Acute Cholecystitis in Thrombotic Thrombocytopenic Purpura

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Introduction

Thrombotic thrombocytopenic purpura (TTP) is a highly fatal thrombotic microangiopathy. The clinical features characterize it are thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, renal dysfunction, and fever. Secondary TTP has a broad range of etiologies and has been associated with a variety of medical conditions including infections, malignancies, pregnancy, autoimmune disorder, HIV, bone marrow transplant and drugs [1, 2]. We report here a case of TTP associated with acute cholecystitis. A review of the medical literature results in only one other published report of TTP occurring in association with cholecystitis [3].

Case

A previously healthy 31-year-old African American male was evaluated for 2 days history of a presumptive episode of hematemesis, abdominal pain and dark stool. He had consumed 2–3 drinks of vodka prior to his event. Denied drug use or smoking. There was no history of allergies or over the counter medications use.

On examination his vital signs were: temperature 98.5 °F, pulse rate of 114 beats per min, respiration rate of 20 per min, and blood pressure 98/58 mm Hg. The patient appeared

weak with icteric sclera. He had no rash or ecchymosis. The neck was supple without masses. Cardiovascular examination was normal except for tachycardia. He had right upper quadrant tenderness with rebound and positive Murphy's sign. There was no organomegaly, bowel sounds were present. Neurological examination was normal. Laboratory examination revealed: hemoglobin 3.6 g/dL, white blood cell count 11 k/cmm with normal differential, platelet count of $17 \times 10^9/L$. Peripheral blood smear revealed schistocytes and thrombocytopenia. White cell morphology was normal. Serum creatinine 1.3 mg/dL, blood urea nitrogen 45 mg/dL, indirect bilirubin 9.4 gm/dl, lactate dehydrogenase 1,823 U/L, reticulocyte count 6 % and serum haptoglobin <8 mg/dl. Antinuclear Antibody titers, amylase, lipase, coagulation profile, hepatitis panel, Thyroid-stimulating hormone, Human immunodeficiency virus, Rheumatoid factor, and direct antiglobulin test were negative. Abdominal ultrasound was consistent with calculus acute cholecystitis. ADAMTS-13 activity obtained before plasmapheresis was 9 %.

A diagnosis of TTP and acute cholecystitis was made. Consumptive coagulopathy was excluded on the basis of a normal coagulation profile. Plasmapheresis was initiated and continued for total of ten exchanges. He was managed conservatively for acute cholecystitis. He was kept NPO, received intravenous fluids, antibiotics, corticosteroids 1 mg/kg/day, packed red blood cells, and folic acid. The patient recovered gradually. On tenth hospital day, he was asymptomatic with hemoglobin of 10.3 g/dL and platelet count of $150 \times 10^9/L$. The patient was discharged on the twelfth hospital day and continues plasmapheresis as an outpatient. His treatment course was complicated by catheter related sepsis. He then required three more sessions of plasmapheresis until the platelet count finally stabilized and hemolysis subsided. He was scheduled for an elective cholecystectomy.

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Discussion

Inhibitory autoantibodies against ADAMTS13, a metallo-proteinase enzyme that cleaves Von Willebrand factor (vWF), is the most common pathophysiology associated with the TTP. Given the rarity of TTP in association with acute cholecystitis, it is difficult to postulate if there is a cause-effect relationship, and if so, which of the disease processes is the inciting factor. It has been suggested the idea that the microthrombi of TTP could cause an exacerbation of an underlying inflammatory process in the gallbladder causing the release of additional mediators and further inflammation [3]. In some cases of TTP, it is thought that damage to endothelial cells, whether by injury or disease, leads to the release of extra large vWF multimers. In a state of severe ADAMTS13 deficiency, extra large vWF multimers persist and may cause platelet activation leading to platelet aggregation and the formation of microthrombi [4]. ADAMTS13 levels may be low due to the development of autoantibodies to the enzyme. In addition, under proinflammatory conditions, ADAMTS13 activity has been seen to be decreased due to various mechanisms, including transcriptional down regulation, proteolytic degradation, and consumption due to high substrate concentration [5]. This imbalance may be further propagated as vWF serves as an acute phase protein with its plasma level increasing in a state of systemic inflammation. It can be theorized that in a pro-inflammatory phase, like that of acute cholecystitis, extra large multimers of vWF is released by damaged endothelium and platelets, which in turn cause a reciprocal activation of endothelial cells and platelets.

Further research is required to explain the mechanism of TTP, the clinical variability of the disease, and its association with other disease processes. Whether a marker specific to the gallbladder or pathogenesis of acute cholecystitis could contribute to the development of TTP, or whether a common inducing factor exists needs to be answered. In a setting of acute bleeding and infection etiology of thrombocytopenia could be unclear. Regardless of the etiology of TTP, given the benefit of exchange plasmapheresis on mortality rates clinicians should maintain a high index of suspicion. Whenever clinically suspected, delays in initiating therapy should be avoided. Early recognition is the principal importance for a favorable outcome.

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