Ischemic Cardiomyopathy with a Rapid Progression from Thrombotic Thrombocytopenic Purpura

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Abstract

An 83-year-old woman who complained of dizziness and nausea visited our hospital. An electrocardiogram showed ST-segment elevation in multiple leads and an echocardiogram showed severe hypokinesis of the anteroseptal wall of the left ventricle. However, emergency coronary angiography showed no stenotic lesions in any coronary arteries. A laboratory examination showed thrombocytopenia, renal dysfunction, and hemolysis. We therefore diagnosed the patient with thrombotic thrombocytopenic purpura (TTP). While we were preparing to initiate plasma exchange therapy, she suddenly developed cardiopulmonary arrest. A postmortem examination revealed microthrombi in the small vessels of the myocardium. We herein report a case of ischemic cardiomyopathy with a rapid progression from TTP.

Key words: thrombotic thrombocytopenic purpura, cardiomyopathy

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is an acute and fatal syndrome with abnormalities in multiple organ systems and is characterized by hemolytic anemia, thrombocytopenia, renal dysfunction, a fever, and a fluctuating neurologic syndrome. Although coronary artery thrombosis in TTP has been reported in several autopsy studies, cardiac complications of TTP, including ischemic cardiomyopathy, have rarely been reported (1-3). We herein report a case of ischemic cardiomyopathy with a rapid progression from TTP.

Case Report

An 83-year-old woman was admitted to the primary care unit of our hospital at 9 a.m. complaining of dizziness and nausea, which had begun on the previous day. On the physical examination, she showed icterus and hematuria, although there were no abnormal neurological findings. Her height was 156 cm, body weight was 60 kg, body temperature was 36.7°C, blood pressure was 130/70 mmHg, and pulse rate was regular at 72 beats/min. A chest radiograph showed no cardiomegaly or pulmonary congestion. An electrocardiogram (ECG) revealed sinus rhythm with ST-segment elevation in multiple leads without Q waves (Fig. 1A). Transthoracic echocardiogram (TTE) showed localized severe hypokinesis of the anteroseptal wall of the left ventricle, and the left ventricular ejection fraction was 50%; there was no valvular disease or pericardial effusion. Furthermore, the blood troponin T rapid qualitative test was positive. Because acute myocardial infarction was suspected, antiplatelet drugs (200 mg of aspirin and 300 mg of clopidogrel) were immediately administered to the patient for percutaneous coronary intervention at the primary care unit, and subsequently, an emergent coronary angiography (CAG) was performed at 10 a.m. There were no stenotic lesions in any coronary arteries, the coronary blood flow was not impaired [Thrombolysis in Myocardial Infarction (TIMI) flow grade 3], and left ventriculography (LVG) showed diffuse hypokinesis of the left ventricle not limited to the anteroseptal wall.

While CAG was being performed, all results of the blood test performed on admission were reported (Table), which...
Figure 1. A: Electrocardiography at admission showing ST-segment elevation in the I, II, aVL, and V2-V6 leads. B: Electrocardiography at shock showing aggravated ST-segment elevation in the I, II, aVL, and V2-V6 leads.

Table. Blood Test on Admission.

| Peripheral blood | Biochemistry | Coagulation |
|------------------|--------------|-------------|
| WBC 7.1 10^9/L   | TP 6.2 g/dL  | PT 82 %     |
| RBC 4.01 10^12/L | Albumin 3.2 g/dL | APTT 45 sec |
| Hb 13.4 g/dL     | T-Bil 7.7 mg/dL |             |
| PLT 8,000 mm^-3  | D-Bil 0.4 mg/dL |             |
| WBC: white blood cell, RBC: red blood cell, PT: prothrombin time, APTT: activated partial thromboplastin time, TP: total protein, ALT: alanine aminotransferase, ALP: alkaline phosphatase, γ-GTP: gamma-glutamyl transpeptidase, BUN: blood urea nitrogen, BNP: brain natriuretic peptide

revealed isolated thrombocytopenia [platelet count (PLT), 8,000 mm^-3], hyperbilirubinemia [total and direct bilirubin (T-Bil, D-Bil), 7.7 and 0.4 mg/dL, respectively] in association with intravascular hemolysis without anemia [hemoglobin (Hb), 13.4 g/dL], mild renal dysfunction [serum creatinine (Cre), 1.3 mg/dL], and elevated cardiac enzyme levels [aspartate aminotransferase (AST), 112 IU/L, lactate dehydrogenase (LDH), 2,547 IU/L, creatine kinase (CK), 809 IU/L, CK-MB, 74 U/L, and troponin T, 5.7 ng/mL]. Moreover, a peripheral blood smear showed schistocytes (Fig. 2). According to these findings, the patient was diagnosed with TTP. At 11 a.m., we transferred the patient from the catheterization laboratory to the intensive care unit and prepared for plasma exchange therapy. At 1 p.m., she suddenly began vomiting and showed a sudden decrease in blood pressure and subsequently developed cardiopulmonary arrest. TTE during resuscitation procedures demonstrated no evidence of tamponade. The blood test performed at that time revealed a further increase of cardiac enzyme levels (AST, 535 IU/L, LDH, 2,845 IU/L, CK, 1,112 IU/L, CK-MB, 179 U/L). Furthermore, ECG showed aggravated ST-segment elevation in multiple leads (Fig. 1B). Despite performing resuscitation procedures, the patient died.

On autopsy, the gross findings revealed diffuse petechial hemorrhages in the myocardium (Fig. 3). In the microscopic findings, microthrombi with necrosis were observed in small vessels involving the heart (Fig. 4). Although there were no stenotic lesions in any coronary arteries, microthrombi diffusely impaired the microcirculation of the myocardium. Thus, her pathological condition was regarded to be ischemic cardiomyopathy. Similar microthrombi were observed in the lungs and stomach (Fig. 5), as well as in the kidney and adrenal gland (data not shown). In addition, the serological test revealed that the activity of a disintegrin and
metalloproteinase with thrombospondin type 1 motifs member 13 (ADAMTS13) was almost 0% (normal range: 50-180%), and there was no inhibitor of ADAMTS13. From these findings, we speculated that cardiogenic shock occurred after global myocardium infarction due to diffuse small vascular occlusion induced by TTP. In this case, there was a discrepancy between the left ventricular wall motion of TTE performed at the primary care unit and that of LVG performed an hour later, suggesting that microvascular occlusion due to TTP had advanced very rapidly.

Discussion

The major cause of TTP is the severely decreased activity of ADAMTS13 (4). The role of ADAMTS13 is to cleave highly active ultra-large von Willebrand factor multimers, which are critical for platelet tethering and normal hemostasis, into smaller protein fragments (5-7). The decreased activity of ADAMTS13 accelerates platelet aggregation, resulting in organ ischemia because of partial vessel occlusion (5). In our case, microthrombi with necrosis were extensively observed in the small vessels in the myocardium. Hawkins et al. reported a systematic review of TTP patients with cardiac abnormality (8). In their study, myocardial infarction was the most frequent cardiac complication associated with TTP. Although clinical evidence was rarely reported, autopsy data revealed that the most common abnormality was thrombi in the arterioles and capillaries. Cardiac hemorrhage and myocardial necrosis were also observed. These findings are similar to our case.

Cases of myocardial infarction associated with TTP had been previously reported, however, few cases developed rapid progression similar to our case. TTP is a rare, but serious complication of clopidogrel use (9). Although the definite mechanism has not yet been elucidated, a lower activity of ADAMTS13 has been reported in patients with clopidogrel-induced TTP (10, 11). Because our patient had taken clopidogrel for coronary artery stenting, clopidogrel may have additively reduced the activity of ADAMTS13 and contributed to the acute progression of TTP.

TTP is an acute life-threatening illness that requires prompt treatment. Plasma exchange therapy is the standard treatment for TTP. The mortality associated with TTP has decreased from 90% to less than 20% due to the initiation of plasma exchange therapy (3, 12, 13). Gaddam et al. reported complete recovery of ischemic cardiomyopathy from TTP using plasma exchange therapy (3). In our case, although we attempted to initiate plasma exchange therapy, the rapid progression of the disease made further intervention impossible.

In this case, it is probable that the use of clopidogrel accelerated TTP and induced subsequent ischemic cardiomyopathy. Therefore, when we treat a patient with TTP and
Figure 5. Photomicrographs of the autopsied lung and stomach. A: The histological appearance of the lung. A pulmonary alveolar hemorrhage is observed. B: Microthrombi-induced microvascular embolization in the lung (arrow). C: The histological appearance of the stomach. A superficial mucosal hemorrhage (white arrow) and a congested vessel (black arrow) are observed. D: Microthrombi-induced microvascular embolization in the stomach (arrow) (H&E staining, original magnification: A: 40×, B: 200×, C: 40×, D: 200×).

cardiac complications, we should therefore carefully select medications and agents for the treatment of cardiovascular disease to avoid inducing a rapid progression of the disease.

The authors state that they have no Conflict of Interest (COI).

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