Acute pancreatitis leading to thrombotic thrombocytopenic purpura/haemolytic uremic syndrome (TTP/HUS) treated with therapeutic plasma exchange and haemodialysis- A Case Report

Bhargav Prajapati1*, Tarak Patel2, Nidhi Bhatnagar3, M. D. Gajjar4, Shital Soni5, Kaminidevi Gupta6

1,6 Resident, 2,5 Assistant Professor, 3 Associate Professor, 4 Professor & Head Department of IHBT, B. J. Medical College & Civil Hospital, Ahmedabad

ABSTRACT
BACKGROUND: Haemolytic uremic syndrome is a disorder in which there is acute kidney injury (AKI) with non-immune haemolytic anaemia and thrombocytopenia. It is most commonly seen in children. There are very few cases reported where pancreatitis was the cause of TTP/HUS. We describe the case of a 30 year old male patient, who was admitted with diagnosis of acute pancreatitis (AP) and developed deterioration of renal function, despite fluid resuscitation. The clinical features, radiological findings and laboratory investigations were in favour of diagnosis of AP with TTP/HUS. Therapeutic plasma exchanges along with haemodialysis were started on alternate days. Renal failure was part of TTP/HUS in this patient with diagnosis of AP. The exact mechanism causing this condition is not clear. Early initiation of therapeutic plasma exchange has a major impact on survival and long term renal function improvement.

Key words: Acute pancreatitis, TTP/HUS, Therapeutic plasma exchange

INTRODUCTION
Haemolytic uremic syndrome, thrombotic thrombocytopenic purpura (TTP), and disseminated intravascular coagulation (DIC) are classified into a group of disorders called thrombotic microangiopathies (TMA).1 The prevalence of acute kidney injury (AKI) in patients with acute pancreatitis (AP) has been reported to be 15%, with mortality from cases complicated by AKI close to 80% compared with 7% among patients with AP but without AKI. Though rare in adults, cases of HUS have also been associated with infections, transplants, autoimmune diseases, drugs and neoplasms. Pancreatitis as a result of TTP or HUS is rare, affecting only 2% of adults with TTP/HUS.5 Very few case reports of pancreatitis causing TTP/HUS have been reported.5-7 Here we report a case of acute pancreatitis complicated by TTP/HUS which was treated successfully with therapeutic plasma exchange after early recognition.

CASE REPORT
A 30 years old male patient was admitted to our hospital with epigastric pain, vomiting, anuria since 7 days. Patient had no history of prior hospitalization. He also denied having any other medical conditions and surgeries. On physical examination, tenderness on epigastrium was present. On admission, patient had urine output of <100 ml/day. The patient was admitted with a diagnosis of acute pancreatitis, dehydration secondary to oral intolerance and acute pre-renal azotaemia. Intravenous fluid hydration was started and the patient was placed on bowel rest. Medications were given to control his epigastric pain, nausea and vomiting. In the next two days his renal function deteriorated progressively and his serum creatinine level was 6.33 mg/dl and serum urea was 85.70 mg/dl with associated oliguria non responsive to hydration therapy. His haemoglobin was 7.40 gm/dl
Acute pancreatitis leading to thrombotic thrombocytopenic purpura/haemolytic

and platelet count was 1,15,000/cmm. There was no evidence of bleeding. Further laboratory investigations showed a raised reticulocyte count of 3.5%, serum amylase 811.70 U/L, serum lipase 3483 U/L, LDH of 3065 IU/L and a negative coomb’s test. The patient was therefore diagnosed with acute pancreatitis with TTP/HUS and the physician advised for therapeutic plasma exchange.

**Table 1: Laboratory findings of the patient on admission day 1, 6 and 17**

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 6</th>
<th>Day 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (gm/dl)</td>
<td>7.40</td>
<td>8.29</td>
<td>7.80</td>
</tr>
<tr>
<td>Platelet count (*10^9/cmm)</td>
<td>115</td>
<td>314</td>
<td>473</td>
</tr>
<tr>
<td>S. Bilirubin (mg/dl)</td>
<td>2.80</td>
<td>3.35</td>
<td>0.6</td>
</tr>
<tr>
<td>S. Creatinine (mg/dl)</td>
<td>6.33</td>
<td>10.37</td>
<td>3.69</td>
</tr>
<tr>
<td>S. Urea (mg/dl)</td>
<td>85.70</td>
<td>139.70</td>
<td>24.30</td>
</tr>
</tbody>
</table>

One volume TPE was performed with removal of 40-45 ml of plasma/kg according to patient’s body weight, height, haematocrit and total body volume on Spectra Optia apheresis machine (Manufacturer: TERUMO BCT). Replacement was carried out by fresh frozen plasma (20-22 ml/kg of body weight) and normal saline (15-20 ml/kg of body weight). Continuous monitoring of vitals, e.g., pulse, blood pressure and respiratory rate was carried out during the procedure to prevent any adverse events related to procedure. Total 4 cycles of TPE were performed on alternate day in 8 days period along with haemodialysis on alternate days. A few days after initiation of this treatment, improvement in renal function as well as platelet count was seen. The patient was discharged on 18th day of admission.

**Table 2: Details of each cycle of therapeutic plasma exchange.**

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Day of admission</th>
<th>Whole Blood processed</th>
<th>Plasma removed</th>
<th>Replacement fluid used (FFP + N.S.)</th>
<th>ACD used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle-1</td>
<td>Day 3</td>
<td>5782 ml</td>
<td>2407 ml (48 ml/kg)</td>
<td>2306 ml (46 ml/kg)</td>
<td>315 ml</td>
</tr>
<tr>
<td>Cycle-2</td>
<td>Day 5</td>
<td>5580 ml</td>
<td>2100 ml (42 ml/kg)</td>
<td>2000 ml (40 ml/kg)</td>
<td>400 ml</td>
</tr>
<tr>
<td>Cycle-3</td>
<td>Day 7</td>
<td>5262 ml</td>
<td>2525 ml (50 ml/kg)</td>
<td>2400 ml (48 ml/kg)</td>
<td>900 ml</td>
</tr>
<tr>
<td>Cycle-4</td>
<td>Day 9</td>
<td>5570 ml</td>
<td>2180 ml (44 ml/kg)</td>
<td>2100 ml (42 ml/kg)</td>
<td>525 ml</td>
</tr>
</tbody>
</table>

**DISCUSSION**

15% of patients with acute pancreatitis have acute kidney injury, usually associated with multiple organ dysfunction. Isolated renal failure is seen in only 3% of patients with acute pancreatitis. 

Reports have shown that the prevalence of acute kidney injury varies with severity of the pancreatitis. The mortality from acute pancreatitis complicated by acute kidney injury can reach 70% to 80% compared with 6% to 7% in patients with pancreatitis but without acute kidney injury. Most of the deaths are in patients with multiple organ failure rather than with isolated acute kidney injury. Though different entities, HUS and TTP are similar in clinical features, laboratory findings and basic mechanism of endothelial cell damage. There are two types of HUS. The first type is associated with diarrhoea, which is self-limited, mostly seen in children and is caused by verotoxin producing E.coli 0157:H7. The other type of HUS is not associated with diarrhoea, mostly seen in adults. Most of the cases are idiopathic, but some of them are found to be associated with infections, bone marrow transplants, autoimmune diseases, drugs and neoplastic diseases. In this patient, rapidly deteriorated kidney function and subsequent development of systemic symptoms led the clinician to consider the possible causal relationship between acute pancreatitis and TTP/HUS. Some hypotheses point toward endothelial injury, in acute pancreatitis, as the inciting factor that sustains the microangiopathic process. The mechanism of endothelial injury could be mediated by pancreatic autoantibodies, interleukin-1 (IL-1), tumor necrosis factor-a (TNF-a) or modified Von Willebrand factor (VWF). Genetic predisposition is clearly important considering that most cases of acute pancreatitis do not result in TTP/HU. It is difficult to identify risk factors for the development of TTP/HUS among patients with acute pancreatitis, because there have been only a few cases reported in the literature, and the pathophysiologic mechanism that leads to the development of TTP/HUS in patients with acute pancreatitis is not sufficiently understood. Unusually large multimers of VWF (ULvWF) have been implicated in the pathogenesis of TTP. Aggregation of the large VWF multimers with platelets...
Acute pancreatitis leading to thrombotic thrombocytopenic purpura/haemolytic occludes terminal arterioles and capillaries. Recently, serum measurement of von Willebrand factor cleaving protease, called ADAMTS-13, has been used to differentiate between TTP/HUS. Patients with TTP may have either a deficiency in the activity of ADAMTS-13 enzyme or they have an inhibitor such as anti-ADAMTS-13, therefore patients with TTP typically have little or no ADAMTS-13 activity in their plasma compared to patients with HUS\(^3\), \(^13\), \(^18\)-\(^21\), although TTP-like illness without identifiable ADAMTS-13 dysfunction has also been recognized\(^22\). Therapeutic plasma exchange, using donor fresh frozen plasma as the replacement fluid, remains the cornerstone of treatment for classic TTP\(^13\)-\(^17\). Although plasma-based therapies are being used first-line for HUS, there is no evidence from clinical controlled trials. It is thought that the donor plasma infusion replaces the missing metalloproteinase, while the removal of the patient’s plasma depletes the ADAMTS-13 inhibitor and possibly also the von Willebrand factor (vWF) polymers.\(^3\) In our case, the patient’s renal function improved after 2nd cycle of initiating the therapeutic plasma exchange. In his report of 20 cases, Boyle describes a 100% survival rate in patients that received plasma\(^7\), other reports also describe renal recovery within 24 hours after initiating plasma exchange).\(^5\), \(^6\) Other possible therapies that can be considered in refractory patients include splenectomy and the use of corticosteroid with variable success rates reported. In isolated case reports, the anti-CD20 monoclonal antibody rituximab has been used successfully in treatment refractory cases of TTP\(^23\).

**CONCLUSION**

In patients with acute pancreatitis, acute kidney injury is a common complication. Most of the times it is associated with multiple organ dysfunction, especially in severe pancreatitis. The physicians should keep TTP/HUS in mind as one of the most important and common causes of acute renal failure in adult patients with diagnosis of acute pancreatitis. Direct or indirect endothelial damage is thought to play a major role in pathophysiology, though the mechanism is not clear. Early diagnosis and therapeutic plasma exchange along with haemodialysis as a mainstay of treatment have been reported to improve survival and improvement in renal function.

**REFERENCES**


