Case Report

Acute pancreatitis induced thrombotic thrombocytopenic purpura

Mohammed Arshad Ali, Jalal Syed Shafiuddin Shaheen, Mohammed Ali Khan

Abstract

Thrombotic thrombocytopenic purpura (TTP) is a rare syndrome of unknown cause with an estimated incidence of one case per million. The disease is characterized by a pentad of symptoms: Thrombocytopenia, microangiopathic hemolytic anemia, neurologic changes, renal dysfunction, and fever. It causes thrombosis in the microvasculature of several organs, producing diverse manifestations. Acute pancreatitis (AP) is a well-described consequence of TTP. Acute pancreatitis triggering TTP is uncommon.

Keywords: Microangiopathic hemolytic anemia, pancreatitis, thrombotic thrombocytopenic purpura

Access this article online

Website: www.ijccm.org

DOI: 10.4103/0972-5229.126084

Quick Response Code:

Introduction

Thrombotic thrombocytopenic purpura (TTP) is rare with an annual incidence of approximately six per million.[1] The minimum diagnostic criteria are microangiopathic hemolytic anemia (MAHA) and thrombocytopenia, which may be accompanied by central nervous system, renal, gastrointestinal, and cardiac involvement. It is due to deficiency or dysfunction of A Disintegrin and Metalloproteinase with a Thrombospondin type 1 motif, member 13 (ADAMTS13) leading to accumulation of ultra-large von Willebrand factor molecules and subsequent von Willebrand factor (vWF)/platelet-rich microvascular thrombosis. Most cases in adults are idiopathic. However, TTP may be secondary.[2]

In acute pancreatitis, pancreatic tissue damage occurs as a result of intracellular activation of enzymes leading to a secondary inflammatory response and release of cytokines.[3]

From:
Department of Anesthesiology and Intensive Care, Salmania Medical Complex, Manama, Bahrain

Correspondence:
Dr. Mohammed Arshad Ali, Department of Anaesthesiology and Intensive Care, Salmaniya Medical Complex, P.O. Box 12, Manama, Kingdom of Bahrain. E-mail: faryas99@yahoo.com

Acute pancreatitis (AP) is a well-described consequence of TTP,[4] but TTP as a consequence of acute pancreatitis is rare.

Case Report

A 43-yrs-old Indian male was admitted to the hospital with abdominal pain of one-day duration. The pain was mainly in the epigastrium, was severe in intensity and radiating to the back, and associated with nausea and vomiting.

His past medical history was insignificant except for alcoholism. His physical examination was normal apart from tenderness over the epigastrium.

Laboratory findings showed an elevated serum amylase of 878 µ/L. His urea was 6.7 mmol/L, creatinine being 87 mmol/L. Total bilirubin was 29 µmol/L with a direct component of 6 µmol/L and indirect bilirubin of 23 umol/L. His aspartate aminotransferase (AST) was 45 IU/L, blood glucose of 7.3 mmol/L, and Lactate dehydrogenase (LDH) was 190 IU/L. His white blood count was elevated to 12,000 cells/mm^3. Hematocrit was 42%, with a hemoglobin of 14 g/dL and platelets were 1,97,000/mm^3. Ultrasound abdomen showed gallstones and a bulky hypo echoic pancreatic tail representing the area of pancreas. Computed tomography abdomen also

showed the tail of pancreas to be edematous with fat stranding and a calculus at the neck of the gall bladder [Figure 1]. Bilateral pleural effusions were also noted which was mild to moderate, more on the left than the right. The patient was diagnosed as acute pancreatitis secondary to gallstones. He was started on the standard treatment for acute pancreatitis.

On the 4th day of admission, his platelets dropped to 14,000/mm^3, along with a fall in hemoglobin to 8.7 g/dL. LDH rose to 2,037 IU/L, associated with an increase in indirect hyperbilirubinemia. The urea and creatinine increased to 17 and 169 mmol/L, respectively. Peripheral smear showed significant schistocytes of 4%. The fibrinogen levels and the coagulation profile remained normal. ADAMTS 13 enzyme assay was not done as the test was not available in our hospital. Based on these typical lab values, a diagnosis of TTP was made as the patient was having thrombocytopenia, MAHA, and renal impairment. The only other differential diagnosis is hemolytic uremic syndrome (HUS). The severe thrombocytopenia with mild renal impairment went in favor of TTP rather than HUS, which is expected to have severe renal impairment with mild thrombocytopenia. The patient underwent pan CT, which ruled out malignancy anywhere else as a triggering factor for TTP. The patient was commenced on plasmapheresis in addition to methylprednisolone, which is an established treatment for both TTP and HUS.

Patient's platelet counts, urea, creatinine along with hemoglobin started to improve after the second session of plasmapheresis. His recovery was complicated by the progression of bilateral pleural effusion, which resulted in respiratory compromise, requiring intubation and mechanical ventilation. Bilateral intercostal drains were inserted and the patient was weaned off the ventilator by the 7th day. He had a total of eight sessions of plasmapheresis and the laboratory parameters were back to normal and the patient was discharged from the hospital on the 20th day of admission. Follow up of the patient a month after discharge from hospital found him to be doing well.

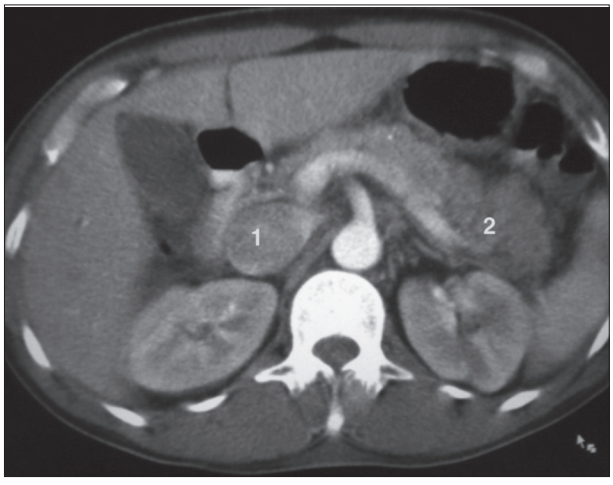

Figure 1: 1.head of pancreas. 2. Tail of pancreas (Bulky, hypo- echoic showing evidence of acute pancreatitis)

Discussion

TTP is a life-threatening disorder characterized by MAHA and thrombocytopenia as a result of microvascular platelet clumping often accompanied by ischemic organ dysfunctions such as neurological abnormalities or renal insufficiency.[5]

In only 10% of published cases of TTP has an initiating factor that has been recognized. Triggering factors for the development of TTP are pregnancy, vascular diseases, cancer, or the use of certain drugs such as mitomycin. Recently, TTP has also been described in Human immunodeficiency virus (HIV)-positive patients. Nevertheless, in the great majority of cases, TTP develops in a previously healthy patient.[6]

In most cases of idiopathic TTP, severe deficiency of ADAMTS13 prevents processing of unusually large vWF multimers released from endothelial cells. The persistence of unusually large vWF multimers seems to be responsible for the formation of microvascular platelet thrombi. In adults, severe ADAMTS13 deficiency is often caused by inhibitory ADAMTS13 auto antibodies. Currently, plasma exchange with replacement of fresh frozen plasma remains the treatment of choice in any patient presenting with acute TTP. The finding of severe autoantibody-mediated ADAMTS13 deficiency in a relevant number of patients provides the rationale for the concurrent prescription of corticosteroids although their value in this situation is unproven.[5]

It is common that TTP severely affects the pancreas. In a post mortem study, Hosler *et al*.,[7] found pancreatic involvement in 30 out of 51 cases diagnosed with TTP. The mechanism for pancreatic injury during TTP is thought to be impairment of pancreatic circulation by thrombotic occlusion of small vessels and subsequent ischemia.[5]

On the other hand, the acute inflammatory response to pancreatitis may trigger the onset of TTP. Swisher *et al*.,[8] reported five patients and reviewed 16 cases from the literature, in which acute pancreatitis preceded clinical and laboratory signs of TTP by a median of 3 days. One postulated mechanism involves diffuse endothelial

injury mediated by inflammatory cytokines that are released as part of the systemic inflammatory response to acute pancreatitis. It has been demonstrated in *in vitro* studies that inflammatory cytokines stimulated endothelial cell release of ultra large vWF multimers and inhibited the cleavage of ultra large vWF by ADAMTS13.[5]

However, early recognition of TTP and its association with acute pancreatitis is imperative, because prompt treatment with daily plasma exchange and steroids could be life saving.[5]

As in several of the cases in the series reported by Swisher *et al.*,[8] our case exemplifies the short interval between the diagnosis of acute pancreatitis and the subsequent manifestations of TTP.

Conclusion

It is becoming apparent that pancreatitis can precipitate acute TTP. The mechanism for this association is multifactorial. A high clinical suspicion is required to make an early diagnosis and allow early initiation of plasma exchange therapy which can lead to a favorable outcome.

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How to cite this article: Ali MA, Shaheen JS, Khan MA. Acute pancreatitis induced thrombotic thrombocytopenic purpura. Indian J Crit Care Med 2014;18:107-9.

Source of Support: Nil, **Conflict of Interest:** None declared.