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CASE REPORT

Complete Recovery of Ischemic Cardiomyopathy from Thrombotic Thrombocytopenic Purpura

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Abstract: A 50 year old male HIV patient on antiretroviral therapy was admitted for chest pain. Upon admission, the patient was found to have elevated cardiac enzymes, acute thrombocytopenia, hemolytic anemia, acute pancreatitis and acute renal failure. The patient was diagnosed with thrombotic thrombocytopenic purpura/haemolytic uremic syndrome and emergency plasma exchange therapy was initiated along with aspirin, beta-blockers, steroids, and antiretroviral therapy. Patient responded well and demonstrated complete resolution of ischemic cardiomyopathy with left ventricular ejection fraction improving from 35% to 55% by the time of discharge. Essentially, prompt diagnosis and treatment can reverse cardiac damage induced by thrombotic thrombocytopenic purpura.

Keywords: thrombotic thrombocytopenic purpura, cardiomyopathy, HIV

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Introduction

While coronary artery thrombosis in thrombotic thrombocytopenic purpura (TTP) has been established in multiple autopsy studies, myocardial infarction as TTP's primary presentation has rarely been reported. Cardiologists and physicians must be aware of this rare cardiac complication of TTP, as any delay in diagnosis or treatment of this manifestation can be lethal. To our knowledge, complete recovery of ischemic heart failure in TTP has never been reported.

Case Report

A 50 year old African-American male HIV patient presented to the emergency department with complaints of chest pain and shortness of breath for one week. He described his chest pain as a pressure like sensation which was substernal, non-radiating, worsening with exercise and associated with dyspnea. He had no complaints of diaphoresis or vomiting. His shortness of breath progressively worsened over the week ultimately resulting in the patient becoming dyspneic with minimal exertion. Patient had no fevers, cough, leg swelling, or palpitations.

Patient was known to have HIV and was on HAART therapy with fosamprenavir 1400 mg twice daily, tenofovir 300 mg once daily, emtricitabine 200 mg once daily and mycobutin 150 mg once daily. Patient was taking metoprolol 25 mg twice daily for hypertension. There was no family history of coronary artery disease, and patient was a non-smoker and non-alcoholic. At presentation, patient had a blood pressure of 152/99 mm of Hg, heart rate of 115/min, respiratory rate of 18/min, and was breathing comfortably with no distress with an oxygen saturation of 100% on room air. Physical examination was within normal limits, revealed no signs of heart failure, and no evident splenomegaly or rash.

Electrocardiogram showed sinus tachycardia with no ST or T wave changes (Fig. 1). Upon admission, labs showed hemoglobin 7.4 gm/dl, RBC count 2.46 Mil/mm^3, platelet count 9,000/mm^3, prothrombin time 11 sec, reticulocyte count 5.96%, serum creatinine 2.9 mg/dl, LDH 1391 U/L, haptoglobin 15 mg/dl, amylase 581 U/L, lipase 257 U/L, troponin 1.85 ng/ml, and CKMB 4.0 ng/ml. Peripheral blood smear showed marked hypochromia, poikilocytosis, anisocytosis, few schistocytes, few helmet cells, and slight stippling. Transthoracic echocardiogram showed a decreased left ventricular ejection fraction (LVEF) of 35%, with moderate diffuse left ventricular hypokinesis, and had no regional wall motion abnormalities. Further workup showed CD4 count of 381 cells/mm^3. Antiphospholipid antibodies were negative, ANA was negative and HIT antibodies were negative.

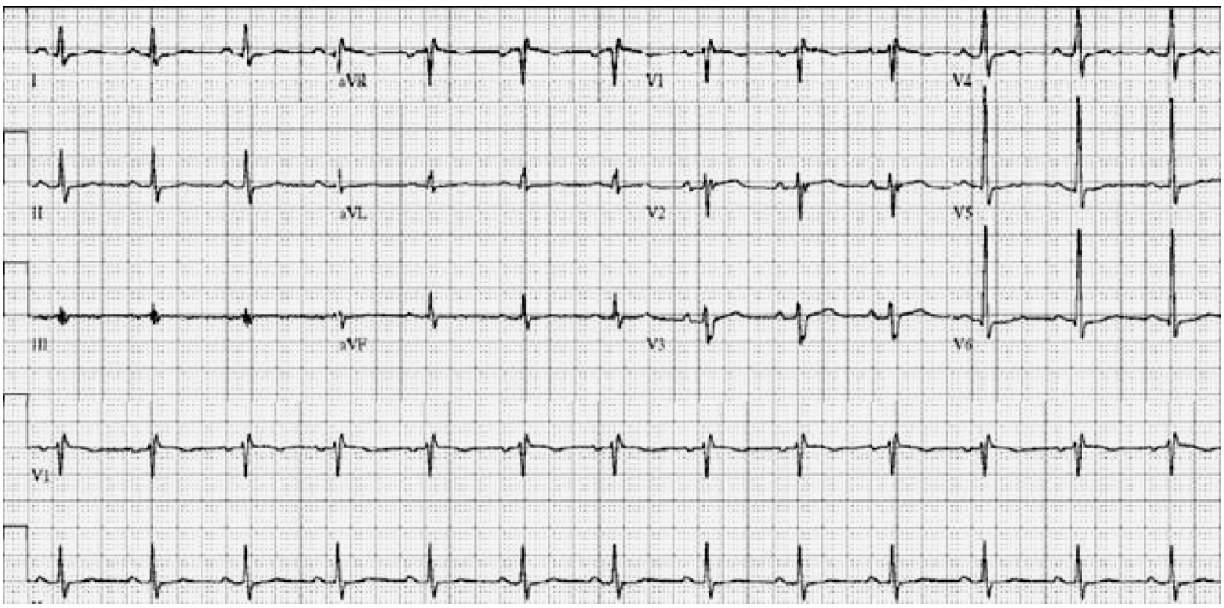

Figure 1. Electrocardiogram showing a sinus rhythm with normal P-waves and PR interval, a normal axis, normal width of QRS complex, with no ST or T wave changes.

Patient was diagnosed with thrombotic thrombocytopenic purpura/hemolytic uremic syndrome, further complicated by non-ST elevation myocardial infarction (NSTEMI), and acute pancreatitis based on the peripheral smear, thrombocytopenia, hemolytic anemia, acute renal failure, elevated cardiac biomarkers and elevated pancreatic enzymes. An emergency Udall Catheter was placed in the patient's femoral vein and plasma exchange therapy was initiated. To decrease anemia induced high output heart failure, he was transfused with three units of packed RBC's. Also, his current home medications including HAART regimen and metoprolol were initiated.

Patient underwent plasma exchange therapy seven times during the course of hospital stay. He was also started on prednisone 60 mg once daily and, after platelet counts were more than 20,000/ml, aspirin 325 mg per day was started for an added therapeutic benefit. Plasma exchange therapy was stopped after platelet counts were stabilized and hemolysis resolved. The aforementioned were evidenced by low LDH levels and stable hemoglobin. Acute pancreatitis and renal failure also resolved. At the time of discharge, patient had a stable hemoglobin of 11.6 gm/dl, platelet count of 180,000/ml, and LDH of 183 U/L. Repeat transthoracic echocardiogram showed complete recovery of left ventricular function with a normal LVEF% of 55%–65% and patient had no symptoms of heart failure. Patient was discharged after 14 days of hospitalization on a tapering regimen of prednisone, along with aspirin, metoprolol and HAART therapy. At 3 month outpatient follow-up, patient had stable hemoglobin of 14 gm/dl and platelet count of 188,000/ml. An out patient exercise stress test was normal, suggesting no significant coronary artery disease.

Discussion

Coronary artery thrombosis in thrombotic thrombocytopenic purpura (TTP) has been established in multiple autopsy studies, but TTP presenting primarily with cardiac symptoms has rarely been reported.[1] Furthermore, treating myocardial infarction in this subset of thrombocytopenic patients with antiplatelet agents like aspirin and clopidogrel has an increased risk of bleeding. Also, the role of beta blockers, ACE inhibitors and statins are less defined in this rare entity. Our experience with this HIV patient showed early diagnosis and initiation of plasma exchange therapy, along with aspirin, prednisone, metoprolol and HAART regimen can reverse this ischemic cardiomyopathy. Severe anemia can cause high output heart failure and hence prompt blood transfusion was given to decrease the workload on the heart.

Thrombocytopenia is the result of decreased bone marrow production, increased sequestration in spleen, or increased utilization in the form of platelet aggregation. Evaluation of acute thrombocytopenia is challenging and requires a careful approach in an attempt to exclude fulminant conditions like DIC (disseminated intravascular coagulation) and TTP. Normal prothrombin time in a thrombocytopenic patient will exclude DIC and the findings of hemolytic anemia will guide in the diagnosis of TTP.[2] Findings of hemolytic anemia include schistocytes on peripheral smear, elevated LDH, low haptoglobin, elevated reticulocyte count and elevated unconjugated bilirubin. Hemolytic uremic syndrome (HUS) is considered if the patient also has prominent renal failure. Other less serious causes of thrombocytopenia include infections, organ transplantation, certain drugs and cancers. Among infections, HIV causing TTP has been reported extensively before the introduction of HAART therapy.[3] Lately, TTP in HIV patients is reported rarely with advanced HIV disease, and isolated thrombocytopenia needs to be differentiated from TTP in these cases.

TTP/HUS is common among women and blacks. TTP causes systemic microvascular platelet clots leading to ischemia in multiple organs thereby affecting the kidneys, gastrointestinal tract, brain and, in rare cases, the heart. The classic pentad of features including fever, thrombocytopenia, hemolytic anemia, neurological abnormalities and renal failure is no longer needed to conclude upon a diagnosis of TTP. TTP is classified as congenital, acquired idiopathic and secondary TTP. The main pathogenesis in TTP is the presence of "unusually large Von Willibrand factor, VWF" with resultant pathological platelet aggregation. These unusually large VWF's are produced by endothelial cells and platelets, which are normally broken down into smaller subunits by a metalloproteinase enzyme called ADAMTS13. Congenital deficiency or inhibitory IgG antibodies to ADAMTS13 can lead to abnormal accumulation of large VWF and aggregation of platelets.[4,5]

However, low ADAMTS13 levels are more specific for congenital and idiopathic TTP while variable ADAMTS13 levels are found in secondary TTP. Secondary TTP from HIV, as seen in our patient, is most likely from endothelial damage by HIV infection causing abnormal release of VWF and increased clearance of ADAMTS13. Studies conducted on HIV patients with TTP showed variable levels of ADAMTS13 levels and autoantibodies, indicating a potentially different pathogenesis behind TTP in the HIV population.[7,8] We did not measure an ADAMTS13 level in our patient as it is not yet a standard investigation protocol and clinical usefulness of ADAMTS13 assays and IgG antibody measurements needs further studies.[6]

Mortality from TTP has decreased from 90% to less than 20% due to the initiation of plasma exchange therapy.[9,10] Plasma exchange therapy includes plasmapheresis and infusion of fresh frozen plasma. Plasmapheresis helps in removing unusually large VWF and autoantibodies against ADAMTS13. Infusion of fresh frozen plasma may add ADAMTS13 enzyme to the blood. Mortality will be high in patients with delayed diagnosis or delayed initiation of therapy. Complications from plasma exchange include sepsis from catheter related local infections, bleeding during catheter insertion due to low platelet count and rare transfusion reactions.[11] Plasma exchange therapy should be continued until platelet counts are stabilized and there are no signs of hemolysis.

Addition of antiplatelet agents like ASA in thrombocytopenia causes an increased risk of bleeding, but trials have shown that ASA is beneficial in preventing platelet aggregation and will improve mortality.[12] The role of adding clopidogrel into the treatment regimen of myocardial infarction in TTP is debatable because clopidogrel by itself can cause TTP in some rare cases.[13] Steroids have been used for a long time in TTP and they are thought to act by decreasing the autoantibody production. There are no major studies indicating the benefits of adding steroids to plasma exchange therapy. But literature review justifies the use of steroids and suggests continuing steroids until recovery. Steroids should be used with caution in HIV patients, as they might increase the chance of opportunistic infections. In selected patients, immunosuppressive drugs like vincristine, cyclophosphamide or azathioprine are used. HIV patients have a higher incidence of TTP and it has been suggested that HIV can cause TTP.[8] Continuation of HAART therapy plays a crucial rule in these patients and relapses have occurred in patients who discontinued HAART therapy after recovery.[14]

In conclusion, TTP in HIV with cardiac involvement should be promptly diagnosed and treated with plasma exchange therapy, steroids, ASA, metoprolol and HAART therapy. Early initiation of therapy in cardiac involvement can reduce mortality and reverse ischemic cardiomyopathy.

Disclosures

This manuscript has been read and approved by all authors. This paper is unique, not under consideration by any other publication, and has not been published elsewhere. The authors and peer reviewers report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material. Written consent was obtained from the patient or relative for publication of this study.

References

1. Hawkins BM, Abu-Fadel M, Vesely SK, George JN. Clinical cardiac involvement in thrombotic thrombocytopenic purpura: a systematic review. *Transfusion*. 2008 Feb;48(2):382–92.
2. Ruutu T, Barosi G, Benjamin RJ, et al. European Group for Blood and Marrow Transplantation; European LeukemiaNet. Diagnostic criteria for hematopoietic stem cell transplant-associated microangiopathy: results of a consensus process by an International Working Group. *Haematologica.* 2007;92:95–100.
3. Gervasoni C, Ridolfo AL, Vaccarezza M, et al. Thrombotic microangiopathy in patients with acquired immunodeficiency syndrome before and during the era of introduction of highly active antiretroviral therapy. *Clin Infect Dis.* 2002;15(35):1534–40.
4. Moake JL, Rudy CK, Troll JH, et al. Unusually large plasma factor VIII: von Willebrand factor multimers in chronic relapsing thrombotic thrombocytopenic purpura. *N Engl J Med*. 1982 Dec 2;307(23):1432–5.
5. Furlan M, Robles R, Solenthaler M, Lämmle B. Acquired deficiency of von Willebrand factor-cleaving protease in a patient with thrombotic thrombocytopenic purpura. *Blood*. 1998 Apr 15;91(8):2839–46.
6. Bianchi V, Robles R, Alberio L, Furlan M, Lämmle B. Von Willebrand factor-cleaving protease (ADAMTS13) in thrombocytopenic disorders: a severely deficient activity is specific for thrombotic thrombocytopenic purpura. *Blood*. 2002 Jul 15;100(2):710–3.
7. Park YA, Hay SN, Brecher ME. ADAMTS13 activity levels in patients with human immunodeficiency virus-associated thrombotic microangiopathy and profound CD4 deficiency. *J Clin Apher*. 2009;24(1):32–6.
8. Bell WR, Braine HG, Ness PM, Kickler TS. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: clinical experience in 108 patients. *N Engl J Med.* 1991;325:398–403.
9. Rock GA, Shumak KH, Buskard NA, et al. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. *N Engl J Med.* 1991;325:393–7.
10. Bell WR, Braine HG, Ness PM, Kickler TS. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: clinical experience in 108 patients. *N Engl J Med.* 1991;325:398–403.

11. Nguyen L, Terrell DR, Duvall D, Vesely SK, George JN. Complications of plasma exchange in patients treated for thrombotic thrombocytopenic purpura. IV. An additional study of 43 consecutive patients, 2005 to 2008. *Transfusion*. 2009 Feb;49(2):392–4.
12. Bobbio-Pallavicini E, Gugliotta L, Centurioni R, et al. Antiplatelet agents in thrombotic thrombocytopenic purpura (TTP). Results of a randomized multicenter trial by the Italian Cooperative Group for TTP. *Haematologica.* 1997;82:429–35.
13. Bennett CL, Connors JM, Carwile JM, et al. Thrombotic thrombocytopenic purpura associated with clopidogrel. *N Engl J Med*. 2000 Jun 15;342(24): 1773–7.
14. Miller RF, Scully M, Cohen H, et al. Thrombotic thrombocytopaenic purpura in HIV-infected patients. *Int J STD AIDS*. 2005 Aug;16(8):538–42.