RECURRENT ATYPICAL HEMOLYTIC UREMIC SYNDROME ASSOCIATED WITH FACTOR I MUTATION IN A LIVING RELATED RENAL TRANSPLANT RECIPIENT

Micah R. Chan, Christie P. Thomas, Richard J. Smith, Jose Torrealba, Millie Samaniego, University of Wisconsin Hospitals and Clinics, Madison, WI; University of Iowa Hospitals and Clinics, Iowa City, IA

Hemolytic uremic syndrome (HUS) is described by the clinical triad of acute renal failure, microangiopathic hemolytic anemia and thrombocytopenia. Approximately 90% of HUS is triggered by infectious agents such as Stx-*E. coli*; the remaining 10% of cases can be genetic, acquired or idiopathic and are collectively known as atypical HUS (aHUS). Approximately 50% of patients with aHUS have a mutation in one of three complement regulatory proteins - complement factor H (CFH), membrane cofactor protein (MCP) or factor I (FI) - that inhibit activation of the alternative complement pathway thereby limiting complement-mediated tissue injury. Identifying these genetic cases is of clinical relevance in patients with aHUS who progress to end-stage renal failure, as most patients with CFH and FI mutations develop recurrent disease that leads to graft loss.

A previously healthy 26-year-old white female presented with fevers, vomiting, abdominal cramping, and dense renal failure. A renal biopsy showed diffuse capillary fibrin deposition and segmental staining for fibrin and IgM along the glomerular basement membrane, consistent with thrombotic microangiopathy (TMA). Six months later, the patient underwent a haploidentical living-related renal transplant from her father. She had excellent graft function initially but within one month was hospitalized with renal failure and biopsy-proven recurrent TMA with negative C4d and donor-specific antibodies. Because of the rapid recurrence of aHUS in the transplanted kidney with evidence of complement activation, we considered the possibility that she may have a defect in complement regulation. Direct sequencing of three complement control genes revealed a heterozygous missense mutation, Y369S, within a functional domain of FI.

This report emphasizes the importance of genetic testing in patients with aHUS prior to renal transplantation, and demonstrates the challenges in the management of these patients.