

## Thrombotic Thrombocytopenic Purpura after Percutaneous Coronary Intervention

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Thrombotic thrombocytopenic purpura (TTP) is a rapidly progressive hematological syndrome defined by the pentad of thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, fever and renal dysfunction. TTP has been associated with major surgical procedures and specific medications. However, there is no known previously reported case in which acute TTP occurred after a percutaneous coronary intervention (PCI). We report a case of TTP after a PCI, that presented with the pentad of symptoms, as well as hepatitis and pancreatitis.

**Key Words :** Thrombotic thrombocytopenic purpura, Percutaneous coronary intervention, Hepatitis, Pancreatitis

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### INTRODUCTION

There are infrequent, yet serious, complications of coronary angiography that are major causes of prolonged hospitalization. Most of these complications are the result of contrast nephropathy, and diabetic patients are especially susceptible to this. Thrombotic thrombocytopenic purpura (TTP) is a disorder characterized by the presence of hematological abnormalities and organ dysfunction. TTP can be a devastating, rapidly progressive, fatal syndrome unless it is appropriately diagnosed and treated<sup>1)</sup>. The determination of an initial diagnosis of TTP only require the confirmation of the presence of thrombocytopenia and microangiopathic hemolytic anemia without any other manifestations<sup>2)</sup>. Although TTP can be caused by coronary artery bypass graft surgery<sup>3, 4)</sup>, abdominal surgeries (such as cholecystectomy and hysterectomy), and several medications (such as ticlopidine and, clopidogrel), its occurrence following percutaneous coronary intervention has not been reported. We report a case of TTP that presented with thrombocytopenia, microangiopathic hemolytic anemia, renal and neurologic abnormalities, fever, hepatitis, and pancreatitis after percutaneous coronary intervention.

### CASE REPORT

A 65-year-old female was admitted with complaints of dyspnea and chest discomfort. She had a 9-month history of dyspnea on exertion prior to her admission and a 20-year history of diabetes. She had no allergies and did not take any illicit drugs. Diagnostic studies included cardiac enzymes, in which the cTn-I was mildly elevated at 0.98 ug/L. On a transthoracic echocardiogram, the ejection fraction was 39% and hypokinesia was present in the anteroseptal, anterior, septal and apical regions. Gated myocardial scintigraphy demonstrated a reversible reperfusion defect and hypokinesia in the anterior and inferior cardiac walls. The clinical diagnosis was a non-ST elevation myocardial infarction. A complete blood cell count revealed a hematocrit of 29.9%, a white blood cell count of 6,750/ $\mu$ L, and a platelet count of  $226 \times 10^3$ / $\mu$ L. Additional laboratory tests performed at the time of admission revealed a blood ureanitrogen level of 40 mg/dL, a creatinine level of 2.0 mg/dL, and a creatinine clearance of 19 mL/min. Liver function tests were normal.

Aspirin and clopidogrel were started as antiplatelet therapy for 3 days before the coronary procedure. Coronary

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angiography revealed a 90% diameter stenosis of the proximal left anterior descending artery (LAD) and total occlusion of the proximal right coronary artery (RCA). After a 0.5 mm balloon predilation, a 3.0×28 mm sirolimus-eluting stent (SES) was successfully deployed at the LAD lesion. An attempt was made to open the chronic total occlusion in the proximal RCA. A floppy wire was successfully passed into the lesion. With balloon predilation, a 3.0×28 mm SES was successfully deployed at the proximal RCA. After stent implantation, the patient complained suddenly of dizziness and became agitated. The blood pressure dropped to 80 mmHg systolic and the pulse rate decreased to 40 beats per minute for a few minutes. A temporary pacemaker was immediately implanted. After stabilization of her vital signs, additional SESs (2.75×33 mm, 2.5×33 mm) were implanted at the distal and mid RCA. After the PCI, the patient was transferred to the cardiac intensive care unit. Although the vital signs were stable, her mental status was characterized by fluctuating confusion and irritability without any focal neurological findings. The body temperature was elevated to 38.4°C at that time. To evaluate the cause of her abnormal mentation, serologic laboratory tests were performed. Arterial blood gas analysis demonstrated a metabolic acidosis. The platelet count was decreased to  $147 \times 10^3/\mu\text{L}$ . The prothrombin time (PT) was 13.9 seconds, the partial thromboplastin time was 43.6 seconds, and the serum ammonia level was normal. Several hours after the PCI, the platelet count rapidly decreased to  $55 \times 10^3/\mu\text{L}$ , and the aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels increased to 1516 U/L and 789 U/L, respectively. This was in contrast to the nearly normal level of alkaline phosphatase (ALP). Lactate dehydrogenase (LDH) increased to 3,504 U/L. On the first day after the PCI procedure, the platelet count decreased to  $35 \times 10^3/\mu\text{L}$  and the hematocrit decreased to 21.9%. The blood urea nitrogen increased to 60 mg/dL, the creatinine to 3.6 mg/dL, the AST and ALT levels peaked at 6,500 U/L and 2,063 U/L, respectively, and the LDH rose to 3,504 U/L. Serum amylase was also increased. The peripheral blood smear was consistent for microangiopathic hemolysis with schistocytes and burr cells. The Coombs direct and indirect tests were negative as were viral markers. An ultrasound study of the abdomen was unremarkable. A chest radiograph demonstrated no abnormality and an abdominal radiograph demonstrated contrast enhancement in both kidneys.

Packed cells and fresh frozen plasma were transfused immediately. After 3 days, the creatinine rose to 5.5 mg/dL. The amylase and lipase levels had steadily risen to 609 U/L and 1,475 U/L, respectively, for several days with no abdominal pain. The patient's general condition and mental status stabilized, and the platelet count increased to  $51 \times 10^3/\mu\text{L}$ , 3 days after the procedure; and to  $117 \times 10^3/\mu\text{L}$ , 1 week later. She was

discharged with a platelet count of  $178 \times 10^3/\mu\text{L}$ , a hematocrit of 28.1%, and a creatinine level of 1.6 mg/dL, with resolution of contrast on the abdominal radiograph. 4 weeks later, the platelet count increased to  $275 \times 10^3/\mu\text{L}$  and the hematocrit improved to 33.1%. After stabilization of all laboratory findings, the EF improved to 49% on a follow-up transthoracic echocardiogram. The patient experienced no adverse cardiovascular events at the time of her 6-month clinical follow-up.

## DISCUSSION

Thrombotic thrombocytopenic purpura (TTP) is a clinical syndrome characterized by hematological abnormalities and ischemic end-organ dysfunction without any clinically apparent etiology. Its frequency is estimated to be only 3.7 cases per year per 1 million people. Although most cases of TTP are considered to be primary or idiopathic, some cases have been reported to have a number of precipitating factors, including cardiovascular surgeries, malignancies, immunological disorders, toxic substances, infectious agents and several medications. Of the medications, ticlopidine and clopidogrel have been associated with TTP following coronary stenting<sup>5, 6</sup>. The greatest risk of developing life-threatening TTP has been reported to occur within 2 weeks after initiating clopidogrel therapy. Even though our patient received clopidogrel (75 mg/day) for 3 days before the procedure, this agent was unlikely to have been the cause of her TTP. The clopidogrel was administered for too short a period of time. In fact, she continued to take clopidogrel during the TTP event and the recovery period.

We also considered the alternative explanations for this patient's clinical presentation and thrombocytopenia. A thorough history and physical examination excluded any infectious process and sepsis. Coagulation studies are usually helpful in differentiating TTP from disseminated intravascular coagulation, although both entities can have a similar morphologic picture in the peripheral blood smear, which is characterized by numerous fragmented erythrocytes (schistocytes).

The patient's prothrombin time, partial thromboplastin time, and fibrinogen level were all within normal limits. Coombs test was also negative, and immunologic disorders were excluded. The infusion of heparin could have been related to the TTP. Low molecular weight heparin was used before and during the procedure. However, heparin-induced thrombocytopenia could not explain the presentation of hemolytic anemia, mentation changes, and renal failure.

It is of interest that this case also included some atypical manifestations of TTP, such as hepatitis and pancreatitis. Ischemic hepatitis is usually asymptomatic. There was a reversible elevation of the serum amino-transferase levels after

the ischemic episode (the levels peaked to more than 20 times the upper normal limit within 1 to 3 days), elevation of the LDH levels, and acute renal failure<sup>7)</sup>. Pancreatitis may also occur as a result of TTP; or, in a few cases, it may trigger TTP<sup>8)</sup>. In this case, there was no abdominal pain or abnormality on imaging studies. However, the patient's amino-transferase levels increased rapidly to nearly 100 times the normal value, with increased levels of pancreatic enzymes. Other causes for the patient's hepatitis, such as viral infections and drugs, were also excluded.

The clinical diagnosis of TTP is generally difficult to make, because there are various clinical presentations and there is rarely a full expression of the pentad. The complete pentad is observed in only 20% of cases. However, early recognition of this disorder can have a substantial impact on the outcome of TTP, and immediate plasmapheresis with plasma exchange has demonstrated the ability to improve significantly the mortality rate and severe morbidity from neurologic disability<sup>9)</sup>. This case demonstrated the variable presentation of TTP and suggested that the PCI itself may be associated with the development of TTP. The increasing number of recent reports of TTP may be related to the worldwide usage of antiplatelet medications and the modification of the diagnostic criteria for TTP. The current introduction of plasmapheresis in the management of this disorder has improved the outcome up to an 82% survival rate<sup>10)</sup>. Our patient received conservative therapy and a single FFP infusion, instead of plasmapheresis. We conclude that the most effective management for this disorder could begin with the physician's early suspicion and diagnosis.

We described a diabetic female who developed TTP after a PCI, and who recovered with conservative therapy and an FFP infusion. The greatest concern in this case was that TTP developed after a percutaneous coronary intervention, which

had not been reported previously in the literature.

## REFERENCES

- 1) Shamseddine A, Saliba T, Aoun E, Chahal A, El-Saghir N, Salem Z, Bazarbachi A, Khalil M, Taher A. *Thrombotic thrombocytopenic purpura 24 year of Experience at the American University of Beirut Medical Center. J Clin Apher* 19:119-124, 2004
- 2) Nabhan C, Kwaan HC. *Current concepts in the diagnosis and management of thrombotic thrombocytopenic purpura. Hematol Oncol Clin North Am* 17:177-199, 2003
- 3) Chang JC, Shipstone A, Llenado-Lee MA. *Postoperative TTP following cardiovascular surgeries. Am J Hematol* 53:11-17, 1996
- 4) Pavlovsky M, Weinstein R. *Thrombotic thrombocytopenic purpura following coronary artery bypass graft surgery: prospective observations of an emerging syndrome. J Clin Apher* 12:159-164, 1997
- 5) Manor SM, Guillory GS, Jain SP. *Clopidogrel-induced thrombotic purpura-hemolytic uremic syndrome after coronary artery stenting. Pharmacotherapy* 24:664-667, 2004
- 6) Steinhubl SR, Tan WA, Foody JM, Topol EJ. *Incidence and clinical course of thrombotic thrombocytopenic purpura due to ticlopidine following coronary stenting. JAMA* 281:806-810, 1999
- 7) Seeto RK, Fenn B, Rockey DC. *Ischemic hepatitis: clinical presentation and pathogenesis. Am J Med* 109:109-113, 2000
- 8) Munoz-Rodriguez J, tricas Leris JM, Andreu Solsona V, Vilaseca Bellsola J. *Ischemic hepatitis in patients with heart failure. An Med Interna* 20:579-581, 2003
- 9) Rock GA, Shumak KH, Buskard NA, Blanchette VS, Kelton JG, Nair RC, Spasoff RA. *Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. N Engl J Med* 325:393-397, 1991
- 10) Bell WR, Braine HG, Ness PM, Kickler TS. *Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: clinical experience in 108 patients. N Engl J Med* 325:398-403, 1991