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. It is less frequent in children and more common in women in their third and fourth decades. 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 plasmapheresis. Although other modalities of treatment like steroids, FFP infusions, antplatelet agents and vincristine have been reported, however their role is not well established. 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 25-300 U/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 10th 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 Moschowitz 
ocurred 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. 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. 
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. Our patient fulfilled clinical as 
well as laboratory criteria of TTP.

The triggering factor of TTP remains 
unidentified in 90% of cases. Massive 
hemolysis of any etiology can trigger acute 
pancreatitis. Hemolysis is also seen in patients 
with acute pancreatitis of other etiologies. 
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. 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. 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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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**REFERENCES**