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CASE REPORT

Thrombotic thrombocytopenic purpura: A rare complication of acute pancreatitis

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Abstract

Thrombotic Thrombocytopenic Purpura (TTP) is a poorly understood entity involving multiple organs and having grave prognosis if not treated promptly. Acute pancreatitis (AP) is a rare cause of TTP and TTP is also a rare complication of acute pancreatitis. TTP is induced in AP by poorly understood mechanism, which involves multiple pathways apart from only ADAMTS13 deficiency. Here, we report a case of a 32-year-old male who developed acute pancreatitis due to chronic alcoholism. He developed signs of TTP from Day 4 of his onset of pain. High clinical suspicion and prompt initiation of plasmapheresis was associated with good outcome. In this case report, we have discussed details of our case and the different mechanisms involved in pathogenesis of TTP in AP and their outcome with prompt management.

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a multisystem disorder characterized by a combination of features of thrombocytopenic purpura, microangiopathic hemolytic anemia, fever, neurological manifestation, and renal failure. The underlying pathophysiological mechanism for TTP is either a deficiency of ADAMTS13 or the development of an antibody against ADAMTS13. ADAMTS13 cleaves ultra-large multimers of von Willebrand factor (ULvWF) into smaller particles. In the absence of ADAMTS13, there is an excess of ULvWF multimers, which forms disseminated platelet-rich microthrombi, causing various organ ischemia. Although various autoimmune disorders, drugs, and pregnancy are associated with TTP, in half of the patients, the cause remains idiopathic.

Acute pancreatitis is an acute inflammation of the pancreas and is associated with an increase in various cytokines levels in its acute phase. Development of TTP in patients with acute pancreatitis does not only involve ADAMTS13, but it is rather a complex pathway. There are only a few case reports available of TTP as a complication of acute pancreatitis. So, here, we report a case of thrombotic thrombocytopenic purpura secondary to alcohol-related acute pancreatitis.

Case report

A 32-year-old male from Punjab, North India, presented to our emergency department with abdominal pain for the last 5 days that was epigastric in location, acute in onset, and severe in intensity. It was associated with multiple episodes of vomiting. The patient had a history of active significant alcoholism, approximately 100 gm/day for the last 10 years. Initially, the patient was managed at a primary care center where he was found to have increased serum amylase (3722 U/L). He was diagnosed with acute pancreatitis secondary to alcohol and was managed conservatively with intravenous (IV) fluid supplementation and analgesics. There was no organ failure or local complications during the initial 3 days. However, he developed fever, decreased urine output, and irrelevant talk with altered sensorium on Day 4 of his pain, for which he was referred to our hospital on Day 5 of abdominal pain.

In our hospital, the patient was shifted to ICU services and was intubated on the same day. On evaluation, the patient had anemia (Hb-6.5 gm/dL), thrombocytopenia (21 000/cumm), and increased creatinine levels (3.49 mg/dL). A peripheral blood smear demonstrated the presence of schistocytes (5%), with an increase in lactate dehydrogenase (LDH) levels (4887 U/L). Based on clinical history and laboratory parameters, we suspected thrombotic thromocytopenic purpura secondary to acute pancreatitis. The patient underwent contrast enhanced computed tomography (CECT) abdomen on Day 6 of abdominal pain, which demonstrated interstitial pancreatitis (Fig. 1). The patient was started on plasmapheresis for thrombotic thromocytopenic purpura. He was also investigated for etiological work-up, including malarial antigen, dengue NS1 antigen, IgM leptospira serology, anti neutrophil antibody (ANA), perinuclear-antineutrophil cytoplasmic antibody (p-ANCA), cytoplasmic- antineutrophil cytoplasmic antibody (c-ANCA), and direct coombs test that were negative. After starting plasmapheresis, the patient's general condition gradually improved, with increase in platelet count after second plasmapheresis. Gradually, the patient's sensorium improved, and he was extubated after three sessions of plasmapheresis. His fever also subsided, and he was shifted to ward after five sessions of plasmapheresis. At Day 20, with normalization of his parameters—Hb-10.8 gm/dL, platelet-3.49 lacs/cumm,

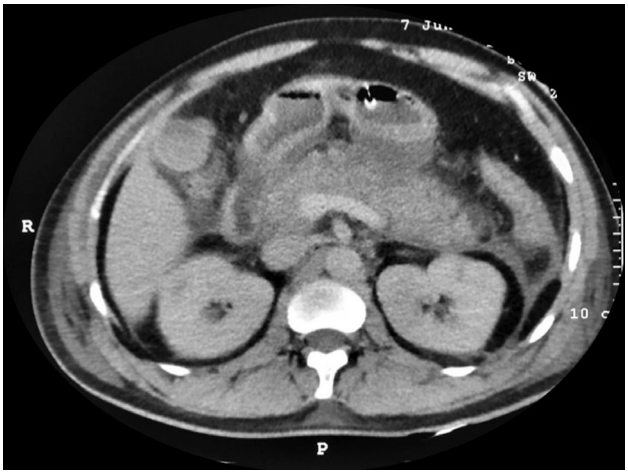

Figure 1 CECT abdomen of patient showing interstitial pancreatitis

creatinine-0.8 mg/dL, LDH-228 U/L—and no evidence of schistocytes on peripheral smear, we stopped his plasmapheresis after seven sessions, and he was discharged on Day 28 in a stable hemodynamic condition.

Discussion

TTP is a rare disease with an obscure etiology. It was initially described as classical triad by Moschcowitz in 1925 with components of microangiopathic anemia, thrombocytopenia, and acute renal failure. Later, in 1966, pentad was described, including fever and neurological symptoms. The disease is mainly initiated by the occlusion of vessels by microthrombi of aggregated platelets and fibrin deposits. Although various theories, including endothelial damage, neutrophilic activation, and immunological phenomena, have been postulated, the actual pathogenetic pathway remains to be explored.[1] Various etiologies, including rheumatological diseases, HIV, pregnancy, and organ transplantation, have been postulated to be a risk factor for thrombotic thrombocytopenic purpura, while half of the cases remain idiopathic.[2,3]

Acute pancreatitis, like other inflammatory condition, is associated with endothelial damage and the release of various cytokines, including interleukin-8 (IL-8) and tumor necrosis factor α (TNF-α), which is associated with the release of a large amount of ultra-large, high-molecular-weight vWF. ADAMTS-13 is consumed in the cleavage of this excess of ULvWF. So, it has been postulated that ADAMTS-13 deficiency is a result rather than effect in acute pancreatitis-induced TTP.[4,5] In acute pancreatitis, a complement system is found to be inappropriately activated due to susceptibility of C3 and C5 to direct cleavage of pancreatic enzymes. An activated complement system is associated with endothelial damage, activation of platelets, neutrophils, and disseminated endothelial microthrombi formation.[6] Nitric oxide (NO) is a potent vasodilatory molecule, which also has an antiplatelet effect. In acute pancreatitis, endothelial damage is found to be associated with a decrease in endothelial NO synthase production. Decrease in NO level predisposes the patient to thrombotic microangiopathy. In rat models, this decrease in NO synthase has been found to be an important mediator in the pathogenesis of acute pancreatitis.[7] The pathogenesis of TTP in acute pancreatitis is associated with multiple interconnecting pathways, including the release of inflammatory mediators, complement activation, endothelial damage, depletion ofNO, and relative deficiency of ADAMTS 13 molecules. In our patient, we did not measure ADAMTS 13 levels due to the nonavailability of the test in our institute.

Diagnosis of thrombotic thrombocytopenic purpura is established by clinical pentad (fever, anemia, thrombocytopenia, altered sensorium, and renal failure) with the exclusion of other causes. However, classical pentad is present in less than 40% of patients, adding a further diagnostic dilemma.[8] The presence of schistocytes in peripheral blood, along with increased LDH levels, may aid in diagnosis, but high clinical suspicion is of paramount importance. Once diagnosis of TTP is suspected, the prompt search of etiological factors such as autoimmune conditions, infections, HIV, drugs, pregnancy is necessary to identify the treatable cause for the same. Our patient presented with classical pentad of TTP, which helped in the prompt diagnosis of the condition, along with high clinical suspicion. In our case, we had performed an extensive etiological evaluation to identify any other cause before attributing it to acute pancreatitis.

Our case developed signs of thrombotic thrombocytopenic purpura on Day 4 of abdominal pain. Swisher et al. has reported five cases of thrombotic thrombocytopenic purpura along with a review of 16 previously reported cases.[9] In their review, they noticed that patients developed TTP after a median of 3 days of development of acute pancreatitis. Swisher et al. also developed diagnostic criteria for the diagnosis of TTP secondary to acute pancreatitis.[9] Our patient also fulfilled the diagnostic criteria for TTP secondary to acute pancreatitis.

Prompt diagnosis and treatment is of paramount importance in the management of thrombotic thrombocytopenic purpura. Plasmapheresis, high-dose methyl prednisolone, rituximab, and recombinant ADAMT13 are the various treatment options available, with plasmapheresis being the first-line choice.[10] Our patient and other reported cases had all received plasmapheresis with good outcome. Complete response is defined as normalization of platelets for two consecutive days, with normalization of laboratory parameters including LDH and clinical recovery.[10] In our case, we continued plasmapheresis till complete response.

Conclusion

Thrombotic thrombocytopenic purpura is a life-threatening but treatable disorder. Acute pancreatitis is a rare etiology for thrombotic thrombocytopenic purpura involving various pathogenetic mechanisms apart from ADAMTS 13 deficiency. A high index of clinical suspicion is required for prompt diagnosis and early treatment, which is associated with good outcome.

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