The Interaction Between Coagulation and Complement Cascades in the Management of Thrombotic Microangiopathies Related to Postpartum Hemorrhage

To the Editor: We read with great interest the report by Kaufeld *et al*.[1] who studied the impact of short-term complement inhibition in patients with thrombotic microangiopathy associated with postpartum hemorrhage.[1] We agree with the authors regarding the need to propose a pragmatic management model by presenting a real-world cohort of patients affected by this infrequent complication. Nonetheless, we believe that some aspects deserve further discussion.

Although critical-care diagnostic algorithm to investigate thrombocytopenia associated with thrombotic microangiopathy categorically separates atypical hemolytic uremic syndrome from disseminated intravascular coagulation,[2] evidence shows that postpartum hemorrhage-related thrombotic microangiopathy may lie at the intersection between these two clinical entities.[3,4] Considering several levels of reciprocal interaction between the coagulation and complement cascades, this statement appears to be justified from a pathophysiological point of view.[3] In fact, the tissue factor-activated coagulatory pathway is known to be triggered by the terminal complement complex. Conversely, kallikrein, plasmin, and thrombin are coagulation factors that act as activators of both complement factors C3 and C5, which are the convergence points of the classical and alternative complement cascades.[3] In this scenario, the degree of alteration of the coagulation system should be included in the clinical variables considered in the genesis of complications and response to treatment.

Furthermore, blood transfusion therapy has been demonstrated to impact as an immune system modulator, which may influence critical patients' outcomes,[5] although this may be difficult to quantify in a real-life emergency setting. The level of several proinflammatory cytokines, including interleukin-1 along with markers of endothelium immuno-activation demonstrated to increase in the hours following red blood cell transfusion.[5] These alterations may also represent an additional element influencing complement function.

In conclusion, we agree that short-term treatment with complement inhibition in patients with postpartum hemorrhage-related thrombotic microangiopathy will deserve further investigation to confirm the benefits demonstrated by preliminary data, considering a relatively limited impact on health care costs. Studying the role played by coagulation activation and transfusion therapy in these patients could help clarify the pathogenesis and better predict the response to treatment.

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