# Acute pancreatitis with Thrombotic thrombocytopenic purpura in an adolescent girl

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## ABSTRACT

Thrombotic thrombocytopenic purpura (TTP) has multiple clinical manifestations and risk factors but the events that actually trigger acute episodes of TTP are often unclear. We describe the case of a 16-year-old girl who presented with acute pancreatitis followed by TTP.

***Keywords:*** acute pancreatitis, microangiopathic hemolytic anemia, thrombocytopenia

## INTRODUCTION

TTP is categorized as a microangiopathic hemolytic anemia (MAHA), which is a group of disorders characterized by hemolytic anemia, thrombocytopenia and small vessel damage (microangiopathy), The reported incidence is six cases per million per year.[1] It is less frequent in children and more common in women in their third and fourth decades.[2] It classically occurs in patients with a hereditary or acquired lack of ADAMTS-13 (a disintegrin and metalloprotease with thrombospondin repeats), a metalloproteinase that cleaves large multimers of von Willebrand factor. The mortality of TTP in untreated subjects is 90% but can be reduced with prompt intervention like plasmapharesis.[1] Although other modalities of treatment like steroids, FFP infusions, antiplatelet agents and vincristine have been reported, however their role is not well established.[2] The events that actually trigger acute episodes of TTP are often unclear. Acute pancreatitis triggering episodes of acute TTP has been reported in few studies, mainly in adults. Here we report a case of an adolescent girl with acute TTP triggered by acute pancreatitis and managed successfully with steroids.

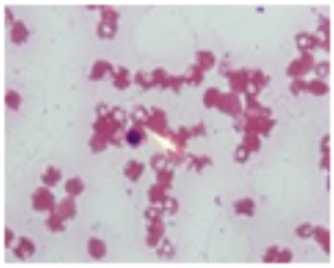
## CASE REPORT

A 16 year-old girl was admitted with severe upper abdominal pain for three days, radiating to back along with vomiting and fever. Her baseline investigations revealed serum amylase and lipase levels of 1062 U/L (N 30-110 U/L) and 1315 U/L (N 25-300U/L) respectively, and the ultrasound appearance was consistent with a diagnosis of acute pancreatitis. Hb on admission was 12.5 g/dl; WBC 15600/cmm; platelet count 1.5 lakh/cmm. Blood film examination revealed a neutrophilic leucocytosis with no evidence of red cell fragmentation. Liver and renal function tests were normal. Etiological workup for acute pancreatitis was also normal. Blood and urine cultures were sterile. She was managed conservatively with IV fluids, analgesics, and Injection Pantaprazole, with resolution of symptoms within 48 hours of admission.

On 3rd day, she complained of severe headache and passed cola colored urine. Examination revealed BP 126/90, severe anemia and jaundice. There were no neurological abnormalities and fundus examination was normal. Urine output was also normal. Repeat investigations revealed Hb of 4.9 g and platelet count of 46,000. serum creatinine was 4.2 mg/dl (N 0.7-1.2 mg/dl), total bilirubin 8.3 mg/dl (N 0.2-1.4 mg/dl), direct bilirubin 2.0 mg/dl (N 0-0.3 mg/dl), indirect bilirubin 6.3 mg/dl (N 0-1.1 mg/dl) ,SGOT 40 IU/L (N 14-36 IU/L), SGPT 50 IU/L (N 09- 52 IU/L), serum

alkaline phosphatase 58 IU/L (N 38-126 IU/L), LDH 4288 U/L (N 313-618 U/L) and reticulocyte count 5%. Her peripheral blood film revealed numerous fragmented red cells, schistocytes (Fig.1) and no malarial parasite.

**Fig.1.** Peripheral blood film showing schistocytes and nucleated red cells



Coagulation test, direct Coomb's test and Anti nuclear antibody test were negative. Serum amylase and lipase levels revealed a downward trend to 186 U/L and 304 U/L on day 4 respectively. Urinalysis revealed presence of hemoglobin, epithelial casts and mild proteinuria.

Considering fever, headache, unexplained thrombocytopenia, microangiopathic hemolytic anemia and renal dysfunction, a diagnosis of TTP, possibly triggered by acute pancreatitis was considered. Due to non availability of plasmapheresis at our centre, she was started on intravenous methyl prednisolone in a dose of 30 mg/kg/day for five days. She received 4 units of packed cell transfusion along with other supportive care. She started showing improvement in laboratory parameters within 72 hrs of starting steroids, with stabilization of hemoglobin, resolution of thrombocytopenia with normalization of renal and liver functions by 10$^{th}$ hospital day (7 days after initiation of steroids). ADAMTS-13 activity could not be done. On follow up at 3 months, she was asymptomatic. Complete blood count, liver function tests, renal function tests as well as ultrasound abdomen on follow up was normal.

## DISCUSSION

TTP is generally a disorder of adults; <10% of cases occur in the pediatric age group. The original case of TTP reported by Moschcowitz occurred in a 16-year old girl. TTP classically occurs in patients with a hereditary or acquired lack of ADAMTS13 that cleaves large multimers of von Willebrand factor.[3]

TTP was originally characterized by a pentad of thrombocytopenia, MAHA, fluctuating neurological signs, renal impairment and fever, often with insidious onset. Unexplained thrombocytopenia and MAHA without another apparent cause are sufficient to diagnose TTP.[4] However other manifestations of hemolysis including high LDH, indirect hyperbilirubinemia, and reticulocytosis are also invariably noted during detailed laboratory workup. Schistocytes are a hallmark of MAHA and are essential for the diagnosis of TTP.[5] Our patient fulfilled clinical as well as laboratory criteria of TTP.

The triggering factor of TTP remains unidentified in 90% of cases.[5] Massive hemolysis of any etiology can trigger acute pancreatitis. Hemolysis is also seen in patients with acute pancreatitis of other etiologies.[6] Acute pancreatitis is an inflammatory disease characterized by local tissue injury which can trigger a systemic inflammatory response. Pancreatitis has been commonly reported as a manifestation of TTP, and occurs as a consequence of pancreatic vascular compromise. However, cases of acute pancreatitis triggering TTP have been rarely reported.[2,4,6,7,8] Swisher et al. reported five patients and reviewed 16 such cases from the literature in which acute pancreatitis proceeded clinical and laboratory signs of TTP by a median of 3 days.[8] The mechanism of MAHA following acute pancreatitis is not well established. The systemic inflammatory response of pancreatitis, mediated by IL-6, IL-8, TNF-α, and

other cytokines, may contribute to the onset of an acute episode of TTP-HUS.[7,8]

Plasma exchange has been the mainstay of therapy and recommended to be initiated urgently. However the presence of antibodies to ADAMTS-13 in acquired TTP has led to the use of immunosuppressive therapies like steroids, vincristine, cyclophosphamide, azathioprine, intravenous immunoglobulin as well as splenectomy. Over the years, several hypotheses like a hypothetical generalized phenomenon of the Sanarelli- Schwartzman type, stabilization of platelet and endothelial cell membranes, inhibition of macrophage activity, an increase in the activity of T-suppressor lymphocytes, leading to inhibited antibody production, were used by various authors as rationales to support and justify the use of corticosteroids in TTP patients.[9] The literature survey is of little help in drawing any conclusion on the actual role of steroids in TTP treatment. A multicentric study to compare the effectiveness of standard- versus high-dose methylprednisolone as an adjunctive treatment to PE in the acute phase of TTP indicate that the association of plasma exchange with high-dose of steroids reduces the percentage of TTP patients that fail to achieve complete remission.[10] Supportive care is also very important in management of patients with TTP. Red blood cell transfusion is frequently required. Platelet transfusion should be used for life-threatening hemorrhage.[1]

To best of our knowledge there are no case reports of TTP in children in association with acute pancreatitis in Indian literature. Our patient a 16 year's old girl had features suggestive of TTP which was preceded by acute idiopathic pancreatitis and could be managed successfully with intravenous steroids only.

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