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# An Unusual Presentation of Thrombotic Thrombocytopenic Purpura

Yaolin Zhou, MD,[a] Stephanie D. Reilly, MD,[b] Radhika Gangaraju, MD,[c] Vishnu V.B. Reddy, MD,[b] Marisa B. Marques, MD[b]
[a]*Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City;* [b]*Department of Pathology, University of Alabama at Birmingham;* [c]*Division of Hematology-Oncology, Department of Medicine, University of Utah, Salt Lake City.*

## PRESENTATION

We describe a patient with sudden and severe postoperative thrombocytopenia whose diagnosis was delayed. The patient was a 58-year-old black man with diabetes mellitus type 2, hypertension, and chronic kidney disease, who presented to our institution with 4 days of abdominal pain. He had a history of remote exploratory laparotomy for an abdominal gunshot wound repair.

## ASSESSMENT

His physical examination was remarkable for obesity (body mass index of 30.4 Kg/m$^2$), abdominal distension, pain, and rebound tenderness. There were no signs of hemolysis. Vital signs included temperature of 37.4°C, heart rate of 80 beats per minute, respiratory rate of 16 breaths per minute, and blood pressure of 174/99 mm Hg. Laboratory studies showed a hemoglobin of 12.5 g/dL, white blood cell count of 9.4 $\times$ 10$^9$/L, platelet count of 211 $\times$ 10$^9$/L, blood urea nitrogen of 26 mg/dL, serum creatinine of 2.3 mg/dL, and troponin I of 0.025 ng/mL (reference range: <0.04 ng/mL).

A computed tomography scan of the abdomen and pelvis revealed low-grade functional obstruction with segmental small bowel thickening and nonspecific mesenteric stranding and adenopathy. The differential diagnosis included Crohn's disease, lymphoma, and mechanical small bowel obstruction due to postsurgical adhesions. He was admitted for further management, but the location of the obstruction was inaccessible by upper or lower endoscopy.

Within 12 hours of admission, the patient underwent laparoscopic resection of a 20-cm segment of ischemic small bowel. He tolerated the procedure well. The following day, the patient was given prophylactic low-molecular-weight heparin and was noted to have mild thrombocytopenia (113 $\times$ 10$^9$/L) and a hemoglobin of 11.7 g/dL. Due to a remote possibility of heparin-induced thrombocytopenia, low-molecular-weight heparin was discontinued, and bivalirudin was initiated. His platelet count decreased to 15.7 $\times$ 10$^9$/L on postoperative day (POD) 2 and his renal function worsened during the course of hospitalization (**Figure 1**). One unit of apheresis platelets was transfused on POD 3 but his platelet count did not increase.

## DIAGNOSIS

On POD 4, the patient was noted to have jaundice, epistaxis, and dark urine, consistent with hemolysis. A hematology consultant reviewed his peripheral blood smear and was schistocytes, and increased reticulocytes. Other laboratory tests showed a D-dimer of 6951 ng/μL (reference range: 110-240 ng/μL), prothrombin time of 17 seconds (reference range: 12.2-14.5 seconds), partial thromboplastin time of 42 seconds (reference range: 23-31 seconds), fibrinogen of 591 mg/dL (reference range: 200-400 mg/dL), and lactate dehydrogenase of 1455 IU/L (reference range: 120-240 IU/L).

The differential diagnosis for the thrombocytopenia included consumption, disseminated intravascular coagulation, and thrombotic thrombocytopenic purpura. Heparin-induced thrombocytopenia was considered unlikely because his platelet count had dropped prior to receiving prophylactic low-molecular-weight heparin, and there was no known previous heparin exposure. Thrombotic

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Requests for reprints should be addressed to Yaolin Zhou, MD, University of Oklahoma Health Sciences Center, 940 Stanton L. Young Blvd., BMSB 451, Oklahoma City, OK 73104.
E-mail address: yaolinz@gmail.com


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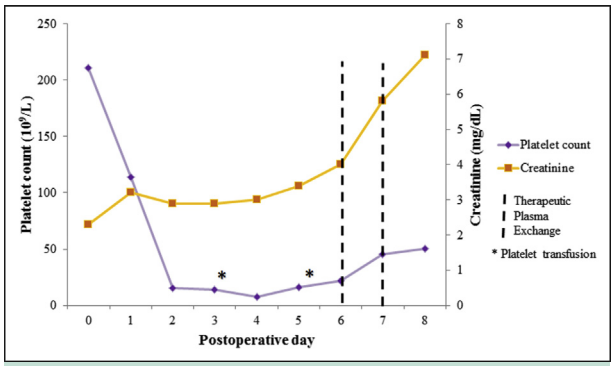


**Figure 1** Time course of platelet count and serum creatinine from admission to death. Daily platelet counts and serum creatinine from admission to postoperative day 8 when the patient expired. The purple line represents the platelet count (left y axis), the orange line represents the serum creatinine (right y axis), asterisks mark when platelet transfusions were given, and the vertical lines, when he had therapeutic plasma exchanges.

thrombocytopenic purpura also seemed unlikely because of the normal platelet count on admission.

On the morning of POD 5, the patient's platelet count fell to 7.3 × $10^9$/L. He received another ineffective platelet transfusion. On POD 6, he developed a generalized seizure followed by a pulseless electric activity cardiac arrest. He was successfully resuscitated, intubated, and transferred to the intensive care unit. Given his persistent profound thrombocytopenia and rapid clinical deterioration, thrombotic thrombocytopenic purpura was suspected and the apheresis team was contacted for the first time. A plasma specimen was collected and sent to the Blood Center of Wisconsin for ADAMTS13 activity testing, and emergent therapeutic plasma exchange was performed.

## MANAGEMENT

Despite therapeutic plasma exchange, our patient continued to experience episodes of cardiac arrest throughout POD 6. On POD 7, he underwent another exchange, but had already suffered irreversible brain injury. Clinical examination and nuclear medicine study performed on POD 8 showed brain death.

The diagnosis of thrombotic thrombocytopenic purpura was confirmed when the ADAMTS13 activity was later reported as <5% (normal ≥67%), with an inhibitor level of 1.8 Bethesda units (normal ≤0.4 inhibitor units). Postmortem examination demonstrated extensive acute neuronal hypoxic injury and microthrombi in several organs. Multiple subepicardial infarctions due to platelet-rich microthrombi were present in the heart (Figure 2). Thrombi were also present in the kidneys and small bowel. Review of the surgically resected intestines showed that the microthrombi were composed of platelets and factor VIII (Figure 3), suggesting thrombotic thrombocytopenic purpura was present at the time of surgery.

## DISCUSSION

Thrombotic thrombocytopenic purpura is rare, with a yearly incidence of approximately 11 cases per 1 million persons in the US and worldwide.[1,2] The currently accepted clinical definition of thrombotic thrombocytopenic purpura is thrombocytopenia and microangiopathic hemolytic anemia without an alternative explanation.[3,4]

Thrombotic thrombocytopenic purpura can be either acquired or inherited.[3,5] The inherited form is caused by genetic mutations in the *ADAMTS13* gene. More common is the acquired form, mediated by autoantibodies against ADAMTS13. The antibodies cause a deficiency of the **A** **D**isintegrin **A**nd **M**etalloprotease with **T**hrombo**S**pondin type 1 motif **13** (ADAMTS13) enzyme, which cleaves von Willebrand factor into its normal-size multimers.

Whether acquired or inherited, deficiency of the ADAMTS13 enzyme leads to widespread formation of aggregates of von Willebrand factor and platelets that block small vessels, leading to end-organ ischemia. Transfusing platelets can intensify the formation of such aggregates in

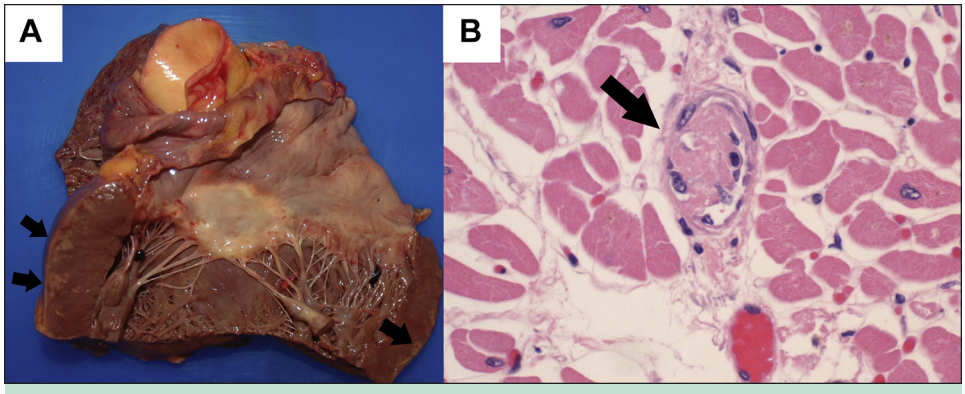


**Figure 2** Pertinent findings at autopsy included (**A**) the heart showing multiple foci of subepicardial acute infarction (gross image) and (**B**) platelet fibrin thrombi in the coronary microvasculature (hematoxylin & eosin stain, 400×).