Scholars Journal of Medical Case Reports **ISSN 2347-6559 (Online)**
Sch J Med Case Rep 2016; 4(10):777-781 **ISSN 2347-9507 (Print)**

(An International Publisher for Academic and Scientific Resources) DOI: 10.36347/sjmcr.2016.v04i10.023

A case of thrombocytopenia mimicking thrombotic thrombocytopenic purpura

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Abstract: A 45-year-old female felt general fatigue over a 7-day period during the summer. For 5 days, she had skin lesions and a fever over 38 °C, so she visited a local clinic. She received a prescription of Loxoprofen and Teprenone due to suspicion of a viral infection. However, her symptoms did not improve, so she visited the same clinic again. Given that she had hypotension, and hypoxia, she was transported to our hospital. Upon arrival, she had swollen lymph nodes on her neck, and multiple scattered spotty erythema over her whole body. A peripheral blood smear showed microangiopathic hemolytic anemia with schistocytes and thrombocytopenia. She was treated with massive infusion of Ringer's lactate and noradrenaline for hypotension; however, her unstable circulation did not improve. In addition, her consciousness became restless, so she was intubated in the emergency room. After admission to the intensive-care unit, she underwent infusion of levofloxacin, minocycline, gamma globulin, glycyrrhizinate for sepsis, thrombomodulin for disseminated intravascular coagulopathy, steroids for septic shock, continuous hemodiafiltration for acute renal failure, and mechanical ventilation for acute respiratory distress syndrome. After these treatments, her unstable circulation and respiratory and renal dysfunction gradually improved. After medical treatment and rehabilitation, she was discharged on Day 20 of hospitalization. The present patient had the "classic pentad" of TTP clinically. Approximately 20% to 50% of patients with TTP experience a relapse. Accordingly, the patient is being followed as an outpatient under careful monitoring.
Keywords: thrombocytopenia; thrombotic thrombocytopenic purpura; intensive care.

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is primarily diagnosed clinically, but the diagnosis is often difficult because of its varied, nonspecific symptoms. Typical TTP presents with the "classic pentad": 1. Severe thrombocytopenia (70%–100% of patients), 2. Microangiopathic hemolytic anemia with multiple schistocytes (70%–100%), 3. Neurologic involvement (50%–90%), 4. Renal abnormalities (about 50%), and 5 [1]. Fever (25%). We herein report a case of thrombocytopenia of unknown origin mimicking thrombotic thrombocytopenic purpura.

CASE PRESENTATION

A 45-year-old female felt general fatigue over a 7-day period during the summer. For 5 days, she had skin lesions and a fever over 38 °C, so she visited a local clinic. She received a prescription of Loxoprofen and Teprenone due to suspicion of a viral infection. However, her symptoms did not improve, so she visited the same clinic again. Given that she had hypotension (blood pressure 70/40 mmHg), and hypoxia (SpO_2 91% under room air), she was transported to our hospital.

Her medical and family history were unremarkable. She had not traveled abroad for several years, and there was no influence of influenza at the time. Upon arrival, her Glasgow Coma Scale score was 15. She had a blood pressure of 78/48 mmHg, a heart rate of 86 beats per minute (BPM), a respiratory rate of 30 BPM, an SpO_2 of 92% in room air, and a body temperature of 36.6 °C. Regarding the physiological findings, she had swollen lymph nodes on her neck, and multiple scattered spotty erythema over her whole body (Figure 1). Her chest roentgen and electrocardiogram were negative. Computed tomography for detecting septic focus demonstrated swelling of the lymph nodes in the neck and splenomegaly (Figure 2) [2]. The main abnormal results of the biochemical analysis of the blood are shown in Table 1. A peripheral blood smear showed microangiopathic hemolytic anemia with schistocytes and thrombocytopenia (Figure 3).

She was treated with massive infusion of Ringer's lactate and noradrenaline for hypotension; however, her unstable circulation did not improve. In addition, her consciousness became restless, so she was intubated in the emergency room. After admission to the intensive-care unit, she underwent infusion of levofloxacin, minocycline, gamma globulin, glycyrrhizinate for sepsis, thrombomodulin for disseminated intravascular coagulopathy, steroids for septic shock, continuous hemodiafiltration for acute renal failure, and mechanical ventilation for acute

respiratory distress syndrome. As she had severe thrombocytopenia under 2.0 × 10^4/μl, she underwent infusion of platelet twice on the second and third hospital day but did not obtain a significant improvement. After these treatments, her unstable circulation and respiratory and renal dysfunction gradually improved. The renal replacement therapy was stopped on the fourth day, and mechanical ventilation and use of vasopressor were established on the eighth hospital day (Figure 4). The results of special laboratory tests were obtained later (Table 2), and a false positive for human immunodeficiency virus and high levels of rheumatoid arthritis and ferritin were recognized. All tests to detect the focus of the infection were negative. After medical treatment and rehabilitation, she was discharged on Day 20 of hospitalization.

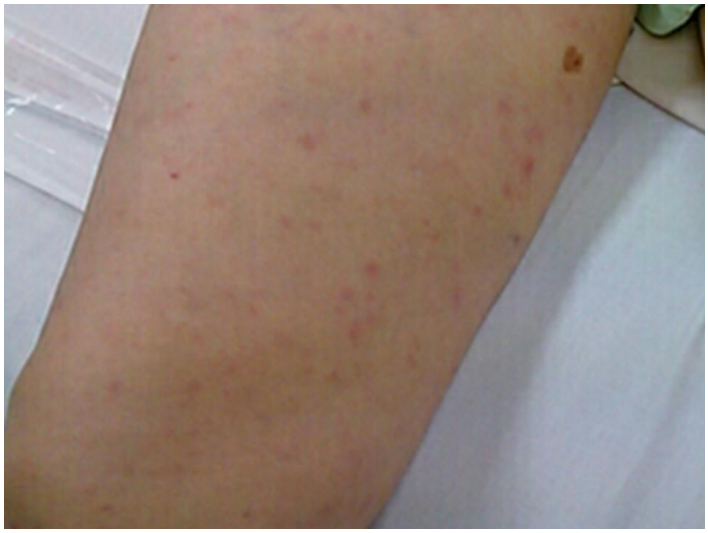

Fig-1: Physical findings. Multiple scattered spotty erythema over the whole body was observed.

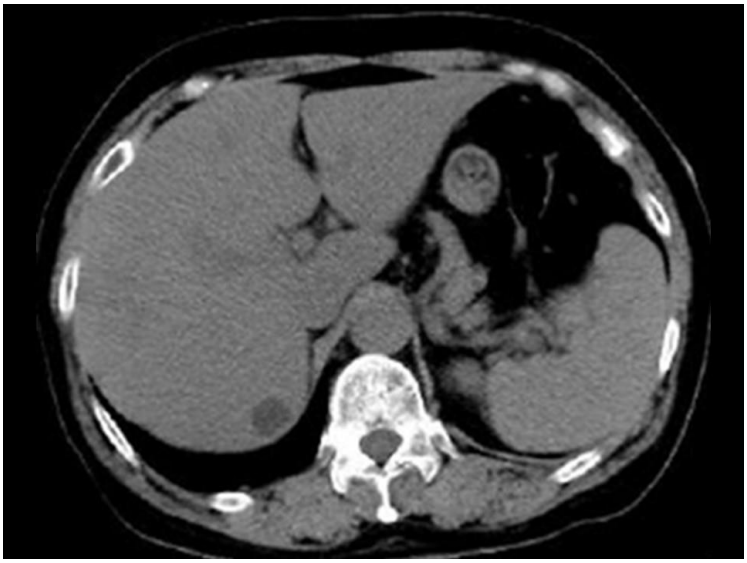

Fig-2: Trunk CT on arrival. CT to detect the septic focus revealed swelling of the lymph nodes in the neck and splenomegaly.

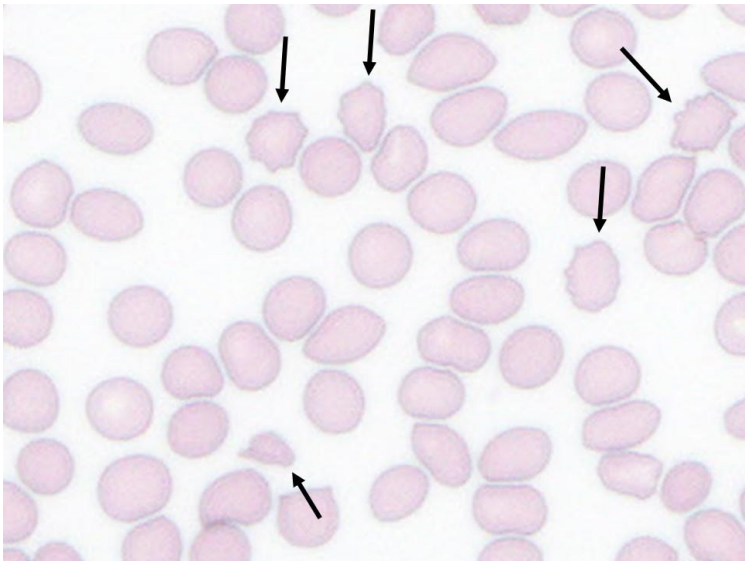

Fig-3: Peripheral blood smear. The blood smear showed microangiopathic hemolytic anemia with schistocytes and thrombocytopenia.

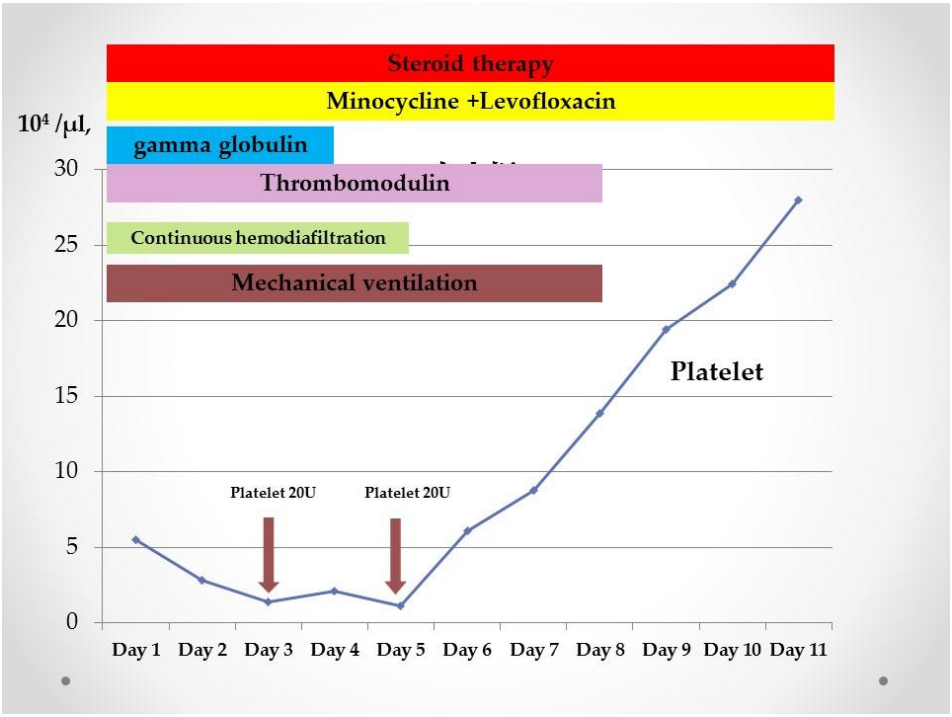

Fig- 4:Time course of intensive care and platelet count. The platelet count improved gradually with intensive care.

Table-1: The laboratory analysis results

Arterial blood gas (room air)			
pH	7.43	pCO_2	30 mmHg
pO_2	67 mmHg	Bicarbonate	19.7 mmol/l
Lactate	2.7 mmol/l		
Cell blood count			
White blood cell count	8200/μl (Seg 94%, Mono 3%, Lymph 3%)		
Hemoglobin	11.1 g/dl	Platelet count	5.5×10^4/μl
Serum biochemical data			
Total protein	7.2 g/dl	Albumin	2.7 g/dl
Lactate dehydrogenase	607 IU/l	Amylase	187 IU/l
Aspartate aminotransferase	155 IU/l	Alanine aminotransferase	102 U/l
Creatine phosphokinase	212 IU/l	Total bilirubin	2.8 mg/dl
Blood urea nitrogen	12.3 mg/dl	Glucose	104 mg/dl
Creatinine	2.20 mg/dl	Sodium	137mEq/l
Potassium	3.9 mEq/l	C reactive protein	22.3 mg/dl
Coagulation			
Activated partial thromboplastin time		51.5 (25.9) sec	
Prothrombin time		13.8 (12.1) sec	
Fibrinogen		382 mg/dl	
Fibrinogen degradation products		54.0 μg/mL	
Urine			
Protein 1+	Glucose 1+	White blood cells –	

Table-2: Results of laboratory findings

Blood culture	negative	Urine culture	negative
Herpes simplex IgM	0.37	Herpes simplex IgG	4.7
Ebstain Barr virus (EBV)			
EBV IgM	10>	EBV IgG	160
EBV EBNA	160		
Mycoplasma CF	4>	Anti-streptokinase	80
Anti-nucleotide antibody	40>		
Orientia tsutsugamushi antibody			
Gilliam IgM	10>	Gilliam IgG	10>
Kato IgM	10>	Kato IgG	10>
Kato IgM	10>	Kato IgG	10>
Scarlet fever (PCR)	negative	Zika virus (PCR)	negative
Dengue fever (PCR)	negative	Chikungunya fever (PCR)	negative
Severe fever with thrombocytopenia syndrome virus (PCR)			negative
Myeloperoxidase-anti-neutrophil cytoplasmic antibody			0.5>
Proteinase 3 - anti-neutrophil cytoplasmic antibody			0.5>
Human immunodeficiency virus			false positive
Rheumatoid arthritis particle-agglutination value			2560
Pathology of skin			
Mild inflammatory change			
PCR: polymerase chain reaction			
CF: complement fixation			

DISCUSSION

The present patient had the "classic pentad" of TTP clinically. ADAMTS13 (an abbreviation for "a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13") is a plasma protein that cleaves von Willebrand factor, which interacts with

platelets to promote blood clotting. If ADAMTS13 is lacking, unusually large multimers of von Willebrand factor can accumulate and trigger intravascular platelet aggregation and microthrombosis, causing the signs and symptoms of TTP.[1] Measuring the levels of ADAMTS13, ADAMTS13 inhibitor, and ADAMTS13 antibody is becoming standard when confirming a diagnosis of TTP[1]; however, we were unable to measure the levels of ADAMTS13 and ADAMTS13 inhibitor during thrombocytopenia because this examination was not covered by the health insurance system in Japan.

According to a French study, among 772 patients with adult-onset thrombotic thrombocytopenic purpura, 378 (49%) had idiopathic thrombotic thrombocytopenic purpura, whereas 394 (51%) had disease associated with miscellaneous clinical situations (infections, autoimmunity, pregnancy, cancer, organ transplantation, and drugs) [3]. Pathophysiologically, 3 distinct forms of thrombotic thrombocytopenic purpura were observed: 585 (75%) patients had autoimmune disease with anti-ADAMTS13 IgG, 166 (22%) had acquired disease of unknown cause, and 21 (3%) had inherited disease (Upshaw-Schulman syndrome) with mutations in the ADAMTS13 gene [3]. In addition, idiopathic thrombotic thrombocytopenic purpura were mainly autoimmune (345 [91%] cases) [3]. As the present patient had a high level of antibodies for autoimmune disease and negative findings for bacterial and rickettsia infection, TTP was thought to have been induced by a viral infection and asymptomatic autoimmune disease.

The British Society for Haematology published revised guidelines for managing TTP.[4] Acquired idiopathic TTP with reduced ADAMTS13 activity requires immediate therapeutic plasma exchange. Daily plasma exchange combines plasmapheresis to remove circulating ultralarge von Willebrand factor-platelet strings and autoantibodies against ADAMTS13, and the infusion of fresh-frozen plasma to replace ADAMTS13. This procedure is the mainstay of therapy and brings 70% to 90% of patients with idiopathic TTP to remission. Patients who are tefractory to therapeutic plasma exchange (10%–20% of cases) have been treated with corticosteroids, splenectomy, or immunosuppressive agents (cyclosporine, azathioprine, or cyclophosphamide) and/or Rituximab (monoclonal anti-CD20) [1]. However, patients with severely decreased ADAMTS13 activity or low titers of ADAMTS13 autoantibodies tend to respond to steroid therapy [1]. Zhang et al. reported that some patients with TTP obtained a favorable outcome using a combination of continuous hemodiafiltration and steroid therapy [5]. We performed multidisciplinary therapies for multiple organ failures induced by an infection of unknown origin and abnormal autoimmune response. Fortunately, these multidisciplinary therapies, which resembled treatment strategies for TTP, were effective in the present case. Approximately 20% to 50% of patients with TTP experience a relapse [6]. Accordingly, the patient is being followed as an outpatient under careful monitoring.

Conflict of interest: The authors declare no conflicts of interest in association with this study.

Acknowledgements
This manuscript received financial support from the Ministry of Education, Culture, Sports, Science and Technology (MEXT)-Supported Program for the Strategic Research Foundation at Private Universities, 2015-2019, concerning [The constitution of a total research system for comprehensive disaster and medical management, corresponding to a wide-scale disaster].

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