Case Report

Suspected Thrombotic Thrombocytopenic Purpura: Urgent Timely Therapeutic Plasma Exchange Improves Patient Prognosis

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Received: June, 2015.
Accepted: February, 2016.

Abstract

We present a case of 62 year male with dyspnea, cough and abdominal pain. There was a diagnostic dilemma for TTP as Hemolytic uremic syndrome, dengue, malaria and autoimmune hemolytic anemia were ruled out by investigations. ADAMTS-13 testing could not be performed due to financial constraints. The deteriorating life threatening condition of the patient compelled us to perform TPE on urgent basis. The close association of pathologist, clinician , intensivist and transfusion specialists improved patient outcome.

Key Words: *Microangiopathic hemolytic anemia, plasma exchange, thrombocytopenia, thrombotic thrombocytopenic purpura*

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a potentially fatal disorder characterized by platelet aggregates in the microvasculature, resulting in blood vessel occlusion that gives rise to tissue ischemia and end-organ damage. The condition is rare and has a reported incidence in adults of 3.7 per million.[1] Women are affected more frequently than men, with a male:female ratio of 1:2.[2] The diagnosis of TTP is usually first suspected clinically. Previously healthy individuals typically present with thrombocytopenia and microangiopathic hemolysis, in some cases accompanied by neurological dysfunction, fever, renal impairment, abdominal pain, chest pain, and cardiac arrhythmias. Prompt diagnosis is mandatory so that emergency treatment can be instituted immediately as delay may result in increased rates of treatment failure and mortality.[3] We present a case of suspected TTP, who was treated with therapeutic plasma exchange (TPE) with a dramatic response.

Case Report

A 62-year-male admitted with complaints of dyspnea, cough, abdominal pain, and weakness in lower limbs since 10 days. He had purpuric spots over upper limb and trunk. Preliminary work up showed: RBC - 2.4 million/µL, hemoglobin - 7.5 g/dL, total leukocyte count - 13,840/µL, polymorphs - 90%, platelet count - 15,000/µL, prothrombin time - 12.7 s, bleeding time - 1 min 20 s, and international normalized ratio - 1.28. Malaria test and dengue antigen test were negative. The peripheral blood examination showed microcytic hypochromic anemia with few schistocytes and tailed poikilocytes. The reticulocyte count was 0.6%. The osmotic fragility test was normal. The serum biochemistry profile showed mildly altered liver function tests: Total bilirubin - 2.5 mg/dL, direct bilirubin - 0.2 mg/dL, total protein - 5.8 mg/dL, albumin - 3.2 mg/dL, globulin - 2.6 mg/dL, AG ratio 1.23, serum glutamic oxaloacetic transaminase - 97 U/L, serum glutamic pyruvic transaminase - 53 U/L, alkaline phosphate - 76 U/L, gamma glutamyl transferase - 27 U/L, and lactate dehydrogenase - 1270 U/L. The electrolytes were normal sodium - 140 meq/L, potassium - 3.9 meq/L, chloride - 105 meq/L, and calcium - 8.9 meq/L. Urinary examination showed microscopic hematuria with positive nitrite test. HIV, hepatitis B surface antigen, and hepatitis C virus were negative. Sputum for acid-fast *Bacilli* was negative. Antinuclear antibodies and immunoblot were negative. Renal function test was unremarkable, urea - 36 mg/dL and creatinine - 0.8 mg/dL.

Based on the above investigations hemolytic anemia, hemolytic uremic syndrome, dengue, malaria, and autoimmune hemolytic anemia were ruled out.

There was a diagnostic dilemma as the classical pentad of TTP was not present with absence of fever and normal renal function. A provisional diagnosis of TTP was thought as the triad of anemia, thrombocytopenia and neurological deficit were present. ADAMTS13 quantification testing facility was unavailable in the house, sending the sample outside for ADAMTS-13 would have cost a lot of time and money which would have been fatal for the patient, the case was suspected as TTP.

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How to cite this article: Sareen R, Jain R, Sharma M, Gupta GN. Suspected Thrombotic Thrombocytopenic Purpura: Urgent Timely Therapeutic Plasma Exchange Improves Patient Prognosis. Glob J Transfus Med 2016;1:32-4.

Access this article online

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Single donor platelet (SDP) transfusion was carried out to improve the platelet count for securing central venous access. There was no improvement in platelet count after SDP infusion. A repeat compete blood count (CBC) was done and schistocytes were noted on peripheral smear examination. A diagnosis of TTP was established and TPE was planned. The patient meanwhile developed chest infection with poor oxygen saturation; he was subsequently taken on mechanical ventilation.

TPE was performed at 48 hourly intervals; 6 cycles with 1.2 plasma volume (PV) using fresh frozen plasma as replacement fluid. After the completion of the second cycle of TPE, 2 units of packed red cells (PRC) were infused to improve oxygenation. A total of 6 TPE cycles were performed. Serum calcium, albumin, and CBC were closely monitored after each cycle [Figures 1 and 2].

There was a dramatic response to treatment after the second cycle with an improvement in platelet counts [Table 1]. Subsequently, with the infusion of 2 PRC units there was a significant improvement in oxygen saturation and ventilator support was gradually weaned off. After fifth cycle, the platelet count was near normal [Table 1]. The patient was taken off the ventilator, and a final cycle of TPE was carried out. CBC showed lowering of schistocytes per high power field (HPF) and a normal platelet count [Table 1]. The patient was advised to add immunosuppressive therapy of rituximab which he could not afford due to cost constraints. Finally, he left the hospital against medical advice.

This case depicts the importance and closes the interaction between pathologist, clinician, intensivist, and blood transfusionist all working in conjunction with a strong clinicopathological correlation and timely intervention.

Discussion

The presence of TTP is suspected when a patient presents with characteristic clinical and laboratory findings without an apparent etiology.[4] These findings include microangiopathic hemolytic anemia, thrombocytopenia, normal renal function with acute renal insufficiency, neurological symptoms, and fever.[5] In the era before effective treatment with TPE, when the vast majority of patients died, and the full clinical course of untreated disease was observed it was common for all five classical features (pentad) to be present.[6] It is now rare for all components of the pentad to be present in the same individual as in our case.[4-7]

For the purpose of treatment, only the presence of microangiopathic hemolytic anemia and thrombocytopenia is sufficient to make an initial diagnosis and initiation of treatment with TPE.[8,9]

The peripheral blood smear examination is of utmost importance in making a diagnosis of TTP as microangiopathy is strongly supported if two or more schistocytes are seen in HPF.[10]

In a study by Burns *et al*., it was concluded that schistocyte count >4–5 per HPF was strongly suggestive of a diagnosis of TTP in appropriate clinical setting and in the absence of other known cause of thrombotic microangiopathy.[11] Our case highlights the importance of involving pathologist as early as possible in evaluating peripheral blood smear, especially for

Figure 1: Therapeutic plasma exchange cycle 1

Figure 2: Therapeutic plasma exchange cycle 6

Table 1: Therapeutic plasma exchange response chart

TPE cycle	Pretreatment	1	2	3	4	5	6	Post-D1	Post-D2	Post-D3
Hemoglobin (mg/dl)	4.8	4	7.5	9.8	9.2	8.6	7.8			
Platelet count (/cmm)	30,000	35,000	75,000	80,000	130,000	140,000	160,000	140,000	150,000	142,000
WBC count (/cmm)	8800	9880	12,500	11,580	12,750	10,360	5010			
PBF schistocyte (/HPF)	08-10	08-10	08-10	06-08	05-06	02-04	0-2			
Lactate dehydrogenase (IU/L)	1270			954			436			

TPE: Therapeutic plasma exchange, WBC: White blood cell, PBF: Peripheral blood film

clinicians who have less familiarity with TTP in a case like this with subtle findings.[11] there was absence of fever in our patient similar to more recent case.[12] ADAMTS13 has not done in our patient as the in-house facility for testing was not available. Moreover, there would have been a time delay had the test been sent to an outside laboratory, which would have delayed initiation of urgent treatment with TPE. The current practice of initiation of early treatment in suspected TTP (presenting with only thrombocytopenia and microangiopathic hemolytic anemia) without an obvious apparent cause and ADAMTS 13 levels is supported in studies by Kremer *et al*.,[8] Raife *et al*.,[9] Wolf *et al*.,[13] and Peyvandi *et al*.[14]

The aphaeresis device used for TPE was based on centrifugation methodology. In these aphaeresis devices, whole blood is pumped into a rapidly rotating separation chamber. Components then separate into layers based on their density, with the most dense element (red blood cells) migrating the farthest from the axis of rotation and the least dense portion (plasma) layering closest to the axis of rotation. Intermediate layers moving from the axis of rotation outward are platelets, lymphocytes, and granulocytes.[15] The other devices with filtration based aphaeresis for performing TPE utilizing filters are not used in the United States. The total volume processed was 1.2 PV as further removal of PV beyond 1.5 PV removes smaller, less clinically significant pathological substance present in plasma while prolonging the procedure and exposing the patient to more replacement fluid and anticoagulants, resulting in increased risk of complications without benefit to the patient.[16] Plasma is used as replacement fluid in limited disorders, TTP being one of them as in our case.[17] In order to obtain the venous access, central venous catheter was used with full aseptic precautions. Care must be taken of the central line with regular flushing before each procedure as the central line complications are life threatening in TPE.[18]

Conclusion

Since patients rarely present with the pentad of TTP, recognition of atypical cases of TTP, and prompt initiation of the management is an important factor in improved patient survival. TTP is a medical emergency that is almost always fatal if exchange plasmapheresis is not initiated early. Our case depicts the importance and close the interaction between pathologist, clinician, intensivist, and transfusionist all working in conjunction to improve the clinical outcome of patients with TTP.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Török TJ, Holman RC, Chorba TL. Increasing mortality from thrombotic thrombocytopenic purpura in the United States – Analysis of national mortality data, 1968-1991. Am J Hematol 1995;50:84-90.
2. Rock GA, Shumak KH, Buskard NA, Blanchette VS, Kelton JG, Nair RC, *et al.* Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. Canadian Apheresis Study Group. N Engl J Med 1991;325:393-7.
3. Pereira A, Mazzara R, Monteagudo J, Sanz C, Puig L, Martínez A, *et al.* Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome: A multivariate analysis of factors predicting the response to plasma exchange. Ann Hematol 1995;70:319-23.
4. Remuzzi G. HUS and TTP: Variable expression of a single entity. Kidney Int 1987;32:292-308.
5. Amorosi EL, Ultmann JE. Thrombotic thrombocytopenic purpura: Report of 16 cases and review of the literature. Medicine (Baltimore) 1966;45:139-59.
6. Ruggenenti P, Noris M, Remuzzi G. Thrombotic microangiopathy, hemolytic uremic syndrome, and thrombotic thrombocytopenic purpura. Kidney Int 2001;60:831.
7. Siegler R, Berry PL, Hogg RL. Comparison of the epidemiologic and clinical features of endemic and sporadic forms of hemolytic-uremic syndrome (HUS) in 210 USA children. Report of the Southwest Pediatric Nephrology Study Group (abstract). Kidney Int 1986;29:1086.
8. Kremer Hovinga JA, Vesely SK, Terrell DR, Lämmle B, George JN. Survival and relapse in patients with thrombotic thrombocytopenic purpura. Blood 2010;115:1500-11.
9. Raife T, Atkinson B, Montgomery R, Vesely S, Friedman K. Severe deficiency of VWF-cleaving protease (ADAMTS13) activity defines a distinct population of thrombotic microangiopathy patients. Transfusion 2004;44:146-50.
10. George JN. How I treat patients with thrombotic thrombocytopenic purpura: 2010. Blood 2010;116:4060-9.
11. Burns ER, Lou Y, Pathak A. Morphologic diagnosis of thrombotic thrombocytopenic purpura. Am J Hematol 2004;75:18-21.
12. Booth KK, Terrell DR, Vesely SK, George JN. Systemic infections mimicking thrombotic thrombocytopenic purpura. Am J Hematol 2011;86:743-51.
13. Wolf G. Not known from ADAMTS-13 – Novel insights into the pathophysiology of thrombotic microangiopathies. Nephrol Dial Transplant 2004;19:1687.
14. Peyvandi F, Ferrari S, Lavoretano S, Canciani MT, Mannucci PM. Von Willebrand factor cleaving protease (ADAMTS-13) and ADAMTS-13 neutralizing autoantibodies in 100 patients with thrombotic thrombocytopenic purpura. Br J Haematol 2004;127:433.
15. Burgstaler EA. Current instrumentation for apheresis. In: McLeod BC, Szczepiorkowski ZM, Weinstein R, Winters JL, editors. Apheresis: Principles and Practice. 3rd ed. Bethesda, MD: AABB Press; 2010. p. 95-130.
16. Szczepiorkowski ZM, Winters JL, Bandarenko N, Kim HC, Linenberger ML, Marques MB, *et al*. Guidelines on the use of therapeutic apheresis in clinical practice: Evidence-based approach from the Apheresis Applications Committee of the American Society for Apheresis. J Clin Apher 2010;25:83-177.
17. Derksen RH, Schuurman HJ, Gmelig Meyling FH, Stuyvenberg A, Kater L. The efficacy of plasma exchange in the removal of plasma components. J Lab Clin Med 1984;104:346-54.
18. McLeod BC. Therapeutic apheresis: Use of human serum albumin, fresh frozen plasma and cryosupernatant plasma in therapeutic plasma exchange. Best Pract Res Clin Haematol 2006;19:157-67.