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LETTER TO THE EDITORS

Response to: Focal segmental glomerulosclerosis recurrence in a young adult with kidney transplant after mRNA COVID-19 vaccination

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Dear Editors,

In response to our report on the response of adolescent kidney transplant recipients to SARS-CoV-2 immunization [1], Fulchiero and Amaral present a thought-provoking case of FSGS recurrence in a kidney transplant recipient following a two-dose mRNA SARS-CoV-2 vaccine series [2]. The case is clinically consistent with a post-transplant recurrence of FSGS and the timing of recurrence in relation to immunization suggests a possible association. While this is an intriguing and plausible hypothesis, we caution an inference of causality. We would also be curious to know if patient developed a serologic response to the vaccine.

Recurrence of numerous glomerular diseases, including minimal change disease, has been temporally associated with the SARS-CoV-2 mRNA vaccine and there are many reports of nephrotic syndrome relapse occurring after various other immunizations [3]. However, post-vaccine recurrence of glomerular disease in transplant patients is not well characterized and, to our knowledge, post-transplant FSGS recurrence has not been previously reported in association with any immunization.

FSGS recurrence is thought to be mediated by an unidentified circulating factor. While numerous potential culprits have been proposed, it is unclear if this factor is represented by an unidentified antibody against podocyte targets or a non-immunogenic permeability factor that leads to toxicity of the podocyte. As the authors note, a T-cell-mediated inflammatory response is hypothesized to facilitate potential vaccine-associated glomerular disease relapses. The mechanism linking T-cell response to proliferation of a potential circulating factor is uncertain. While theoretically possible that mRNA vaccination leads to downstream B-cell activation and autoantibody circulating factor production, the lack of similar reports in a setting of widespread vaccination in an at-risk population makes this unlikely.

We have continued to follow our original cohort of pediatric and adolescent kidney transplant recipients who have received a 2- and 3-dose mRNA vaccine series, including those with FSGS as an original disease process. Thus far, there have been no instances of glomerular disease recurrence, relapse, nor any new diagnoses of acute rejection in this cohort.

There is still much to be learned about the immune mechanisms of mRNA vaccines in the immunocompromised host. While the preponderance of data suggest immunization is safe, efficacious, and beneficial, we concur with the authors' conclusion that continued vigilance for unexpected outcomes in kidney transplant recipients is important.

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Declarations

Conflict of interest The authors declare no competing interests.

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