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AN UNUSUAL PRESENTATION OF THROMBOTIC THROMBOCYTOPENIC PURPURA FOLLOWING HEPATITIS A INFECTION: A CASE REPORT

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Abstract

Introduction: Thrombotic Thrombocytopenic Purpura (TTP) is a fulminant thrombotic microangiopathy often manifested as clinical pentad of fever, thrombocytopenia, hemolytic anemia, renal failure and neurological abnormalities. ADAMTS13 deficiency has been noted as causative factor however secondary TTP/HUS preceded by various insult is also noted. Insults like burn, malignancy, viral infections and sepsis has been associated with TTP/HUS. Association of TTP/HUS with hepatitis A infection is rare and not reported.

Case Summary: 27 years old male was admitted with acute onset fever, drowsiness, decreased urine output and icterus. Physical examination was unremarkable except icterus. He was found to have IgM positive for hepatitis A along with evidence of microangiopathic haemolytic anemia. He was diagnosed to have Hepatitis A along with TTP/HUS on the basis of laboratory and clinical findings and plasmapheresis was started, following which he dramatically improved. No recurrence of TTP/HUS has been noted so far on follow up.

Conclusion: We present an interesting case of Hepatitis A as a possible trigger for Thrombotic thrombocytopenic purpura. Any hemolytic microangiopathy in hepatitis A should be carefully looked for a possibility of TTP.

Keywords: Thrombotic thrombocytopenic purpura, Hepatitis A, TTP/HUS, HAV

Introduction

Thrombotic Thrombocytopenic Purpura [TTP; TTP/HUS] is a fulminant microangiopathic haemolytic condition often manifested as clinical pentad of fever, thrombocytopenia, haemolytic anemia, renal failure and neurological abnormalities. ADAMTS13 deficiency has been noted as causative factor however secondary TTP/HUS preceded by various insults is also noted. Insults like burn, malignancy, viral infections and sepsis has been associated with TTP/HUS (1,2). Association of TTP/HUS with hepatitis A infection is rare and has not been reported. We present a rare occurrence of TTP/aHUS following Hepatitis A infection which was treated successfully with plasmapheresis.

Case summary:

27 years old male from Indian state of Uttarakhand presented with a high-grade fever for 3-4 days, drowsiness for 1-2 days and decreased urinary output. His physical examination was unremarkable except fever and icterus. There was no organomegaly or lymphadenopathy. Microbiological investigation was positive for hepatitis A infection [IgM positive] and the patient was put on symptomatic treatment. The peripheral blood smear examination revealed microangiopathic haemolytic anemia. Direct Coombs test was negative. A provisional diagnosis of TTP/HUS was made on the basis of classical clinical pentad of symptoms and plasmapheresis was initiated. However, ADAMTS13 assay is not available at our

institute. The laboratory findings of the patient at presentation and post plasmapheresis are given in Table 1. The patient responded well to the four sessions of plasmapheresis, improved dramatically and no recurrence of TTP/HUS was noted later on.

Table 1: Laboratory investigations pre and post plasmapheresis.

Parameters	Pre-Plasmapheresis	Post-Plasmapheresis
HB (g/dl)	7.66	10.46
TLC (1000/cumm)	27.35	11.04
Platelets (1000/cumm)	40	250
Schistocytes (%)	8%	2%
Retic (/100RBC) (%)	6%	1.2%
PT (sec)	18.6	17
APTT (sec)	32	32
D-Dimer (micro/ml)	0.54	-
LDH (U/L)	1265	-
Creatinine (mg/dl)	8.46	1.3
Total Bilirubin (mg/dl)	64.91	1.73
Direct Bilirubin (mg/dl)	48.88	0.65
Indirect Bilirubin (mg/dl)	16.03	1.08
AST (IU/L)	133	60
ALT (IU/L)	64	64
Coombs Test	Negative	-
Procalcitonin	Negative	-

Discussion:

TTP is a life threatening thrombotic microangiopathy. TTP occurs due to uncontrolled VWF (von Willebrand Factor)-dependent platelet adhesion, that results in the formation of extensive intravascular thrombi involving mainly the microvasculature. Ultra-long VWF multimers persist in the circulation, platelets bind to these VWF multimers on the surface of endothelial cells or at sites of endothelial injury to the vessel and forms large platelet aggregates. These aggregates are enough to cause hemolysis, consume platelets, and induce tissue ischemia. The plasma metalloprotease called ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13), secreted from hepatic stellate cells and endothelial cells, cleaves a specific Tyr-Met bond in the A2 domain of VWF and prevents large multimers to persist in the circulation in turn preventing the cascade of events (3).

Although autoantibodies to ADAMTS13 are present in most of the sporadic cases and decreased ADAMTS13 activity supports the diagnosis of TTP yet, ADAMTS 13 assay is not always required for early diagnosis and treatment (4).

Inflammatory conditions such as hepatitis may promote thrombotic microangiopathies through endothelial injury or activation that induces the secretion or promotes the adhesion of VWF (von Willebrand Factor). It also inactivates ADAMTS13 and render VWF resistant to proteolysis(5,6).

In our case the diagnosis of TTP was considered due to the presence of classical clinical pentad of TTP and laboratory findings. Other microangiopathies were also ruled out on the basis of the same. The microangiopathic haemolytic anemia was associated with acute hepatitis A event, which resolved completely plasmapheresis and no recurrence was noted later on.

Conclusion:

We report an interesting case of TTP triggered by Hepatitis A infection. Hepatitis A's association with autoimmunity has been reported earlier (7). There is a possibility in a susceptible patient, it can alter immune response and produce antibodies against ADAMTS13 and triggers TTP. Putting those with pre-existing ADAMTS13 deficiency at even higher risks. Therefore, haemolytic anemia in hepatitis A should be carefully looked for a possibility of TTP.

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