

Thrombotic thrombocytopenic purpura: The fatal consequences of treatment delay

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Thrombotic thrombocytopenic purpura (TTP) is a medical emergency that is most often fatal if appropriate treatment is not promptly initiated. For patients with suspected diagnosis of TTP (thrombocytopenia and microangiopathic hemolytic anemia without an alternative explanation), it is recommended urgent Plasma Exchange therapy (PEX), in order to reverse the reduced von Willebrand factor-cleaving protease (ADAMTS13) activity. We herein report a new case of serious acquired thrombotic thrombocytopenic purpura.

A 78-year-old Caucasian woman was admitted to our hospital for sudden onset of confusion and trouble speaking one hour before. She had a past history of essential hypertension and complete heart block (2005) treated with a pacemaker.

The physical examination showed fluctuant anomic aphasia, without impairment of comprehension, repetition or presence of dysarthria. Right central facial palsy and right upper limb weakness (4+/5) were also noted. Her blood pressure was 130/78 mmHg, heart rate of 110 rpm and axillary temperature of 38.5°C. Laboratory workup showed: hemoglobin 5.0 g/dL [range: 11.5-15.5], platelet of 65.000/ μ L [150.000-370.000] using a sodium citrate collection tube, WBC 18.300/ μ L [3.700-11.600] (53% neutrophils; 11% lymphocytes), LDH 916 IU/L [84 - 246], CRP 87.1 mg/dL [0.0-3.0], creatinine 0.76 mg/dL [0.55-1.02], urea 56 mg/dL [15-39], ALT 26 IU/L [13-56], indirect bilirubin 1.0 mg/dL [0.1-0.9], K 4.0 mmol/L [3.5-5.1], fibrinogen 170 mg/dL [150-450]. Then, peripheral blood smear was performed, revealing schistocytosis of 3.5% [<1.0] and negative Coombs' test. Brain CT did not show any significant abnormalities.

TTP was suspected on the basis of these results, and thus, fresh frozen plasma (15 mL/kg/day) and intravenous methylprednisolone were started (1 mg/kg/day). Packed red cells transfusion was also given. There was a quick recovery in her clinical status, with only residual central facial palsy. The patient was hospitalized and PEX was scheduled the next morning.

During that same night, the patient showed quick neurologic deterioration (GCS 3, with fixed nonreactive pupils), which prompted another brain CT showing left-sided acute subdural hematoma and subarachnoid hemorrhage, as well as subfalcine and transtentorial herniation. Then, after discussion with the family, agreed treatment limitation was adopted, and exitus was confirmed 12 hours later. Autopsy was not performed.

We searched MEDLINE (1950 to week 1, December 2016) and EMBASE (1980 to week 49, 2016) using keyword searching related to "Thrombotic thrombocytopenic purpura" and "intracranial hemorrhage". Neurologic impairment have been commonly reported,

although, usually transient and reversible [1-2]. Multifocal hemorrhagic lesions are quite rare, to our knowledge, this is the third case reported [3]. Even despite the low incidence of single or multiple intracranial bleeding, it is worth consideration, since these previously healthy middle-aged adults, responds well to appropriate therapy.

In the management of TTP, PEX therapy has been advocated as the standard treatment. However, PEX may not be immediately available, and for patients with an expected delay, infusion of donor plasma is commonly used, to the cost of more adverse events [4], since plasma infusion does not remove the antibody to ADAMTS13 and moreover the volume of plasma and amount of ADAMTS13 delivered is significantly less than in PEX [5].

Corticosteroids are also used, although documentation of their efficacy is questionable. Furthermore, it is remarkable in our patient, the temporal relationship between starting methylprednisolone and development of intracranial hemorrhage. A sudden rise in blood pressure, a known adverse effect of corticosteroids, could have initiated or worsened intracranial bleeding.

Our case illustrates that PEX therapy should not be delayed in TTP, and while waiting, plasma infusion or immunosuppressive therapy may not be adequate substitutes. Awareness and close monitoring of a patient's medical condition is mandatory, since TTP can be a treatable and curable condition.

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