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Thrombotic thrombocytopenic purpura and neurologic manifestations – Case report and integrative review.

ORIGINAL

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Abstract

Introduction: Thrombotic thrombocytopenic Purpura (TTP) is a rare and pontentially life-threatening condition caused by ADAMTS13 enzyme complex deficiency. It leads to microthrombi formation in the microvasculature, which may cause several organs manifestations. It mainly affects kidneys and nervous system leading to severe complications. The best treatment of TTP nowadays is Plasma Exchange (PEx). The most commom neurologic manifestation of TTP is headache, but stroke, mental confusion and others can also be present.

Objective: To describe a case of atypical neurologic manifestation of TTP and to perform an integrative review.

Case Report: Female patient, 32 years old was admitted to the emergency room with important dyspnea. She also presented hypotension, tachycardia and low oxygen-hemoglobin saturation. After these symptoms were stabilized, she was hospitalized for further investigation. During her hospitalization, she developed microangiopatic anemia, thrombocytopenia and renal failure, she also had a historic of neurologic manifestations such as strenght decrease in lower and upper limbs, gagging, dysphagia. She was diagnosed with TTP and we indicated a hospital transference for her to realize this procedure.

Discussion: The Thrombotic thrombocytopenic purpura is a rare disease that mainly affects women. We present a case of atypical neurologic manifestations of TTP consisting with headache.

Keywords
Implicit association; explicit measure; food choice; healthy eating.

Conclusion: We conclude that to be alert in patients in the emergency department with neurologic manifestations. Once the patient did not present any of the most commom neurologic symptons, it is a rare case.

Introduction

Thrombotic thrombocytopenic purpura is a rare condition. Annual incidence is between 4 to 13 cases per million in different countries around the world. It occurs due to the decreased activity or the deficiency of ADAMTS13, (a desintegrin and metalloproteinase, with a thrombospondin type 1 motif, member 13) a Von Willebrand Factor (VWF)-cleaving protease, leading to accumulation of large VWF multimers, resulting in microthrombi formation in the microvasculature . In addition, there is also the possibility of blood presence of auto-antibodies Anti-ADAMTS13, which can further reduce the ADAMTS13 activity. Clinically, TTP arises as a microangiophatic anemia (with the presence of schistocytes in the peripheral blood, thrombocytopenia and variable damage in multiple organs. Kidneys and Central Nervous System are the most commonly affected. Fever occurs occasionally. The main neurologic manifestations are headaches, seizures and floating strenght decrease. Atypical neurologic manifestations are rarely described. We report here a case of atypical neurologic manifestation in TTP and then we performed an integrative review of literature focusing on the most important points.

Methods

Search on PubMed on 05/29/2016 using the terms "Neurologic Manifestations " [MeSH] AND "Purpura", thrombotic thrombocytopenic" [Mesh]. Integrative Review and Case report.

Results

The search resulted in 135 articles in total. All the designs of studys were included. Articles from the last 10 years were included. Articles in english were included. Articles in pediatric population were excluded. Articles in experimental animals were excluded, plus the editorials,comments, replys and images. Other issues were excluded. After applying the inclusion and exclusion criteria, 10 articles were remaining.

Case Report

Female patient, 32 years old, was brought by the emergency mobile care service and admitted in the emergency room for a severe dyspnea. At physical examination, she presented hypotension, tachycardia (HR=128), Temperature= 37,4°C. She had crackles in both bases, SatO2 68%. She was conscient and oriented but she did not present motor response. It was placed a Venturi Mask Oxygen 50% and rapid infusion of normal saline was made. The patient had an important improvement on the vital signs, with normal blood pressure, O2 saturation and heart rate. Laboratorial exams: Hemoglobin: 16,1mg/dL; Hematocrit: 56,5%; Leukocytes 12.600/mm³ (86% neutrophils); platelets 357.000/mm³; creatinine 0,20mg/dL; urea 27,4mg/dL; sodium 137mEq/L; potassium 5,7mEq/L. Relatives related that 7 months before, the patient began to feel some hip radiating to lower limbs pain with predominance on the right side. 2 months after, she

developed pain in the upper limbs associated with proximal muscle weakness. 1 moth after these new symptoms, the patient was bedridden, needing help to perform basic daily activities, however, she did not have dysautonomia, or strenght oscillations. 2 months before the hospitalization, she presented progressive dysphagia, multiple gagging, loss of cervical support and orthopnea. There was no chronic use of medications or relevant family history.

During hospitalization, she was submitted to antibiotic therapy with piperacillin + tazobactam. On the second day of hospitalization, the patient developed cardiac arrest (assystolia), the resuscitation process was performed for 10 minutes and it was succesfull. On the ninth day of hospitalization, the patient presented a microangiopathic anemia, thrombocytopenia, high seric levels of urea and creatinine and hemolysis markers – increased levels of lactate dehydrogenase (2691U/L), reticulocytes with a 6% relative value and an absolute value of 132,000/mm³. TP= 17,8s aPTT=33,6, ADAMTS13 activity was 4%. The hematologist was contacted and after studying the case, raised the diagnostic hypothesis of Thrombotic thrombocytopenic purpura, indicating Plasma Exchange, requesting transfer to specialized service and starting therapy with fresh frozen plasma. Tha patient was transfered to a specialized service, where she was submitted to PEx. After the PEx, she had an improvement on the clinical status and received hospitalar discharge after ten days.

Discussion

Thrombotic thrombocytopenic purpura is a rare disease with an annual incidence of around 10 cases per 1 million people . This is a serious condition with a mortality rate of approximately 90% if left

Author:	Year:	Diagnosis	Sex:	Age:	N° of cases:	Mainly Neurologic Manifestation:
Saultz et al.	2015	TTP(21)/ aHUS(10)	Male(3)/ Female(28)	51 (median – range 19-69)	31	Headache
Geethakumari et al.	2013	TTP/ Cardiac papillary fibroelastoma	Female	49	1	Stroke
Sandouk et al.	2012	TTP/ DRESS Syndrome	Male	50	1	Stroke
Mehta et al.	2012	TTP/ Multiple Myeloma	Female	70	1	Mental Confusion/Lethargy
Binder et al.	2010	TTP/ SLE	Female	16	1	Headache/ MentalConfusion
Patel et al.	2010	TTP/DVP	Male	58	1	Strenght decrease
Bezov et al.	2010	TTP/HIV (1) TTP/DVP (1)	Male (1) Female (1)	29 (1) 65 (1)	2	Headache
De Jong et al.	2010	TTP/DM /Hypertension	Male	55	1	Coma
Thomas et al.	2008	TTP/Mitral Prolapse/ Depression	Female	25	1	Headache
McCormick	2007	TTP/ Raynaud phenomenon	Female	38	1	Numbness and tingling transient

untreated and 20% if treated properly. Therefore, it is important to note that an early diagnosis and proper treatment are essential as regards the improvement on survival chances. [1-3]

The disease can have three etiologies: autoimmune, acquired idiopathic, genetic inheritance (Upshaw - Schulman syndrome). [1] The pathophysiology of TTP, regardless of etiology, is mainly linked to the activity of circulating enzyme complex ADAMTS13, responsible for the cleavage of the Von Willebrand factor, a glycoprotein which main function is platelet adhesion and aggregation, facilitating coagulation. [4,5,10] In the absence of ADAMTS 13 or its decreased activity, there is an environment conducive to excessive link between Von Willebrand Factor and platelets, causing greater adhesion, aggregation and microthrombosis. [10-11] In autoimmune form is striking the presence of anti - ADAMTS13 autoantibodies, primarily of the IgG class, whereas in the idiopathic form, the main factor of susceptibility is the presence of HLA-DRB1 * 11 in Caucasians. [12] In Upshaw - Schulman syndrome, occurs mutations in the ADAMTS13 gene, over 50 different mutations have been identified. [10-12].

The classic pentad (microangiopathic hemolytic anemia, thrombocytopenia, neurologic manifestations, renal manifestations, fever) of clinical manifestations occurs in less than 10 % of the cases, it is necessary for the initial diagnosis only the presence of microangiopathic hemolytic anemia and thrombocytopenia without any apparent cause. [4,6] The main clinical manifestations are renal, acute renal failure is the most common among this group, and neurological, which are seizures, floating focal deficits, changes in the level of consciousness and headache the most commons. Fever may be present, requiring deeply investigation for infectious diseases.[7,13-15].

In this review, considering the case reports, the neurological manifestations were: headache (40%), stroke (30%), confusional state (20%) and other (10%) . The most prevalent neurological complication in PTT is headache . Saultz et al (2015) in a prospective cohort of 31 patients showed that headache has a higher incidence and higher severity in patients diagnosed with TTP than in the general population.

Diagnosis is made through the association of clinical and laboratorial findings, especially the dosage of ADAMTS13 activity and presence of autoantibodies Anti ADAMTS13 IgG. [8,9] It is important to note that various diseases are part of the differential diagnosis and may present similarly to TTP, the Hemolytic Uremic Syndrome is the main condition described [16]. Other conditions that can mimic TTP are disseminated intravascular coagulation, Evans Syndrome, Antibody antiphospholipid syndrome, severe vasculitis, malignant hypertension, disseminated metastatic cancer. [17] Some anticancer drugs such as Gemcitabin, Mitomycin C, Cisplatin, may also be related to the appearance of TTP. [18]

Regarding treatment, PEx should be the first choice because 80% of the patients treated with PEx survive. Immunosuppressants, glucocorticoids and fresh frozen plasma may also be used. Some studies show cases of death as a complication of plasmapheresis, which makes it clear that, although it is a good treatment option, does not come without risks and new therapies need to be developed. [8,19-27]

Conclusion

It is important to arise the diagnostic possibility of thrombotic thrombocytopenic purpura in patients admitted to emergency services with neurological symptoms to clarify, in order to diagnose the earliest as possible suspected cases, despite its relative rarity, since early treatment implies better prognosis outcome. We can also conclude that headache is the main neurologic manifestation in patientes with TTP.

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