New Biomarker of Preeclampsia in Kidney Transplant Recipients

To the Editor: We read the article by Kattah et *al.*[1] with great interest. The authors demonstrated that pregnancy was a risk factor for long-term allograft function and increased chronic vascular injury in postpregnancy biopsies of kidney transplant recipients (KTRs). Furthermore, the authors mentioned that one of the possible causes of these worse consequences may be preeclampsia. However, the diagnosis of preeclampsia would be more difficult in KTRs than in non-KTRs.

Regarding allograft dysfunction during pregnancy in KTRs, there are numerous differential diagnoses such as rejection, recurrent primary disease, calcineurin inhibitor nephrotoxicity, or urinary obstruction, as well as preeclampsia.[2] Ideally, definitive diagnosis requires allograft biopsy; however, noninvasive examination is preferred because its safety during pregnancy has not been established.[3] We hypothesize that the soluble fms-like tyrosine kinase-1/placental growth factor (sFlt-1/PlGF) ratio might be useful in differentiating between them. Although this test results were right in differentiating preeclampsia from other causes,[4] its use in KTRs has not yet been reported.

We identified the potential benefit of the sFlt-1/PlGF ratio for kidney injury during pregnancy in a 32-year-old woman with IgA nephritis as the primary disease. The patient had hypertension from the 28th week of gestation; thus, gestational hypertension was diagnosed, and magnesium sulfate and nifedipine were started on hospitalization. Glomerular hematuria began at 33 weeks of gestation, and proteinuria and allograft function rapidly worsened at approximately 34 weeks (Figure 1). Because the sFlt-1/PlGF ratio was markedly elevated to 205 (reference range: <38.0) at 35 weeks of gestation, preeclampsia was suspected rather than rejection or recurrent IgA nephritis. In this regard, we did not plan to perform an allograft biopsy or any treatment for rejection. Eventually, the patient was induced to deliver at 36 weeks of gestation. At 10 weeks postpartum, proteinuria and hypertension were completely resolved, and kidney function improved to

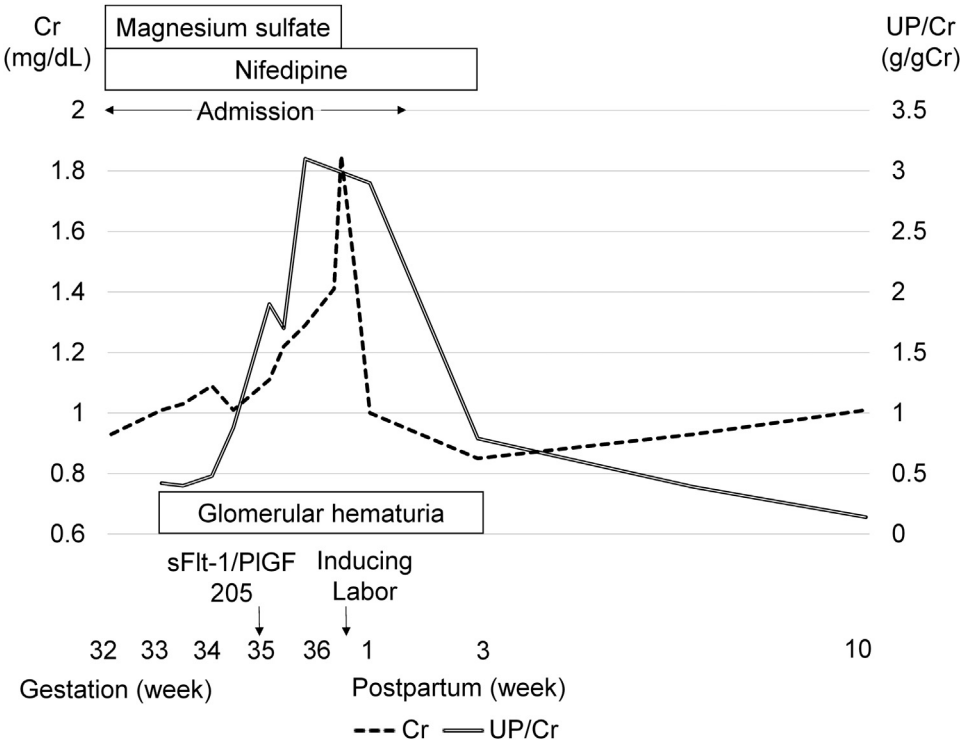

Figure 1. Laboratory data and treatment during the clinical course during and after pregnancy. *sFlt-1/PlGF*, soluble fms-like tyrosine kinase-1/placental growth factor ratio, *UP/Cr*, urinary protein/creatinine.

baseline; thus, the diagnosis of preeclampsia was also retrospectively made without kidney allograft biopsy.

Because preeclampsia in KTRs can be a risk factor for subsequent transplant kidney dysfunction, following the study by Kattah *et al.*,[1] we may proactively consider measuring the sFlt-1/PlGF ratio for early diagnosis if preeclampsia is suspected.

CONSENT

We obtained informed consent from this patient and she accepted the presentation of their clinical course. The consent details are stated in the electron medical record at St. Mariann University Hospital.

AUTHOR CONTRIBUTIONS

RN and MY participated in the writing of the paper and in the approval of final manuscript.

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Response to "New Biomarker of Preeclampsia in Kidney Transplant Recipients"

The Author Replies: Drs. Noda and Yazawa's interest and response to our article is much appreciated.[1] They present a case that highlights one of the most difficult clinical scenarios in obstetric nephrology—differentiating preeclampsia from other intrinsic kidney disease processes. In the kidney transplant population, the differential is even broader, with rejection, infection, and recurrent disease, all potentially causing dysfunction in the allograft.

The use of sFlt-1/PlGF ratio shows great promise in ruling out preeclampsia in many clinical scenarios, especially preterm preeclampsia.[2] Angiogenic markers remain for investigational use only in the United States.[3] Bramham *et al.*[4] have performed longitudinal assessments of angiogenic markers in women with established hypertension and chronic kidney disease, including women with kidney transplants. They found that whereas sFlt-1 and PlGF levels, and the sFlt-1/PlGF ratio, were significantly different between women with superimposed preeclampsia and women without preexisting disease, PlGF ratio at less than fifth percentile had the highest predictive value, and sFlt-1 did not improve on diagnostic accuracy.[4] Larger studies in kidney transplant patients with longitudinal measures will be helpful in validating these findings.

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