

Adamts13 Mutation Revealed By a Recurrent Ischemic Stroke in a Young Male Patient Responding to Steroid Therapy Alone: A Case Report

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ABSTRACT

ADAMTS 13 deficiency can lead to recurrent cryptogenic strokes, especially among young patients. We describe the first case of recurrent stroke due to ADAMTS13 deficiency that responded to steroid therapy alone.

Keywords

Autoimmune haemolytic anemia, Autoimmune thrombocytopenia, ADAMTS 13 mutation, Thrombotic thrombocytopenic purpura.

Case Report

We report the case of a 49-year-old right-handed male, with a history of repeated cryptogenic strokes. He was admitted for impaired consciousness and right brachiofacial hemiparesis with motor aphasia of acute onset (NIHSS score at 10). The patient presented abundant melena 48 hours before admission. Cerebral MRI showed an acute fronto-insular stroke with mild hemorrhagic infarction and stroke sequelae in the right parieto-temporal region. The previous strokes were classified cryptogenic after ruling out immunological, infectious and cardiological causes. At admission, the blood count showed anemia (hemoglobin=6.90 g/dL). This level decreased to a minimum value of 5.76 g/dL despite the transfusion of 2 packed red blood cells. Oesophagogastroduodenoscopy was normal. A thrombocytopenia appeared on the fifth day of hospitalization; the lowest value was 77.000/mm³. Consequently, B12 vitamin and folate levels were dosed and found normal. Medical history confirmed that he had no similar cases in his family, no history of anemia, no infectious disease, no fever, no rash, no infection, and no recent heparin therapy. Physical examination did not find splenomegaly nor adenomegaly.

Given the regenerative bi-cytopenia with a rich myelogram, the

autoimmune hypothesis was raised. Genetic study revealed an ADAMTS 13 mutation. The ADAMTS 13 activity was measured at 17% (60,6 - 130,6%), which was in favor of thrombotic thrombocytopenic purpura (TTP). Plasma exchange was discussed. As a temporizing measure, the patient received a high dose of steroids (1g per day during 3 days intravenously); leading to a fast remarkable raise in platelets and red blood cells, with amendment of the gastro-intestinal bleeding. We hypothesize that all the patient's strokes were related to the ADAMTS 13 deficiency. The patient's neurological evolution was satisfactory with corticosteroid therapy (NIHSS score at 7). The patient was discharged under oral corticosteroid therapy. Twelve months later, no new signs of stroke occurred. Rankin Score at 3 months was at 2.

TTP is a thrombotic microangiopathy due to an ADAMTS 13 deficiency that can lead to recurrent strokes in young patients [1]. The plasma metalloproteinase ADAMTS 13 plays a key role in the cleavage of the ultra-large VWF multimers into smaller less procoagulant multimers. Micro-thrombi are composed of platelets and ultra large von Willebrand factor multimers in the small blood vessels, leading to organ dysfunction [2].

That is why in this population of patients, a complete blood count and platelet count should be performed regularly in order to look for autoimmune cytopenia. This should be done even more

regularly and urgently if the patient presents with a hemorrhagic disorder. The occurrence of normocytic normochromic anemia possibly associated with thrombocytopenia not responding to blood transfusion should raise the autoimmune hypothesis, among others. This hypothesis should be considered even though the association of these two entities is rare. The correction of the above-mentioned disorders with corticosteroid therapy is an additional argument in favor of this mechanism.

To our knowledge, only 5 cases of TTP revealed by recurrent strokes have been reported in the literature [1-6]. The patients presented either lacunar strokes, right MCA infarction, or multiple strokes. Our patient presented with two large strokes: an acute cortical fronto-insular stroke associated to a very mild hemorrhagic infarction, as well as an old stroke in right parieto-temporal region. On the other hand, the five patients were treated with either fresh frozen plasma or plasmapheresis sessions [1-6]. The patients did not relapse. Our patient was treated with initial intravenous high dose steroids (followed by gradual tapering of the drug as an oral maintenance therapy). The patient responded favorably. One year after the initial diagnosis the patient did not relapse (neither neurologically nor hematologically). A long-term follow-up would be useful to observe new relapses and study the effect of corticosteroid alone for the treatment of TTP in this patient's population.

Conclusion

In conclusion, neurologists should raise the hypothesis of ADAMTS 13 deficiency when confronted to repeated history of ischemic stroke in young adults, even more when it is associated

to regenerative cytopenia. Our observation raises the potential beneficial effect of high dose steroids.

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