A Novel Nanobody: Capalacizumab, in the Modern Era of TTP Treatment

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Thrombotic thrombocytopenic purpura (TTP) is a potentially lethal thrombotic microangiopathy. Treatment for TTP is centered around plasmapheresis, rituximab, and steroids. We present a case of a TTP successfully treated with capalacizumab, a novel nanobody. A 45-year-old male with history of alcohol abuse presented with vomiting, diarrhea and encephalopathy. Physical exam was remarkable for tachycardia and tachypnea. Initial labs were significant for lipase 6,073 U/L, total bilirubin 2.7mg/dl, AST 199 U/L, ALT 88 U/L and creatinine 3.78 mg/dl. His renal function deteriorated necessitating hemodialysis. The hemoglobin dropped from 14.1 gm/dl to 8.7 gm/dl, platelets from 90,000/mm3 to 20,000/mm3 with LDH 2205 U/L, haptoglobin 11 mg/dl and total bilirubin rose to 4.7 mg/dl. PT/INR was normal. Peripheral smear showed 2+ schistocytes. Coombs test was negative. For the diagnosis of TTP, he was started on high dose steroids, rituximab and capalacizumab with daily plasmapheresis. The encephalopathy, blood counts and renal function improved dramatically within days. He completed 17 days of plasmapheresis and a 30-day course of capalacizumab. Treatment for TTP is traditionally centered on plasmapheresis, rituximab, and steroids leading to survival in 80-90% patients. Caplacizumab, a novel anti-von Willebrand factor humanized single-variable-domain nanobody that acts to inhibit platelet-vWF multimers has been introduced in addition to these treatments. In the initial phase 2, single-blind, randomized trial of 75 patients, laboratory remission (normalization of platelet count to >150,000/mm3) was achieved faster in those given caplacizumab plus usual care than in those given usual care plus placebo. Post-hoc analysis revealed a shorter course of daily plasmapheresis as well as fewer thrombotic events in the study group. These findings were confirmed in another randomized, double-blinded trial of 145 patients published by the same authors, again revealing a shorter time to platelet normalization and fewer days of plasmapheresis with caplacizumab plus usual care. However, results of both trials have raised questions of bias towards study group when looking at hazard ratios for survival rather than survival curves, and it is unclear whether relapse is more common in caplacizumab group. It is also unclear if immunoglobulin-mediated prevention of platelet-vWF multimers is physiologically equivalent to normally-functioning platelets. As with any novel treatments, further studies are indicated, especially those not funded by the drug manufacturer. Our patient did have a favorable response using caplacizumab in addition to steroids, rituximab, and plasmapheresis.