Response to "Features of Postpartum Hemorrhage-Associated Thrombotic Microangiopathy and Role of Short-Term Complement Inhibition": Still a Long Way to Go

The Author Replies: We read with interest the work entitled "Features of Postpartum Hemorrhage-Associated Thrombotic Microangiopathy and Role of Short-Term Complement Inhibition."[1] The authors contend that postpartum patients presenting with thrombotic microangiopathy may benefit from short-term C5 inhibition. Several lines of argumentation tend to mitigate this claim. First and foremost, no comparison is provided between patients who received C5 inhibition (72.5%) and those treated without these agents. Therefore, in the absence of a control group, the author's conclusion rests heavily on the assumption that the outcome of kidney function following postpartum thrombotic microangiopathy is poor. This hypothesis is not supported by the current literature. In 1 multicenter retrospective investigation reporting on patients with postpartum thrombotic microangiopathy, including preeclampsia ($n = 33$) and postpartum hemorrhage ($n = 20$), Meibody *et al.*[2] recorded a median estimated glomerular filtration rate of 82 ml/min, 89.5 ml/min (86–92) at 12-month follow-up, respectively. None but 2 patients with preeclampsia received eculizumab. In fact, the final kidney function course depended primarily on the occurrence of cortical necrosis with a median last follow-up estimated glomerular filtration rate of 6 ml/min (5–31). However, patients experiencing cortical necrosis would not be considered eligible to receive a complement inhibitor trial, given the potentially irreversible nature of kidney lesions, further narrowing down the expected gains from C5 inhibition. Finally, the understanding of the paper's results may fall within the scope of what authors have termed the "modifier gene" concept, whereby the disease results from the interaction of genetic predisposition and a second "hit," in this case pregnancy and its complications.[3,4] This conceptual framework is suggested in the Supplementary Appendix wherein the authors distinguish pathogenic variants from risk haplotypes. Unfortunately, not only is this assumption not spelled out explicitly, but the authors claim quite contrarily that none of the patients with postpartum hemorrhage exhibited susceptibility variants. Pending robust clinical evidence, we suggest that the current use of complement inhibitors should be grounded in the implementation of fast-track genetic testing to identify the small fraction of patients with pathogenic variants who have demonstrated proven benefit from these treatments in the short-term and long-term.[5]

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