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A Case of Thrombotic Microangiopathy Induced By Suspected Bacterial Infection

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Abstract: A 43-year-old female had experienced general fatigue for 1 month. For two weeks, she was admitted for dehydration to a local medical facility and she developed a fever, oligouria, and abdominal pain treated by antibiotics without a culture examination. However, her circulation became unstable, so she was transferred to another hospital. There, she was diagnosed with septic shock and renal failure, liver dysfunction, anemia, and thrombocytopenia and was immediately transported again to our hospital the same day. Upon arrival, after tracheal intubation, computed tomography for detecting septic focus failed to reveal the origin. A peripheral blood smear showed microangiopathic hemolytic anemia with schistocytes and thrombocytopenia. She received a diagnosis of thrombotic microangiopathy (TMA)—specifically, thrombotic thrombocytopenic purpura. After admission to the intensive-care unit, she underwent infusion of vasopressors, antibiotics, gamma globulin and steroid for sepsis, continuous hemodiafiltration for acute renal failure, plasma exchange, and mechanical ventilation. After these treatments, her unstable circulation and respiratory and renal dysfunction gradually improved. Thrombocytopenia worsened to 7,000 μl on the fifth hospital day but increased gradually. Mechanical ventilation and the use of vasopressors were diminished following renal replacement therapy. All tests to detect the focus of the infection were negative except for positive findings of procalcitonin and beta-D glucan. ADAMTS13 and ADAMTS13 inhibitor were negative. She additionally received anti-fungal drug and platelet transfusion. After medical treatment and rehabilitation, she was discharged on Day 36 of hospitalization. We herein report a rare case of TMA suspected of being induced by bacterial infection. Physicians should perform a culture study before the administration of antibiotics.
Keywords: thrombotic microangiopathy; sepsis; culture

INTRODUCTION

Thrombotic microangiopathy (TMA) is a rare, lethal disease and is primarily diagnosed clinically, but the diagnosis is often difficult because of its varied, nonspecific symptoms [1-3]. TMA can be classified as 1) thrombotic thrombocytopenic purpura (TTP), which is diagnosed under the classic pentad (severe thrombocytopenia, microangiopathic hemolytic anemia with multiple schistocytes, neurologic involvement, renal abnormalities, and a fever with decreased activity of a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13 [ADAMTS13]); 2) bacteria (*Escherichia coli* or *Streptococcus pneumoniae*)-induced hemolytic uremic syndrome; 3) complimentary abnormality-induced; and 4) unknown etiology, including autoimmune, malignancy, pregnancy, organ transplantation, drug-induced, or essential [4]. ADAMTS13 is a plasma protein that cleaves von Willebrand factor, which interacts with platelets to promote blood clotting [5]. 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. Measuring the levels of ADAMTS13, ADAMTS13 inhibitor, and ADAMTS13 antibody is becoming standard when confirming a diagnosis of TTP [6-8]. We herein report a case of TMA suspected of being induced by a bacterial infection.

CASE PRESENTATION

A 43-year-old female had experienced general fatigue for 1 month. For two weeks, she was admitted for dehydration to a local medical facility. After this admission, she developed a fever, oligouria, and abdominal pain treated by antibiotics without a culture examination. However, her circulation became unstable, so she was transferred to another hospital. There, she

was diagnosed with septic shock and renal failure, liver dysfunction, anemia, and thrombocytopenia and was immediately transported again to our hospital the same day. She had a medical history of hypokalemia of unknown origin and depression. Her family history was unremarkable. She had not traveled abroad for several years, and there was no indication of influenza at the time.

Upon arrival, her Glasgow Coma Scale score was 13. Her blood pressure was unmeasurable due to vasopressor use, and she had a heart rate of 72 beats per minute, a respiratory rate of 25 breaths per minute, an SpO_2 of 87% in 10 L per minute of oxygen, and a body temperature of 36.2 °C. Regarding the physiological findings, her conjunctiva was anemic, and she had multiple spotty purpura scattered over her whole body. Her chest roentgen and electrocardiogram findings were negative. After tracheal intubation using a sedative, computed tomography for detecting septic focus failed to reveal the origin, but atelectasis, pleural effusion, and consolidation at her breast were noted [9]. 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.

She was treated with massive infusion of Ringer's lactate and noradrenaline for hypotension; however, her unstable circulation did not improve. She received a diagnosis of TMA—specifically, TTP. After admission to the intensive-care unit, she underwent infusion of antibiotics, gamma globulin and steroid for sepsis, continuous hemodiafiltration for acute renal failure, plasma exchange, and mechanical ventilation for acute respiratory distress syndrome. She did not undergo infusion of platelets. After these treatments, her unstable circulation and respiratory and renal dysfunction gradually improved. Thrombocytopenia worsened to 7,000 μl on the fifth hospital day but increased gradually. Mechanical ventilation and the use of vasopressors were diminished following renal replacement therapy. The results of special laboratory tests were obtained later (Table 2). All tests to detect the focus of the infection were negative except for positive findings of procalcitonin and beta-D glucan. She additionally received anti-fungal drug and platelet transfusion. After medical treatment and rehabilitation, she was discharged on Day 36 of hospitalization.

Table-1: **The laboratory analysis results**

Arterial blood gas (room air)			
pH	7.49	pCO_2	32 mmHg
pO_2	71 mmHg	Bicarbonate	24.9 mmol/l
Lactate	7.7 mmol/l		
Cell blood count			
White blood cell count	19,300/μl (Stab 13%, Seg 82%, Lymph 4%)		
Hemoglobin	6.3 g/dl	Platelet count	2.3×10^4/μl
Serum biochemical data			
Total protein	4.2 g/dl	Albumin	2.0 g/dl
Lactate dehydrogenase	489 IU/l	Amylase	90 IU/l
Aspartate aminotransferase	55 IU/l	Alanine aminotransferase	58 U/l
Creatine phosphokinase	3248 IU/l	Total bilirubin	4.2 mg/dl
Blood urea nitrogen	124.2 mg/dl	Glucose	169 mg/dl
Creatinine	3.54 mg/dl	Sodium	108 mEq/l
Potassium	3.9 mEq/l	C reactive protein	19.8 mg/dl
Coagulation			
Activated partial thromboplastin time	30.9 (27.a) sec		
Prothrombin time (international normalized ratio)	1.12		
Fibrinogen	516 mg/dl		
Fibrinogen degradation products	14.4 μg/mL		

Table-2: Results of special laboratory findings

Blood culture	negative
Urine culture	negative
Procalcitonin	positive
Beta-D glucan	positive
Anti-nucleotide antibody	<40
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	negative
Rheumatoid arthritis particle-agglutination value	negative
Pathology of mass at breast	mammopathy
Esophago-gastro-duodenoscopy	negative
Colonoscopy	negative
Analysis of thoracic fluid	transudate

DISCUSSION

The present patient had the "classic pentad" of TTP clinically. However, ADAMTS13 and ADAMTS13 inhibitor in our case were negative. Our case was also negative for autoimmune disease, malignancy, pregnancy, and organ transplantation. The drugs she had received at the previous medical facilities had not been reported to induce thrombocytopenia. While all culture were negative, the high levels of C-reactive protein, left deviation of leukocytosis, and positive findings of procalcitonin strongly suggested bacterial infection. The negative cultures were induced by prior use of antibiotics at other hospitals. Accordingly, our case was therefore diagnosed to have hemolytic uremic syndrome according to the classification of TMA.

Two clinical problems occurred in the present case. One was an undetermined bacterial infection that antibiotics did not deescalate. This was because the physician administered the antibiotics without performing a culture examination. Antibiotics should be given after a culture examination [10]. The other problem was a delay in obtaining the results of ADAMTS13. Because this examination was not covered by the health insurance system in Japan, we had to ask another medical facility to evaluate the level of ADAMTS13. As a result, the patient underwent plasma exchange until obtaining the results for ADAMTS13 could be obtained. A system for promptly obtaining data on the ADAMTS13 level covered by the Japanese health insurance system is needed.

CONCLUSION

We herein report a rare case of thrombotic microangiopathy suspected of being induced by bacterial infection. Physicians should perform a culture study before the administration of antibiotics.

Conflict of interest

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

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