Microangiopathic disease (MAP) is characterized by intravascular hemolysis resulting in anemia with presence of schistocytes on a peripheral blood smear, and with a rise in serum lactate dehydrogenase (LDH) followed by a fall in serum haptoglobin levels and with thrombocytopenia. In virtually every case of MAP, the kidney shows some degrees of injury, ranging from the appearance of proteinuria and active urinary sediment to acute kidney injury and incremental decreases in GFR. Three primary MAP’s have now been identified, based on the underlying pathophysiology and characterized according to the expectations for renal injury and the disease-specific treatment. These syndromes include classical hemolytic-uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), and atypical hemolytic-uremic syndrome (aHUS). Classical HUS is associated with enteric infection, most commonly shiga-like toxin-producing E.coli O157:H7 (STEC-HUS), with a dominant prevalence in childhood. TTP specifically arises from decreased activity of ADAM TS13, a metallopeptase that cleaves large multimers of Von Willebrand factor (vWF) causing inactivation of vWf; the deficiency of ADAM TS13 resulting in sustained presence and activity of vWF multimers. Lastly, aHUS has been linked to uncontrolled activation of the complement system by the lack of counter-regulatory factors, chiefly, factors H, I, or B. This deficiency in regulation can result from production of anti-factor F antibodies or a host of genetic mutations that affect factors F, I, or B production of activity. In addition to these well-defined syndromes, MAP with kidney injury can occur sporadically in a wide variety of unrelated disease processes. In every instance, prompt disease-specific treatment can prevent or ameliorate severe or long-term renal damage. For classical HUS, use of antibiotics to address the infection is not indicated and may be counter-productive while plasmapheresis is not beneficial. Supportive care with dialysis when indicated is the preferred mode of care. A diagnosis or strong presumption of TTP demands initiation of plasmapheresis as soon as possible with administration of corticosteroids. Rituximab may be started as initial therapy or added for disease resistance to steroid and aphaeresis. Absence of evidence for classical HUS or TTP, aHUS must be considered, given the high risk for progressive kidney damage. Eculizumab, a monospecific antibody that inhibits complement factor C5 and interferes with the terminal portion of the complement cascade is the required treatment for aHUS. The expense of this drug makes it desirable to secure the correct diagnosis of the complement-mediated basis of disease by measuring factors H, I, and B activity. In the presence of normal activity of these factors, other diseases that may give rise to sporadic MAP need to be considered. A case-based analysis will be used to outline a reasonable approach to management of MAP with renal involvement.

Biography

Roy Michael Culpepper received the MD Degree from the University of Alabama in Birmingham School of Medicine where he also completed Nephrology Fellowship. He has served on the Faculty at Loma Linda University, School of Medicine, the Health Science Center of the University of Texas in Houston, the Medical College of Virginia, and, for the past 25 years, at the University of South Alabama, College of Medicine where he is Professor of Medicine and past Director of the Division of Nephrology and Dialysis Services. He has served on the National Board of Directors of the National Kidney Foundation and has held grants from the NIH and various pharmaceutical grants for clinical research.

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