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# Ravulizumab in Preemptive Living Donor Kidney Transplantation in Hereditary Atypical Hemolytic Uremic Syndrome

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Dear editor, we here report the first case of successful living donor kidney transplantation using complement inhibition by ravulizumab in a 33-y-old woman suffering from hereditary atypical hemolytic uremic syndrome (aHUS). Atypical HUS is the prototype for complement-mediated diseases that typically present with acute renal failure, albuminuria, and hematological abnormalities.[1] In 2018, our patient developed acute-on-chronic kidney failure and increasing albuminuria during her first pregnancy. A stable chronic kidney disease with elevated serum creatinine and albuminuria of unknown cause was already diagnosed in 2004 (Figure 1). Arterial hypertension was well controlled by angiotensin-converting enzyme inhibitors. After premature delivery because of kidney failure and albuminuria, we performed a kidney biopsy. We identified a double contour appearance of capillary walls as one hallmark of chronic thrombotic microangiopathy, thus confirming the diagnosis of aHUS. Interstitial fibrosis was estimated to be about 40%. We rapidly initiated complement inhibition with eculizumab, a C5 inhibitor.[2] Although detection of a specific risk mutation is not essential to the clinical diagnosis of aHUS, 50% to 70% of patients show one or more of numerous known genetic alterations.[3] In this case, genetic testing revealed a heterozygous variant in the complement factor H (*CFH*) gene (c.157C>T p.(Arg53Cys)). *CFH* is an essential inhibitory part of the complement cascade, accelerating the decay of the C3 convertase with >100 reported genetic mutations.[4] Mutations in *CFH* correlate with early onset of disease and worse renal prognosis.[4,5] In 2020, a phase 3 study on ravulizumab, a new anti-C5 antibody, demonstrated improved hematological and renal outcomes in aHUS.[6] Ravulizumab was engineered from eculizumab but allows recycling of the antibody to expand the half-life compared with eculizumab.[7] In consent with our patient, we switched from eculizumab to ravulizumab because of its time-saving infusion interval of once every 8 wk to support our young patient and mother of a small child continuing her university studies. Renal anemia and metabolic acidosis subsequently forced us to prepare our patient for kidney transplantation. Before eculizumab was introduced, renal transplantation of aHUS patients was challenging, and the renal prognosis was poor because of 50% to 90% recurrence rates. Patients with *CFH* mutations reached the highest relapse rates of thrombotic microangiopathy.[8] As eculizumab demonstrated efficacy after kidney transplantation in aHUS and ravulizumab shares its mechanism, we expected noninferiority compared with eculizumab and continued ravulizumab treatment during transplantation, which was performed without shifting infusion intervals.[9] In April 2021, the patient received kidney donation from her 30-y-old husband. S-creatinine and albuminuria rapidly declined after transplantation. Neither hematological parameters nor kidney biopsy 2 wk after transplantation revealed signs of thrombotic microangiopathy. Six months after transplantation, the patient presents with stable creatinine and no albuminuria. Given concerns of safety or on drug interactions, clinicians might hesitate to use ravulizumab in patients who progress to end-stage kidney disease and are candidates for living donation transplantation. Hence, patients might be deprived of the benefit from the extended half-life of this drug. To our knowledge, usage of ravulizumab has not been reported for patients undergoing renal transplantation. Thus, we provide first evidence for the efficacy of ravulizumab to prevent recurrence of aHUS in a genetically high-risk situation before and after renal transplantation.

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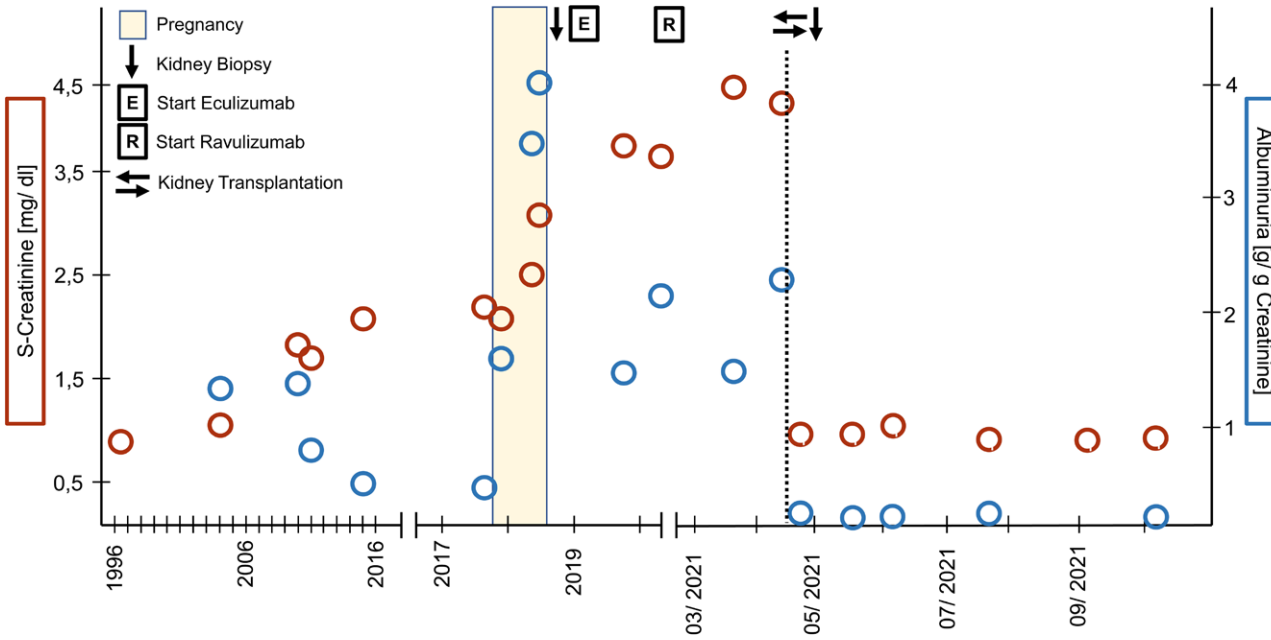


**FIGURE 1.** Time course of the patient's medical history depicting the course of serum creatinine (red circles), albuminuria (blue circles), duration of pregnancy (bright yellow square), time points of kidney biopsies (arrows pointing down), start of treatment with eculizumab (E) and ravulizumab (R), and time point of kidney transplantation (arrows pointing left and right).


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