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Sepsis Mimicking TTP-Case Report and Review of Literature

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ABSTRACT

Here we report a case of Sepsis mimicking as thrombotic thrombocytopenic purpura in a cancer patient with Urothelioma. A 61-year-old man with High grade Urothelial Carcinoma of left renal pelvis (Multifocal disease) Stage-4 presented with Fever on and off since 1 week and shortness of breath at rest since 2 days and hematuria since 1 day.Later in the course, he developed thrombocytopenia followed by MAHA (Micro Angiopathic haemolytic Anaemia), and other lab abnormalities .Thrombotic thrombocytopenic purpura (TTP) was suspected, and total plasma exchange was considered. Since serum procalcitonin,Total leucocyte count was very high and also had elevated prothrombin time, ADAMTS13(a disintegrin and metalloproteinase with thrombospondin type 1 motifs, member 13) was sent for confirmation showed that ADAMTS13 activity of more than 10% for which plasmapheresis was delayed , later patient was treated for sepsis , but patient did not respond and succumbed . This case shows that Sepsis can mimic TTP making diagnosis and treatment extremely difficult. In this type of clinical dilemma to do total plasma exchange (TPE) which is the main modality of treatment for TTP ADAMTS13 activity helps us to prioritise treatment.

Keywords: Urothelioma, Sepsis, TTP

Introduction

Thrombotic thrombocytopenic purpura (TTP) is often described as a pentad of thrombocytopenia is accompanied by an elevated lactate dehydrogenase (LDH) level, anemia, fever, renal dysfunction, and neurological abnormalities caused by unregulated vonWillebrand factor- (VWF-) dependent platelet thrombosis. In case of cancer patients (TTP) can be manifestation of the malignancy itself or a complication of its therapy. In cancer patients in 1979, Antman et al. in the review on MAHA (Micro Angiopathic Haemolytic Anaemia) and cancer proposed that the haemolysis and thrombocytopenia were primarily caused by mechanical obstruction of the vascular lumen by tumour cell emboli. They concluded that a variety of systemic malignancies could cause clinico pathological features of TMA without coagulation abnormalities like disseminated intravascular coagulation. MAHA is difficult to treat without reversing the basic underlying disease process. Thrombocytopenia (platelet count < 150,000/μl) is common in critically ill patients, with an estimated incidence of 20%–40% at some point during the intensive care unit (ICU) stay [3]. To date, studies have focused on the incidence, risk factors and clinical outcomes for the development of thrombocytopenia, in general ICU populations. The data available about the incidence of secondary consumptive thrombocytopenia, like disseminated intravascular coagulation (DIC) and thrombotic thrombocytopenic purpura (TTP) in patients with sepsis are limited [1, 2].

Case

A 61-year-old man with a history of recently diagnosed with High grade Urothelial Carcinoma of left renal pelvis(Multifocal disease) Stage-4, presented with Fever on and off since 1 week and shortness of breath at rest since 2 days, haematuria since 1 day. Patient was admitted in the ICU, Clinically Orthopenic, Pulse-110/min, Blood Pressure-140/80 mm Hg, Spo2- with 1L O2 -96%. His initial lab values on arrival at our hospital were as follows: platelets 2,19,000 cells per cubic mm, haemoglobin (Hb) 7.1 g/dl, leucocytes 26,670 cells per cubic mm, blood urea nitrogen 27, blood urea nitrogen/creatinine 21.07, INR 1.94,PCT 17.23, CRP 24, PRO-BNP 224,Urine routine showed plenty of RBCs and 1-2 puss cells, CT thorax showed no evidence of pulmonary consolidation/pleural effusion. CT thorax showed no evidence of pulmonary consolidation/pleural effusion, ECHO showed normal LV chambers and no RWMA. In view of raised PCT and TLC, with the background of fever and breathlessness, sepsis was suspected, blood and urine cultures sent and antibiotics were initiated.

On day 3 of admission, Hb 6.5, HCT 20.1,TLC 28 950 cells per cubic mm, PLT dropped to 70000, creatinine 2.1,BUN 41, INR 1.87(after transfusing 20ml/Kg of FFP) PCT 30.32. The symptoms gradually worsened, patient developed altered sensorium, worsening anemia, renal function, and thrombocytopenia with raising PCT titers. In view of thrombocytopenia, worsening renal function, altered sensorium, high suspicion of TTP was considered and following labs were done-T.bili-8.4, direct bilirubin 2.3, LDH 984, reticulocyte count 7%, serum ferritin 1300, TIBC 170, folic acid 11, peripheral smear suggestive of microangiopathic

hemolytic anemia with neutrophilic leukocytosis, coombs direct and indirect negative for agglutination. In view of worsening renal function and oliguria, patient was offered hemodialysis, since clinical and biochemical indices pointing towards TTP total plasma exchange (TPE) was considered as an option. However, since patient had leukocytosis, and prolonged PT/INR, sepsis and DIC also considered and coagulation profile done, which showed fibrinogen 238,FDP<10microgram/ml, cultures at the end of 48 hour didn't grow any organism. Since DIC was ruled out,TTP total plasma exchange (TPE) was considered but since patient INR was prolonged, we decided to consider ADAMTS13 activity test before doing total plasma exchange(TPE), which showed ADAMTS13 activity19.9 and anti-ADAMTS13 antibody 12IU/ml, %, the level was normal as per standard.

Hence total plasma exchange (TPE) was deferred. Patient was treated for sepsis with antibiotics (meropenem and colistin) and other supportive treatment, but patient deteriorated, had refractory hypotension and succumb to death.

Literature Review

There are a few similar cases in the literature that are presented with infection and TTPA 44- year-old woman, who had no special medical history or familial history of TMAs, was admitted on suspicion of septic shock. Physical examination revealed gangrene on her soles. Blood tests revealed a decreased platelet count, disseminated intravascular coagulation (DIC), renal dysfunction, hemolysis, and infection investigators excluded thrombotic thrombocytopenic purpura and Shiga toxin-producing Escherichia coli-induced HUS, and clinically diagnosed as Atypical HUS and did plasma exchange .In their case Plasma exchange only improved lactate dehydrogenase levels. Later Subsequent tests revealed elevated serum levels of soluble C5b-9, and genetic testing revealed compound heterozygous c.184G>A (Val62Ile) and c.1204T>C (Tyr402His) single-nucleotide polymorphisms in complement factor H and diagnosed as complement-mediated TMA accompanied by DIC. Another case described by Jeffrey R Schreiber, etal, showed initial presentation as TTP and later found S. pneumonia septicemia it is reported as TTP coincident with S pneumonia septicemia. Since the latter was detected after TTP was diagnosed. The largest of all Oklahoma TTP-HUS Registry showed 31 patients who were initially diagnosed with TTP and treated with plasma exchange but whose presenting clinical features were subsequently attributed to a systemic infection. one more case report from srilanka Medhini Boteju et al reported Cytomegalovirus induced refractory TTP in an immunocompetent individual [4-7].

Discussion

TTP is a rare disease; the exact incidence is not clear, with the available studies incidences is between 1 and 13 cases per million people depending on geographic location. TTP most often occurs after 40 years of age, but congenital forms can occur in children. TTP is more common in women with a 2:1 female to male predominance. The mortality in TTP without treatment is 90%, but this drops to a mortality of 10% to 20% with proper treatment. However, even with successful treatment relapse occurs in up to 36% of patients. The cause for TTP is idiopathic most of the times, but some are associated with chemotherapy, bone marrow transplantation, infections and autoimmune disease. The pathophysiology of TTP is the deficiency of an important cleavage protease (i.e., ADAMTS13) which causes excessive amounts of ultra-large von Willebrand factor (UL-vWF) multimers in the circulation, These UL-vWFmultimers bind to and activate platelets, causing spontaneous aggregation of platelets and activation of coagulation cascade, leading to formation of multiple platelet thrombi inside the capillaries and the small arterioles, resulting in the development of specific TTP clinical and laboratory manifestations [8-9].

Although most of the other cases we described from the literature presented with TTP on presentation and later was attributed to systemic infection we should have high index of suspicion for TTP in patients with systemic infections and all other contributing factors like autoimmune disease, drugs, should be considered and treated since treatment of TTP with plasma exchange, and underlying cause significantly reduces mortality. In case of clinical dilemma in differentiating between systemic infections, DIC, ADAMTS13 levels will help us in diagnosing TTP.

Conclusion

TTP should be considered in all patients with systemic infection presenting with MAHA, and thrombocytopenia. It is critical to have a high index of suspicion for TTP in this context because delay in diagnosis may lead to death and early recognition of TTP and proper treatment can lead to rapid improvement of symptoms and can prevent unnecessary therapy resulting in further complications it is also imperative to use ADAMTS13 effectively before considering Plasma exchange as it can lead to coagulation abnormalities which can be life threatening.

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