plasma exchange.

Relapse was defined as a recurrence of TTP after a patient previously achieved a CR.

Symptom-to-plasma exchange interval was the interval time between the beginning of TTP-related symptoms and the initiation of the plasma exchange.

Relapse-free interval was the time between achieving CR and experiencing relapse.

Event-free interval was the time between achieving CR and death or relapse.

Plasma exchange

Plasma exchange was an exchange of 1-1.5 plasma volumes with fresh frozen plasma or cryo-removed plasma using the automatic apheresis machine (Spectra Optia, Terumo BCT, Japan). The procedure was performed daily until the platelet count increased to the level ≥ 150 x 10^9/L and LDH decreased to a normal level. Plasma exchange was gradually reduced in frequency and discontinued later on.

Steroid administration

High dose steroid was given at the time of diagnosis and subsequently tapered when a patient showed a response.

Statistical analysis

All data were analyzed by SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL, USA) and presented as frequency, mean, median, standard deviation (SD), percentage, maximal and minimal values as appropriate.

Results

Demographic data

Between 2004 and 2013, there were 16 cases diagnosed TTP with severe deficiency of ADAMTS13 levels (< 10%). Ten were females (62.5%), and six were males (37.5%). The mean age and SD of patients was 46.1 ± 24.4 (range 14-93) years.

Clinical characteristics

Of 16 documented TTP, 14 were idiopathic (87.5%), whereas two were HIV-associated TTP (12.5%). One (patient number 7) was found to be HIV positive at the time of admission, and he had never received antiretroviral therapy. The other (patient number 8) had HIV infection one year prior to the diagnosis of TTP, and he was noncompliant with antiretroviral medications. Of the two cases with HIV-associated TTP, three months before admission, CD4 count of patient number 8 was 136 cells/μL.

Neurologic abnormalities were the most common clinical symptoms presented in 14 patients (87.5%). Alteration of consciousness was the most frequent neurological manifestation (8 patients) followed by seizures (4 patients), hemiplegia (1 patient) and paresthesia (1 patient). Bleeding was the second most common presentation accounting for 81.3% of patients. Petechiae and/or ecchymoses were noted in ten patients (62.5%), while hematuria were documented in two and subarachnoid hemorrhage in one patient, respectively. Fever was observed in seven patients (43.75%), whereas renal abnormalities were documented in four patients (25%). There was only one patient with the complete pentad.

Laboratory investigation and imaging

The laboratory data were presented as mean ± SD (range) as follows: hemoglobin 8.5 ± 1.5 (5.9-11.1) g/dL; white blood cell count 7.3 ± 2.2 x 10^9 (3.1-12.6 x 10^9)/L; platelet count 20.8 ± 23.8 x 10^9 (6-81 x 10^9)/L; ADAMTS13 level 4.3 ± 2 (2.4-9.0)%; serum creatinine 1.27 ± 0.94 (0.5-3.6) mg/dL; LDH 2,071 ± 1,340 (503-4,716) U/L; prothrombin time (PT) 11.8 ± 0.9 (10.8-13.7) second; activated partial thromboplastin time (APTT) 25.8 ± 3.0 (21.4-32.0) second. Peripheral blood examination revealed microangiopathic hemolytic anemia with numerous schistocytes and low number of platelets in all cases. To investigate secondary causes of TTP, two patients

were diagnosed with HIV infection, while five females had positive ANA without any autoimmune-related symptoms such as rashes and arthritis. Their clinical characteristics and laboratory parameters did not fit into any specific autoimmune or connective tissue diseases. Therefore, idiopathic TTP was diagnosed in 14 (87.5%) patients, while two (12.5%) were HIV-associated TTP.

Computed tomography of brain was performed in 12 patients with neurologic abnormalities. Eight patients had negative results, while four patients had abnormal findings: one with subarachnoid hemorrhage at the left high parietal cortex and left side of suprasellar cistern; one with left frontal and insular lobe hypodensity; one with generalized brain edema and one with brain atrophy.

The clinical characteristics and laboratory profile of each individual were summarized in Table 1.

Treatment

TTP patients at the KCMH were classified by age into two groups. Patients under the age of 15 years were admitted to the Department of Pediatrics, while those with the age over 15 years were admitted to the Department of Medicine. The two pediatric cases (number 15 and 16) did not undergo plasma exchange but received prednisolone of 1 mg/kg/day. Patient number 15 also received plasma infusion. All adult cases received plasma exchange but varied in doses and types of immunosuppressive drugs (Table 2).

The median of symptom-to-plasma exchange interval was 9.5 (1-33) days. Patient number 7 and 13 were rapidly diagnosed with TTP and received plasma exchange within 2 days after the presentation of their symptoms. However, patient number 7 received only one cycle of plasma exchange and expired shortly due to very aggressive course of the disease. The most common cause of delay was attributed to the delay in seeking medical attention and referral process to the KCMH (8 patients, 57.1%, patients number 2, 3, 5, 6, 9, 10, 12 and 14) followed by misdiagnoses (3 patients, 21.4%, number 4, 8 and 11). Patient number 4 was misdiagnosed as dengue hemorrhagic fever and later as immune thrombocytopenia purpura (ITP), then referred to the KCMH on day 21 after ITP treatment had failed. Patients number 8 and 11 were also initially misdiagnosed as ITP. Patient number 1 was diagnosed with TTP with mild clinical bleeding symptoms without fever, neurologic and renal involvements. She received cryo-removed and fresh frozen plasma transfusion with a transient response. When her platelet count declined to 20 x 10^9/L at the third week of the treatment, plasma exchange was performed. All but one patient (number 3) received immunosuppressive drugs.

Clinical outcomes

A complete remission (CR) was achieved in 11 patients (68.8%) while five patients died. Five of 11 (45.5%) patients experienced their first relapse within the first year. Four relapsed cases (patients number 1, 2, 12 and 15) achieved a second CR by plasma infusion and an immunosuppressive drug. The outcome of one remaining patient is not known as she was treated at another hospital. Three patients had a second relapse, and all later achieved CR. Patient number 12 was the only one that achieved third CR by plasma exchange and an immunosuppressive drug while the other two were treated by only an immunosuppressive drug. Only one young female patient had a third relapse but achieved CR. The overall survival of TTP patients at the KCMH was 68.8%. Both patients with HIV-associated TTP died before CR. The overall survival of idiopathic TTP was 78.6%.

Of five deaths, two (patients number 8 and 9) were unresponsive to treatment, two (patients number 7 and 10) had a delay in initiating plasma exchange and one from invasive aspergillosis due to prolonged corticosteroid use (patients number 5). In this patient, the platelet count decreased from 12 x 10^9/L to 6 x 10^9/L despite plasma exchange after discontinuation of pulse dexamethasone. Therefore, pulse dexamethasone was resumed for 10 days, then reduced to 30 mg/day for 15 days then changed to prednisolone 60 mg/day and tapered. Plasma exchange was continued daily for

Table 1 Patient characteristics and clinical manifestations

No.	Date of DX (D/M/Y)	Sex	Age	Predisposing factor	Fever	Neurological	Bleeding	ADAMTS13 activity (%)	Hb (g/dL)	Plt ($x10^9$/L)	LDH (U/L)	Cr (mg/dL)
1	26/7/2004	F	72	Unknown	-	-	+	6	9.8	81	3,520	0.80
2	29/4/2005	M	45	Unknown	+	+	+	5	6.2	9	1,562	0.90
3	13/7/2005	M	37	Unknown	-	+	+	3	9.9	14	1,680	1.10
4	2/6/2006	F	19	Unknown	+	+	+	8	5.9	20	2,554	0.90
5	21/6/2007	F	58	Unknown	+	+	+	3	6.8	12	2,182	1.40
6	21/6/2010	F	61	Unknown	+	+	+	3	7.6	10	1,785	1.20
7	16/8/2010	M	43	HIV infection	-	+	-	3	9.0	14	4,633	3.49
8	16/5/2011	M	37	HIV infection	-	+	-	3	7.7	14	702	0.87
9	16/3/2011	F	85	Unknown	-	+	+	3	11.1	11	1,783	0.86
10	14/10/2013	M	93	Unknown	-	+	+	2	9.9	80	599	3.60
11	16/3/2013	M	66	Unknown	-	+	-	4	10.4	7	4,716	1.70
12	29/4/2006	F	24	Unknown*	+	+	+	6	9.1	12	961	0.50
13	14/9/2007	F	28	Unknown*	-	+	+	5	9.0	8	2,493	1.10
14	23/1/2012	F	42	Unknown*	-	+	+	3	8.6	24	503	0.60
15	2/8/2005	F	14	Unknown*	+	+	+	3	7.9	10	2,808	0.53
16	20/7/2011	F	14	Unknown*	+	-	+	9	7.2	6	657	0.70
Mean			46.1					4.3	8.5	20.8	2,071	1.27

*indicate patients who had positive ANA

Table 2 Treatment and outcome

No.	Symptom-to PEX interval (days)	Number of PEX	Immunosuppressive drugs	Relapse free interval(days)	Outcome	Follow-up time (years)
1	33	5	1st diagnosis: Prednisolone 40 mg/day 1st relapse: Pulse dexamethasone 40 mg/day for 7 days and cryo-removed plasma infusion 2nd relapse: Pulse dexamethasone 40 mg/day for 4 days	195	CR ⟶ 1st relapse ⟶ CR ⟶ 2nd relapse ⟶ CR	3
2	10	16	1st diagnosis: Pulse dexamethasone 40 mg/day for 4 days 1st relapse: Pulse dexamethasone 40 mg/day for 4 days and FFP infusion	365	CR ⟶ 1st relapse ⟶ CR	3
3	21	10	No immunosuppressive drugs used	No relapse	CR	4
4	21	17	Pulse dexamethasone 40 mg/day for 4 days	No relapse	CR	7
5	7	27	Pulse dexamethasone 40 mg/day for 4 days 5 days later start pulse dexamethasone 40 mg/day for 10 days then dexamethasone 30 mg/day for 15 days followed by high dose prednisolone of 60 mg/d then tapering	Death	Death (invasive aspergillosis)	Death
6	14	8	Dexamethasone 40 mg/day for 8 days	No relapse	CR	4
7	2	1	Dexamethasone 40 mg/day	Death	Death (TTP)	Death
8	8	7	Dexamethasone 20 mg/day for 4 days followed by vincristine 1 mg IV drip in 8 h	Death	Death (TTP)	Death
9	8	4	Dexamethasone 40 mg/day	Death	Death (TTP)	Death
10	27	1	Dexamethasone 40 mg/day for 4 days	Death	Death (TTP)	Death
11	6	27	1st line treatment: Dexamethasone 40 mg/day for 4 days 2nd line treatment: Dexamethasone 40 mg/day for 4 days combined with vincristine 1 mg IV 3rd line treatment: Dexamethasone 40 mg/day for 4 days and chlorambucil 16 mg/day for 5 days every 4 weeks	CR	CR (after chlorambucil)	1
12	9	1st diagnosis: 10 times 2nd relapse: 2 times	1st diagnosis: Pulse dexamethasone 40 mg/day for 4 days 1st relapse: Pulse dexamethasone 40 mg/day for 4 days and FFP infusion 2nd relapse: Pulse dexamethasone 40 mg/day for 4 days, FFP infusion and PEX	120	CR ⟶ 1st relapse ⟶ CR ⟶ 2nd relapse ⟶ CR	7

*PEX, plasma exchange; CR, complete remission; FFP, fresh frozen plasma

Table 2 Treatment and outcome

No.	Symptom-to PEX interval (days)	Number of PEX	Immunosuppressive drugs	Relapse free interval(days)	Outcome	Follow-up time (years)
13	1	14	Dexamethasone 20 mg/days for 2 days followed by dexamethasone 15 mg/day for 4 days	240	CR → pneumonia (4 months after Dx) → 1st relapse (treated at another hospital)	Did not come to KCMH since 1st relapse
14	14	27	Pulse dexamethasone 40 mg/day for 4 days	No relapse	CR	2
15	No PEX	No PEX	1st diagnosis: Prednisolone 1 mg/kg/d and FFP infusion for 26 days 1st relapse: Prednisolone 1.3 mg/kg/d and FFP infusion 2nd relapse: Prednisolone 1.4 mg/kg/d and FFP infusion 3rd relapse: Prednisolone 1 mg/kg/d (50 mg/day)	240	CR → 1st relapse → CR → 2nd relapse → CR → 3rd relapse → CR	5
16	No PEX	No PEX	Prednisolone 1 mg/kg/d	No relapse	CR	3

*PEX, plasma exchange; CR, complete remission; FFP, fresh frozen plasma

about one month without response. Unfortunately, the patient had invasive pulmonary aspergillosis and expired.

Patient number 11 was initially refractory to plasma exchange and pulse dexamethasone. Thrombocytopenia persisted after one month of plasma exchange. Pulse dexamethasone was repeated, and weekly intravenous vincristine was added for 3 weeks as the second line treatment but failed to improve platelet count. Chlorambucil and pulse dexamethasone were initiated as the third line immunosuppressive therapy. His platelet count and LDH returned to normal within a week. The 5-day course of chlorambucil combined with pulse dexamethasone were given every 4 weeks for 6 cycles and the patient remained in CR.

The event-free interval and relapse-free interval were 208 ± 102 (120-365) and 232 ± 89 (120-365) days, respectively. Patient number 1 had lacunar infarction 2 years before she was diagnosed with TTP. Approximately 6 months after CR, she had TTP-related symptoms and recurrent lacunar infarction with right hemiparesis. Pulse dexamethasone and cryo-removed FFP transfusion were given, and she finally achieved CR. Patient number 13 had a community-acquired pneumonia 4 months after attaining CR. Complications of plasma exchange were seen in three patients: one with catheter obstruction, one with hypotension and the other with catheter-related blood stream infection (CRBSI). Hemoculture of the patient with CRBSI grew Methicillin-resistant *Staphylococcus aureus* (MRSA), but the catheter tip culture yielded no growth.

Discussion

In our series, the preponderance of females and the median age were comparable to the other studies of TTP.[4,7,10] Most of the cases were idiopathic TTP. The HIV-associated TTP patients in our study had a much higher mortality rate (100%) than those in Hart et. al. study (4%), which accentuated the importance of initiation of HAART along with plasma exchange in treating HIV-associated TTP patients.[11] Therefore,

an effective antiretroviral therapy as well as plasma exchange should be initiated promptly in patients with HIV-associated TTP.

Neurologic symptoms were the most common manifestations followed by bleeding and fever, respectively. This finding was similar to the regional UK TTP study.[12] Apart from neurologic manifestations, most patients exhibited mild mucocutaneous bleeding, but a minority of patients had more severe bleeding events such as hematuria or subarachnoid hemorrhage. Only one case had a full pentad.

In our study, the mean hemoglobin level (8.5 g/dL) and platelet count (20.8 x 10^9/L) of the patients were comparable with those of patients with severe ADAMTS13 deficiency from other studies, which showed mean hemoglobin level of 7.68 g/dL[10], hematocrit of 21%[4] and 25%[7] and platelet count of 11-12 x10^9/L.[4,7,10] The mean serum creatinine in our study (1.27 mg/dL) was also comparable to those of other studies ranging from 1.1-1.6 mg/dL.[4,7,10]

TTP is an autoimmune disorder characterized by autoantibodies binding to ADAMTS13 resulting in substantially decreased ADAMTS13 activity. Several autoimmune diseases are associated with secondary TTP such as SLE, rheumatoid arthritis, Sjögren's syndrome and mixed connective tissue disease.[13,14] There were five female patients with positive ANA only without specific autoimmune diseases. Other cohort showed that idiopathic TTP patients with positive ANA never developed SLE during a mean follow-up period of 21.3 months.[15] Another study of TTP in association with autoimmune manifestations reported 22 cases with positive ANA among 31 cases with severe ADAMTS13 deficiency (< 5%), and one in ten of this cohort with positive ANA was later diagnosed with SLE.[16] In a review of TTP in association with SLE, there were 30 cases (73.2%) with TTP after SLE diagnosis, six (14.6%) with TTP before SLE diagnosis and five (12.2%) with TTP presented simultaneously with SLE. Of the six cases with TTP prior to SLE, the diagnosis of SLE was made at a median of 2 years (2 weeks to 9 years) following TTP.[17] As autoimmune diseases may develop after TTP, follow-up is essential.

Plasma exchange should be immediately performed when a patient is diagnosed with TTP. Most adult patients received plasma exchange therapy as well as immunosuppressive drugs, while only one adult patient was treated solely by plasma exchange. Interestingly, the two pediatric cases, who were treated with oral prednisolone with or without plasma infusion, can achieve CR without plasma exchange. Four adult patients with first relapse could also achieved CR by plasma infusion and immunosuppressive drug. Adjuvant corticosteroid treatment may benefit patients with severe ADAMTS13 deficiency by suppression of autoantibodies binding to ADAMTS13.[7] We previously demonstrated that two protracted TTP patients (case 1 and 2) with severe ADAMTS13 deficiency rapidly responded to the administration of pulse dexamethasone alone without plasma exchange.[18] We also observed that low dose steroid was not effective in normalizing the platelet count.[18] In this cohort, we found that one patient (case 11) was refractory to plasma exchange and pulse dexamethasone with or without vincristine achieving CR by a combination of pulse dexamethasone and chlorambucil. Therefore, immunosuppressive drugs can shorten the course of disease and reduce exposure to blood products in TTP with severe ADAMTS13 deficiency. However, prolonged administration of high-dose steroid increases the risk of fatal fungal infection. Therefore, shorter course immunosuppressive therapy is preferred.

Apart from guiding treatment, a severe deficiency of ADAMTS13 also gives us information about survival and an increased relapse rate.[19] Another TTP study in Thailand from Chiang Mai University (CMU)[20] was almost similar in baseline characteristics to our study, but ADAMTS13 levels were not determined and a higher mortality rate (60%) was reported. The inferior outcomes from the CMU series might be partly explained by different treatment protocols. Due to the unknown ADAMTS13

status, the CMU cohort might include patients with TTP-mimicking disorders, which do not respond to plasma exchange and/or immunosuppressive therapy.

Of all adult cases undergoing plasma exchange, the CR rate (64.3%) was lower than other studies (80-85%).[5,10] Furthermore, the overall survival rate of 68.8% was also lower than other studies (80-89%).[5,6,7,10] When HIV-associated TTP was excluded, the survival rate in the idiopathic subgroup was 78.6%. The relapse rate (45.5%) in our study was comparable to other studies. Besides rapid recognition and immediate initiation of plasma exchange, the plasma protocol itself should be re-evaluated. Additional immunosuppressive drugs such as vincristine and chlorambucil were used in two patients who showed no response to combination of plasma exchange and pulse dexamethasone. However, one patient had severe symptoms and expired one day after receiving vincristine, whereas the other achieved CR rapidly after the initiation of chlorambucil combined with dexamethasone.

Limitation of this study is that the study is a retrospective analysis of TTP patients, resulting in some missing data. Additionally, the sample size was small.

Conclusion

Our study demonstrated clinical and laboratory characteristics of TTP patients with low ADAMTS13 levels, which were comparable to other studies. However, several clinical outcomes, especially CR rate and survival rate, were lower. Immunosuppressive drugs played an important role in treating idiopathic TTP in our cohort.

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ลักษณะทางคลินิกและผลการรักษา Thrombotic Thrombocytopenic Purpura ที่มี ADAMTS13 ระดับต่ำมาก ในโรงพยาบาลจุฬาลงกรณ์

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บทคัดย่อ

บทนำ *Thrombotic thrombocytopenic purpura (TTP) เป็นภาวะทางโลหิตวิทยาที่พบน้อยแต่มีความรุนแรงทำให้เสียชีวิตได้ ปัจจุบันงานวิจัยและข้อมูลเกี่ยวกับภาวะนี้ในประเทศไทยยังมีจำกัด* ***วัตถุประสงค์*** *เพื่อศึกษาข้อมูลพื้นฐานอาการและอาการแสดง การวินิจฉัย ผลตรวจทางห้องปฏิบัติการ การรักษา และการตอบสนองต่อการรักษาของผู้ป่วย TTP ที่มี ADAMTS13 ระดับต่ำมาก (น้อยกว่าร้อยละ 10) ในโรงพยาบาลจุฬาลงกรณ์* ***ผู้ป่วยและวิธีการ*** *เป็นการศึกษาเชิงพรรณนาแบบย้อนหลังของผู้ป่วย TTP ที่มี ADAMTS13 ระดับต่ำมากในโรงพยาบาลจุฬาลงกรณ์ตั้งแต่เดือนกรกฎาคม พ.ศ. 2547 ถึงเดือนพฤศจิกายน พ.ศ. 2556* ***ผลการศึกษา*** *ผู้ป่วยได้รับการวินิจฉัยภาวะ TTP ที่มี ADAMTS13 ระดับต่ำมาก จำนวน 16 ราย เป็นผู้ป่วยผู้ใหญ่ 14 ราย และผู้ป่วยเด็ก 2 ราย มีอายุเฉลี่ย 46.1 ปี แบ่งเป็นชนิดไม่ทราบสาเหตุ 14 ราย (ร้อยละ 87.5) และชนิดมีสาเหตุเกี่ยวกับไวรัสเอชไอวี จำนวน 2 ราย (ร้อยละ 12.5) ความผิดปกติทางระบบประสาทเป็นอาการแสดงทางคลินิกที่พบบ่อยที่สุด โดยพบในผู้ป่วยจำนวน 14 ราย (ร้อยละ 87.5) ผลตรวจทางห้องปฏิบัติการของผู้ป่วย เช่น ระดับฮีโมโกลบินและจำนวนเกล็ดเลือด มีผลใกล้เคียงกับผลการตรวจของผู้ป่วยที่มี ADAMTS13 ระดับต่ำมากจากการศึกษาอื่น ผู้ป่วยผู้ใหญ่ (อายุมากกว่า 18 ปี) ทั้งหมด 14 รายได้รับการรักษาด้วย plasma exchange ในการวินิจฉัยครั้งแรก แต่ได้รับยากดภูมิคุ้มกันในชนิดและขนาดแตกต่างกัน ค่ามัธยฐานของช่วงเวลาตั้งแต่เริ่มมีอาการจนถึงเริ่มการรักษาด้วย plasma exchange 9.5 วัน อัตรา complete remission และอัตราการรอดชีวิตของผู้ป่วยมีค่าเท่ากันเท่ากับร้อยละ 68.8 ในขณะที่อัตราการรอดชีวิตของกลุ่มย่อยชนิดไม่ทราบสาเหตุคิดเป็นร้อยละ 78.6 อัตราการกลับเป็นซ้ำใน 1 ปีแรกคิดเป็นร้อยละ 45.5 ในผู้ป่วยจำนวน 5 รายที่มีอาการกลับเป็นซ้ำครั้งแรก มี 4 รายได้ complete remission ด้วยยากดภูมิคุ้มกัน โดยไม่ได้ทำ plasma exchange* ***สรุป*** *อาการ อาการแสดงและผลตรวจทางห้องปฏิบัติการของผู้ป่วย TTP ที่มี ADAMTS13 ระดับต่ำมากในโรงพยาบาลจุฬาลงกรณ์คล้ายคลึงกับการศึกษาอื่น อย่างไรก็ตามผลการรักษาและอัตราการรอดชีวิตอยู่ในระดับต่ำกว่าการศึกษาอื่น นอกจากนี้ยังพบว่าการให้ยากดภูมิคุ้มกันมีบทบาทสำคัญในการรักษา TTP ในการศึกษานี้*

Keywords : ● *Thrombotic thrombocytopenic purpura* ● *Severe ADAMTS 13 deficiency* ● *Treatment outcomes*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต 2558;25:43-53.