Pancreatitis Associated With TTP: A Cause or Effect?

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Pancreatitis Associated With TTP: A Cause or Effect?

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Background:

Thrombotic thrombocytopenic purpura (TTP) is a disorder characterized by platelet aggregation and the formation of platelet thrombi, leading to thrombocytopenia and microangiopathic hemolytic anemia, with or without renal failure or neurologic abnormalities, and without another cause identified.[1]

Acute TTP can be acquired or secondary. Secondary causes of TTP are well documented and include medication, infection, malignancy and autoimmune disorders.

Pancreatitis has been shown to be associated with TTP, however, it still remains unclear what the causal relationship is between the two.[2-3]

TTP remains a medical emergency with an accurate and quick diagnosis necessary to reduce mortality. Glucocorticoids and daily exchange plasmapheresis (EP) are standard treatment; rituximab and other immunosuppressive agents are generally saved for refractory cases.[4]

Case Presentation:

A 60-year-old Caucasian male presented to the ER with a 2 week history of sharp epigastric pain. Abdominal exam revealed a soft, non-distended abdomen with epigastric tenderness. Initial laboratory examination showed a Hb of 13.5 g/dL and platelets of 17,000/uL. Lipase was elevated at 2473 u/L and total bilirubin was elevated to 2.6 mg/dl with an increased indirect fraction. LDH was elevated at 1432 IU/L. Numerous schistocytes were observed on peripheral smear. CT scan of the abdomen showed findings consistent with acute pancreatitis and MRCP showed no evidence of cholelithiasis, or choledocholithiasis. ADAMTS13 activity was less than 10% with an elevated ADAMTS13 antibody at 41 U/ mL (Reference range < 12U/mL). Patient was started on prednisone 1mg/kg daily in addition to daily EP. After five days of EP, there was normalization of his platelets. EP was continued two days post platelet normalization and patient was discharged home on a tapering dose of steroids. Patient returned to the ER 2 days after discharge with a recurrence of thrombocytopenia. On this admission, patient had no reoccurrence of abdominal pain and lipase was normal. EP was reinitiated and he required a 5 week hospital stay due to refractory thrombocytopenia. He was consequently started on rituximab and completed 4 weekly doses. Post rituximab, platelets stabilized and remained within the normal range.

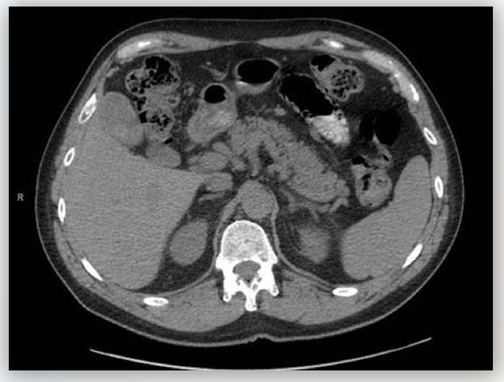

Figure 1: CT scan of abdomen showing acute pancreatis.

Discussion:

In the majority of case reports of patients with pancreatitis and TTP, ADAMTS13 activity was only moderately reduced with no detectable inhibitor.[2-3] These findings are suggestive of secondary TTP.

In this patient, the absence of a recognized etiology for pancreatitis, combined with marked thrombocytopenia on presentation and evidence of severe ADAMTS13 deficiency with an inhibitor, suggests acquired TTP. To further support this interpretation, the patient had a relapse of TTP without further episodes of pancreatitis.

Current guidelines for treatment of acquired TTP suggest continuing EP for a minimum of 2 days after normalization of platelet counts.[4]

Although measurements of ADAMTS13 activity are not required for the diagnosis of TTP, they may help to discriminate between acquired versus secondary TTP.[4]

Patients with ADAMTS13 activity< 10% or an anti-ADAMTS13 antibody have been shown to have an increased risk of relapse.[5]

The use of rituximab has been shown to reduce and delay the incidence of relapse, and has been shown to be an effective treatment for refractory TTP.[6]

Conclusion:

This case demonstrates an acquired TTP that presented with pancreatitis. In patients presenting with features of TTP and other systemic symptoms, the presence of a significantly decreased ADAMTS13 level with the presence of an inhibitor may be used to discriminate between acquired TTP and secondary TTP and therefore help to distinguish those patients who would most benefit from EP and glucocorticoids. In addition, ADAMTS13 levels help to identify those patients who are at increased risk for relapse. This patient with severe ADAMTS13 activity quickly relapsed after discontinuing EP. In addition, this case demonstrates the role of rituximab in relapsed/refractory TTP.

References:

1 George, J.N., Nester, C.M. (2014) Syndromes of thrombotic microangiopathy. *N Engl J Med,* 371(7):654-66.
2 Swisher, K.K., Doan, J.T., Vesely, S.K., Kwaan, H.C., Kim, B., Laemmle, B., Kremer Hovinga, J.A. & George, J.N. (2007) Pancreatitis preceding acute episodes of thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: report of five patients with a systemic review of published reports. *Haematologica,* 92, 936-943.
3 McDonald, V., Laffan, M., Benjamin, S., Bevan, D., Machin, S. & Scully, M. A. (2009), Thrombotic thrombocytopenic purpura precipitated by acute pancreatitis: a report of seven cases from a regional UK TTP registry. *British Journal of Haematology,* 144: 430–433. doi: 10.1111/j.1365-2141.2008.07458.x
4 George, J.N. (2010) How I treat patients with thrombotic thrombocytopenic purpura. *Blood,* 116 (20).
5 Peyvandi, F., Lavoretano, S., Palla, R., Feys, H., Vanhoorelbeke, K., Battaglioli, T., Valsecchi. C., Canciania, M.T., Fabris, F., Zver, S., Reti, M., Mikovic, D, Karimi, M., Giuffrida, G., Laurenti, L. & Mannucci, P.M (2008). ADAMTS13 and anti-ADAMTS13 antibodies as markers for recurrence of acquired thrombotic thrombocytopenic purpura during remission. *Haematologica,* 232-239.
6 Scully, M., McDonald, V., Cavenaugh, J., Hunt, B.J., Longair, I., Cohen, H. & Machin, S.J. (2011) A phase 2 study of the safety and efficacy of Rutiximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. *Blood,* 118, 1746-1753.