CORRESPONDENCE

The Differential Diagnosis and Treatment of Thrombotic Microangiopathies

by PD Dr. med. Martin Bommer, Dr. med. Manuela Wölfe-Guter, PhD, Dr. med. Stephan Bohl, and PD Dr. Dr. med. Florian Kuchenbauer
in issue 19/2018

Supplementary Therapeutic Recommendations

We read the review article by Bommer et al. with great interest (1). The authors provided a comprehensive and excellent overview of the different forms of microangiopathies with a focus on adulthood. As they rightly state, hereditary forms—such as atypical hemolytic-uremic syndrome (HUS) and severe hereditary ADAMTS13 deficiency—are very rare. A definite diagnosis of Upshaw-Schulman syndrome (USS) has been possible only since the beginning of the millennium, since the discovery of von-Willebrand-factor-cleaving protease (ADAMTS13). The diagnosis is hampered by the fact that some patients present with non-specific symptoms (2). A diagnostic window opens up in the neonatal period, when some USS patients may present with thrombocytopenia or hyperbilirubinemia. When the typical causes for that are ruled out, USS should be kept in mind. The relevant tests for ADAMTS13 activity have become readily available in the meantime.

We wish to add therapeutic recommendations for hereditary ADAMTS13 deficiency. In the authors' view, plasmapheresis is indicated in this setting, as it is for the acquired form via ADAMTS13 antibodies. For the latter, plasmapheresis is absolutely indicated because the main objective is a reduction in the causative ADAMTS13 antibodies. In our experience, however, for USS, merely supplying ADAMTS13 by means of one or two transfusions of 20 mL/kg bodyweight (KG) of plasma at an interval of 12–24 h is almost always sufficient, because as a rule, ADAMTS13 antibodies are not present. This measure is also more readily available than plasmapheresis, which imposes enormous logistical and time burdens on patients and staff.

A substantial therapeutic improvement for USS in future will be recombinant ADAMTS13 concentrate, which is currently being studied in clinical trials. DOI: 10.3238/arztebl.2018.0608a

References

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Conflict of interest statement

Dr Hassenpflug received consultancy fees and study support (third party funding) for participating in clinical studies of recombinant ADAMTS13 from Shire.
Prof Schneppenheim received fees for consultancy services and lectures, and financial support (third party funding) for conducting molecular genetic studies in the context of recombinant ADAMTS13 registration trials from Shire.

In Reply:

We were delighted by the great interest in our review article on the differential diagnosis and treatment of thrombotic microangiopathies (1). The multitude of potentially involved specialty disciplines in particular presents huge challenges in terms of the appropriate explanation of relevant differential diagnoses and differential therapeutic measures. Hassenpflug and Schneppenheim name several aspects that distinguish thrombotic-thrombocytic purpura (TTP) in children and adolescents from TTP in adults:

- An early diagnosis of hereditary TTP by means of determining ADAMTS13 activity in unclear findings of hemolysis/thrombopenia in neonates makes sense as in children and adolescents, about one-third of all cases of TTP are due to an ADAMTS13 mutation. By contrast, the probability for hereditary TTP in adults is notably below 5% (2).
- The appropriate treatment in case of active TTP in patients with known congenital TTP can consist merely of fresh plasma substitution. In these cases, the—extremely laborious—plasmapheresis is not necessary. Testing for ADAMTS13 activity/antigen and ADAMTS13 antibodies in order to distinguish between hereditary and acquired TTP with an analysis period of a few hours is desirable but not (yet) available in all hospitals. Since acquired, antibody mediated TTP is much more common (>95%) especially in adulthood, plasmapheresis is still recommended in adult cases of unclear etiology. DOI: 10.3238/arztebl.2018.0608b

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Conflict of interest statement

Dr Bommer has received consultant honoraria and study support (third-party funds) for clinical studies from Ablynx and speaking honoraria from Alexion Pharmaceuticals, Sanofi Genzyme, and JAZZ Pharmaceuticals.