

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/pjnns>

Case report

Acute neurological symptoms of Moschcowitz disease—Case report



Anetta Lasek-Bal*, Katarzyna Kosarz-Lanczek, Zofia Kazibutowska

Department of Neurology, Medical University of Silesia Hospital No. 7, Professor Leszek Giec Upper Silesian Medical Centre, Katowice, Poland

ARTICLE INFO

Article history:

Received 5 April 2014

Accepted 2 July 2014

Available online 11 July 2014

Keywords:

Neurologic sign

Moschcowitz disease

Thrombotic purpura

ABSTRACT

Thrombotic thrombocytopenic purpura (TTP, Moschcowitz disease) is characterized by thrombotic microangiopathy leading to microvascular occlusion and ischemic dysfunction of various organs including the brain. In the course of the rare disease most patients develop neurological symptoms of varying severity and characteristics. The case presented is that of a 34-year-old female patient with profound thrombocytopenia, anemia and rapidly progressive neurological deterioration into coma with normal result of brain imaging. TTP was recognized on the basis of hematological analysis. The initiated steroid therapy and plasma exchange failed to prevent the turbulent course of disease in the patient, who died exhibiting symptoms of multiple organ failure caused by thrombotic microangiopathy. TTP remains to be a diagnostic challenge, particularly in the case of atypical symptoms or when neuroimaging and laboratory results are inconclusive. Before using the corticosteroids and plasma exchange, TTP had a case fatality rate of approx. 90% (Podolak-Dawidziak, 2013). Nowadays recovery is possible when vigorous treatment is introduced early in the course of this disease.

© 2014 Polish Neurological Society. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

1. Case report

A 34-year-old woman was admitted to the Department of Internal Medicine due to general weakness and subfebrile state, both of which appeared four days earlier. In the week before admission, she had a mild infection of the upper respiratory tract; otherwise her individual and family interview did not reveal any burden. She did not use any chronic treatment. The following results were found in the course of

diagnostic procedures: thrombocytes $8000/\mu\text{l}$, red blood cell (RBC) count $2.9 \times 10^6/\mu\text{l}$, low hemoglobin (Hb) 8.14 g/dl, white blood cell (WBC) count $9400/\mu\text{l}$; normal biochemical hepatic and renal parameters and normal results of abdomen ultrasound examination, gastroscopy and chest X-ray.

On the second day of hospitalization, a transient speech disturbance in the form of motor aphasia and numbness of the right cheek appeared twice within a few hours; these lasted several minutes and resolved without residual symptoms. The consulting neurologist found no significant deviations in the

* Corresponding author at: Oddział Neurologii, Samodzielny Publiczny Szpital Kliniczny Nr 7 Śląski Uniwersytet Medyczny, Górnośląskie Centrum Medyczne im. Prof. Leszka Gieca, ul. Ziołowa 45/47, postal code 40-735 Katowice, Poland. Tel.: +48 32 359 83 06; fax: +48 32 202 95 92.

E-mail address: alasek@gcm.pl (A. Lasek-Bal).

<http://dx.doi.org/10.1016/j.pjnns.2014.07.002>

0028-3843/© 2014 Polish Neurological Society. Published by Elsevier Urban & Partner Sp. z o.o. All rights reserved.

physical examination. During hospitalization, thrombocytes and red blood cells were supplemented; however, that failed to cause any significant improvement in the morphotic parameters.

Again, on the third day of hospitalization, the patient experienced speech disturbances. Neurological examination revealed mixed aphasia with predominant motor aphasia, without other clinical symptoms. Computed tomography of the head did not reveal any lesions. Within several hours, the following signs appeared: body temperature of 38.5 °C, increasing quantitative disturbances of consciousness. On the following day, the patient was transferred to the Department of Neurology, where, at the admission, the following were found: body temperature of 38.1 °C, stupor (8/15 points on the Glasgow Coma Scale), normal pupils, slight right-sided hemiparesis with the Babinski sign present, no meningeal syndrome. Magnetic Resonance Imaging (MRI) of the head (with contrast enhancement and including DWI) did not reveal any pathology within the intracranial structures. The blood test revealed the following results: thrombocytes 5000/ul, RBC 2.6×10^6 /ul, present erythroblasts, Hb 8.12 g/dl, WBC 13,400/ul, D-dimers 9000.5 ng/dl (N up to 550 ng/dl), normal ionogram, bilirubin and creatinine.

Due to profound thrombocytopenia lumbar puncture was abandoned. Antibiotic therapy, virusostatic treatment, steroid therapy and freshly frozen plasma were included as treatment. There was a further increase of disorders of consciousness, high body temperature and absence of meningeal symptoms. On the second day of hospitalization in the Department of Neurology, there was an increase in creatinine concentration 1.17 mg/dl (N 0.5–0.95) and bilirubin concentration 4.47 mg/dl (N up to 1.2); proteinuria of 100 mg/dl also occurred. The results obtained showed high levels of L-lactate dehydrogenase (LDH): 2137 U/l (N 135–214), normal haploglobin levels and antiglobulin test results, normal result of serological tests for HIV infection, connective tissue diseases, anti-cardiolipin antibodies, plasmatic coagulation factors and procalcitonin.

After the analysis of the course of disease, the nature of neurological symptoms and the results of imaging tests, it was hypothesized that the nervous system was secondarily affected in the course of immune-mediated hematological disease. Given the persistent thrombocytopenia, anemia and increasing kidney disorders thrombotic thrombocytopenic purpura (Moschcowitz disease), hemolytic uremic anemia, disseminate intravascular coagulation (DIC) and Evans syndrome were considered in the first place. The consulting hematologist found schistocytes in the peripheral blood smear and ultimately confirmed the diagnosis of Moschcowitz disease. Steroid therapy, supply of freshly frozen plasma and red blood cell concentrate were continued. One session of plasma exchange (PE) was performed, after which the patient's state improved in terms of the state of wakefulness, mobility of the right limbs; fever subsided. On the second day after admission to the Department of Neurology, the patient was transferred to the Department of Hematology for further treatment, including the continuation of PE. However, the patient's condition has significantly worsened and she died showing the symptoms of acute respiratory failure. Autopsy indicated multiple organ failure in the course of

thrombocytopenic purpura, with small hemorrhagic infarction in the pancreas and an area of myocardial necrosis. Histological evaluation showed diffuse vascular lesions with severe involvement of large artery branches, medium-sized arteries and small vessels with arterial occlusion.

TTP was first described in 1924 by Moschcowitz in relation to a patient with the following triad of symptoms: thrombocytopenia, hemolytic anemia and variable atypical neurological symptoms [2]. The first description of the disease presented in the literature is an accurate characterization of the clinical image of TTP in our patient.

Thrombotic thrombocytopenic purpura (TTP, Moschcowitz disease) is a thrombotic microangiopathy with thrombocytopenia caused by intravascular platelet aggregation. Formation of blood clots in the capillaries and small arterioles is caused by endothelial damage and the presence of von Willebrand factor multimers (unusually large multimers of von Willebrand factor, UlvWF) binding to thrombocyte receptors. The metalloproteinase binding antibody ADAMS13 (disintegrin and metalloproteinase with thrombospondin-1-like domain) that disintegrates the UlvWF molecules, which prevents their proper degradation, is present in the acute phase of the disease. Additionally, damage occurs to the erythrocytes, which is associated with the presence of platelet aggregates in the microcirculation and is confirmed by the presence of schistocytes in peripheral blood smear [3]. Ischemia of various organs, including the nervous system, occurs as a result of disturbances in the microcirculation. The disease, more often affecting women aged 30–40, starts suddenly and is often preceded by a mild upper respiratory infection. TTP may be either drug-induced or it may accompany a neoplastic disease. Its clinical course reveals the presence of fever, symptoms of hemorrhagic diathesis and hemolysis (anemia, icterus), petechiae on the skin of limbs and trunk and on the mucous membrane of oral cavity, abdominal pain and neurological symptoms with varying characteristics in the majority of patients. The DIC syndrome develops in approximately 10% of patients [1].

The laboratory results reveal normocytic anemia, erythroblasts and schistocytes, thrombocytopenia, reticulocytosis, increased bilirubin, increased LDH activity, proteinuria and negative Coombs reactions. The course of the disease is violent at times, and if untreated, it leads to death in approximately 90% of patients [1,4].

Steroids (Methylprednisolone 0.75 mg/kg intravenously every 12 h for 1–4 weeks) with transfusion of freshly frozen plasma (40–60 ml/kg/d) and PE are applied in treatment. In patients refractory to PE, Rituximab is recommended (intravenously 375 mg/m² within the first 3 days or 375 mg/m² weekly for 4–8 weeks). In patients with exacerbation during steroid therapy or treatment with Rituximab-vincristine is applied (1.4 mg/kg intravenously for 3 days and from the 4th day) follow up by cyclophosphamide or azathioprine. The role of splenectomy in the current management of TTP is limited. It causes improvement in some patients within the remission period after the first relapse. The supplementation of red blood cells is also important. The application of platelet concentrate increases thrombosis [1,5–7].

The case presented here relates to a female patient with TTP whose neurological symptoms were dominant in the

course of the disease. According to the literature, the most common symptoms of damage to the nervous system are headaches, motor deficits, seizures and coma [8,9]. In most cases, coma is preceded by focal symptoms or seizures [10]. It has less often been described in the absence of focal neurological deficits or seizures [11]. Kelly et al. presented two cases with confusion and drowsiness developing into coma who both fully recovered after plasma exchange [12]. The cause of neurologic symptoms in TTP is cerebral angiopathy leading to cerebral hypoperfusion in relation to endothelial dysfunction, impaired reactivity of the small cerebral arteries, damage to the blood-brain barrier and vasogenic edema. MRI reveals ischemic and/or hemorrhagic foci; an image resembling reversible posterior encephalopathy has been also described. Infarcts of the brain may be multifocal cortical or lacunar; they may be located within periventricular region and in the areas supplied by large cerebral arteries [13]. Thrombocytopenia and the increase in blood pressure in the course of renal failure play an important role in the hemorrhagic transformation of ischemic foci or spontaneous brain hemorrhages. The lack of lesions in our patient's MRI of the head, despite the neurological symptoms, may be associated with the early period of examination when the neurological symptoms were caused by microcirculation.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES

- [1] Podolak-Dawidziak M. Niedokrwistości. Interna Szczeklika-Podręcznik Chorób Wewnętrznych 2013. Kraków: Medycyna Praktyczna; 2013 [chapter D 6].
- [2] Moschcowitz E. An acute febrile pleiochromic anemia with hyaline thrombosis of the terminal arterioles and capillaries: a hitherto undescribed disease. *Proc NY Pathol Soc* 1924;24:21–4.
- [3] Blombery P, Scully M. Management of thrombotic thrombocytopenic purpura: current perspectives. *J Blood Med* 2014;5:15–23.
- [4] Sundram F, Roberts P, Kennedy B, Pavord S. Thrombotic thrombocytopenic purpura associated with statin treatment. *Postgrad Med J* 2004;80(947):551–2.
- [5] Scully M, McDonald V, Cavenagh J, Hunt BJ, Longair I, Cohen H, et al. A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. *Blood* 2011;118 (August (7)):1746–53.
- [6] Jiang H, An X, Li Y, Sun Y, Shen G, Tu Y, et al. Clinical features and prognostic factors of thrombotic thrombocytopenic purpura associated with systemic lupus erythematosus: a literature review of 105 cases from 1999 to 2011. *Clin Rheumatol* 2014;33(3):419–27.
- [7] Allford SL, Hunt B, Rose P, Machin S, Haemostasis and Thrombosis Task Force, British Committee for Standards in Haematology. Guidelines on the diagnosis and management of the thrombotic microangiopathic haemolytic anaemias. *Br J Haematol* 2003;120:556–73.
- [8] de Jong F, Te Boekhorst PA, Dippel DW, Jacobs BC. Coma in thrombotic thrombocytopenic purpura. *BMJ Case Rep* 2010;23:2010.
- [9] Godlewski A, Szczech J. A case of Moschcowitz syndrome (thrombotic thrombocytopenic purpura). *Neurol Neurochir Pol* 1987;21(November–December (6)):548–51.
- [10] Pandey S. Seizure in patients with thrombotic thrombocytopenic purpura. *Arch Neurol* 2010;67(12):1536.
- [11] Scully M, Yarranton H, Liesner R, Cavenagh J, Hunt B, Benjamin S, et al. Regional UK TTP registry: correlation with laboratory ADAMTS 13 analysis and clinical features. *Br J Haematol* 2008;142:819–26.
- [12] Kelly FE, Treacher DF, Williams FM, Hunt BJ, Howard S. Coma in thrombotic thrombocytopenic purpura. *J Neurol Neurosurg Psychiatry* 1999;66:689–90.
- [13] Bas D, Oguz KK, Topcuoglu MA. Atypical reversible posterior leukoencephalopathy syndrome in thrombotic thrombocytopenic purpura. *Intern Med* 2008;47(21):1931–4.