Use of Eculizumab During Pregnancy in Kidney Transplant Recipients With Atypical HUS

To the Editor: Duval *et al.*[1] recently described a kidney transplant recipient who developed atypical hemolytic uremic syndrome, and was treated with eculizumab during pregnancy with a successful outcome. We described a similar case recently (Cheung CK, Evans K, Williams M, et al. A successful pregnancy in a patient following renal transplantation for atypical HUS managed with eculizumab. UK Kidney Week; June 2018. Available at: https://britishrenal.org/ukkw2018-2/abstracts-2/. Accessed September 29, 2019).

Our case was a 24-year-old woman, with end-stage renal disease of uncertain etiology who underwent a live kidney transplant. Subsequently, a transplant biopsy for graft deterioration showed recurrent atypical hemolytic uremic syndrome. She was commenced on eculizumab 1200 mg every 2 weeks, and her graft function stabilized (estimated glomerular filtration rate 45 ml/min per 1.73 m^2). She later expressed a desire to become pregnant, did not have significant proteinuria, and was taking tacrolimus and azathioprine. After becoming pregnant, her eculizumab dose was increased at 16 weeks (Table 1), with monitoring for hemolysis and complement activity (C3, C4, C5, CH50, AH50 assays) every 2 weeks. At 29+5/40, she developed edema, hypertension, increased proteinuria, decline in renal function and platelets, and increased lactate dehydrogenase. An emergency cesarean delivery was performed, and placental histopathology later confirmed preeclampsia. A female infant weighing 950 g was delivered, with patent ductus arteriosus (which subsequently closed), and was fed with expressed breastmilk. The patient was given two 900-mg eculizumab infusions in the first postnatal week, which was later reduced. Hemoglobin and platelets stabilized, and kidney function returned to prepregnancy levels. Total complement activity remained suppressed throughout pregnancy. Both mother and child are currently well.

These reports suggest that preemptive increased dosing of eculizumab to prevent breakthrough haemolysis, with close monitoring for hemolysis and complement activity, represents a safe and viable strategy during pregnancy in kidney transplant recipients with atypical hemolytic uremic syndrome.

Table 1. Eculizumab dosing during the pregnancy

Gestational age	Eculizumab dosage, mg	Infusion frequency
Booking	1200	Every 2 wk
16 wk	1500	Every 2 wk
28 wk	900	Weekly
Within 24 h of delivery	900	Additional infusion
7 d postnatal	1200	Weekly
14 d postnatal	1200	Every 2 wk

1. Duval A, Olagne J, Cognard N, et al. Pregnancy in a kidney transplant woman under treatment with eculizumab for atypical hemolytic uremic syndrome: is it safe? *Kidney Int Rep.* 2019;4:733–739.

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The Authors Reply: We thank Cheung *et al.*[1] for their valuable comment and their contribution to the literature by describing a second case of successful pregnancy in a kidney transplant recipient receiving eculizumab for atypical hemolytic uremic syndrome.

These 2 reports[2] show the relevance of the issue of conception in transplanted women with atypical hemolytic uremic syndrome while undergoing C5-inhibitor therapy. Moreover, it gives guidelines on the management of these high-risk pregnancies. In both cases, the preemptive increase in eculizumab dosage permitted an efficient complement blockage throughout pregnancy, allowing the prevention of atypical hemolytic uremic syndrome flare.

Although these preliminary data seem promising concerning graft, maternal, and fetal outcomes, it is important to highlight the lack of pharmacologic data on eculizumab therapy in transplanted pregnant women and the absence of current knowledge on the potential long-term impact of this therapy in children. Hence, prenatal counseling and pre- and postpartum close specialized follow-up of both mother and child are critical.

1. Cheung CK, Nettleton KJ, Williams ML, et al. Use of eculizumab during pregnancy in kidney transplant recipients with atypical HUS. *Kidney Int Rep*. 2019;4:1658.

2. Duval A, Olagne J, Cognard N, et al. Pregnancy in a kidney transplant woman under treatment with eculizumab for atypical hemolytic uremic syndrome: is it safe? *Kidney Int Rep*. 2019;4:733–739.

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