Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

or boosters of this particular vaccine in this patient would be unwise until this potential relationship is more clear.

ACKNOWLEDGMENTS

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

AUTHOR CONTRIBUTIONS

Author contributions were evenly divided, and included but not limited to patient care, research, writing the article, and subsequent revisions.

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Kidney International (2021) **100,** 463–464; https://doi.org/10.1016/j.kint.2021.05.007

Relapse of primary membranous nephropathy after inactivated SARS-CoV-2 virus vaccination

To the editor: Coronavirus disease 2019 (COVID-19) vaccine is one of the most effective public health interventions to end the COVID-19 outbreak. There are insufficient data on the use of COVID-19 vaccines in patients with autoimmune disease, but vaccines appear to be safe, and experience from previous vaccine studies does not indicate an increased risk of relapse/recurrence.[1] However, theoretically, unwanted immunologic events, such as autoimmunity, may be triggered by vaccines. We describe a patient with membranous nephropathy (MN) who stayed in remission for 8 years and experienced a relapse after vaccination with a purified inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus vaccine called CoronaVac (produced in China by Sinovac).

A 66-year-old female patient presented with lower-extremity edema 2 weeks after the first dose of Sinovac's COVID-19 vaccine. She had been diagnosed with biopsy-proven primary MN 8 years earlier. At that time, secondary causes of MN, such as malignancy, infections, and drugs, were excluded, but anti–phospholipase A2 receptor (anti-PLA2R) antibody could not be tested because it was not available. She was treated with steroid, cyclosporine, and lisinopril 10 mg/d. Complete remission was achieved within 3 months, and all immunosuppressive treatments were discontinued at 6 months while lisinopril 10 mg/d was continued. Renal functions and urinary protein excretion remained in the normal range without immunosuppressive therapy for 8 years. Her medical history also showed hypertension for 1 year and diabetes mellitus and hyperlipidemia for 6 years. On admission, urea was 93 mg/dl, creatinine was 2.78 mg/dl, serum albumin was 2.6 g/dl, spot urine protein-to-creatinine ratio was 9.42 mg/mg, and anti-PLA2R antibody was positive (120.53 relative units/ml [<14, negative; >20, positive]). Secondary causes of MN, such as malignancy, infections, and drugs, were excluded. No diabetic retinopathy was noted. A diagnosis of MN relapse was established given the clinical symptoms and laboratory examination results.

To our knowledge, cases of nephrotic syndrome in MN form have been reported after influenza vaccination.[2,3] A case of minimal change disease with full-blown nephrotic sydrome and acute kidney injury 10 days after the Pfizer-BioNTech COVID-19 vaccination has also been reported.[4] In addition to this case, we observed 2 patients who developed anti-PLA2R–positive MN after SARS-CoV-2 infection. Our observation suggests that the SARS-Cov-2 virus may cause a loss of tolerance to the PLA2R antigen. Consequently, close follow-up of patients with MN after SARS-CoV-2 vaccination is recommended. Further studies are needed to determine whether relapse of MN is specific for inactivated SARS-CoV-2 virus vaccination and to decipher the mechanisms of immune dysregulation in those patients.

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Kidney International (2021) **100,** 464–465; https://doi.org/10.1016/j.kint.2021.05.001

Relapse of IgG4-related nephritis following mRNA COVID-19 vaccine

To the editor: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination is currently recommended for patients with chronic kidney disease and immunocompromised patients because their risk of developing severe forms of coronavirus disease 2019 (COVID-19) is higher than other patients. Several reports have highlighted the increased risk of immune disease recurrence following mRNA vaccination, including minimal change disease, membranous nephropathy, or even acute allograft rejection.[1,2] We report the case of a 66-year-old man who was diagnosed with IgG4-related disease (IgG4-RD) nephritis in December 2019. At this time, he presented with asthenia associated with acute kidney injury, evaluated by serum creatininemia (SCr) at 450 μmol/L and aseptic leukocyturia (120/mm^3) without proteinuria or hematuria. Although anti-DNA antibodies were negative, anti–SSA-52 antibodies were highly positive (113 UI/L; normal range, <10 UI/L) and were associated with hypocomplementemia C3 (0.51 g/L; normal range, 0.9–1.8 g/L) and C4 (<0.02 g/L; normal range, 0.1–0.4 g/L). Serum IgG4 antibodies were elevated at 6.9 g/L (normal range, 0.03–2.01 g/L). A positron emission tomographic scan revealed intense bilateral kidney fixation and fat infiltration. A kidney biopsy revealed IgG4-related nephritis with storiform fibrosis and an IgG4-to-IgG ratio >40 (Figure 1). Initial treatment consisted of steroids (1 mg/kg), quickly followed by 4 weekly rituximab perfusions (375 mg/m^2) due to steroid resistance.[3] Kidney function improved, along with a decrease in SCr to 180 μmol/L, disappearance of leukocyturia, and normalization of serum complement and IgG4 levels, permitting steroid withdrawal. Anti–SSA-52 antibodies also strongly decreased and became negative in June 2020. A positron emission tomographic scan was performed on January 18, 2021, for IgG4-RD follow-up, and showed no pathologic fixation nor renal infiltration. The patient was vaccinated with an mRNA vaccine (BNT162b2 mRNA; Pfizer BioNTech) on January 28, 2021, and February 17, 2021. Two weeks later, he presented with intense asthenia with arthralgias and myalgias. SCr was elevated at 210 μmol/L on March 5, 2021, increased to 250 μmol/L on March 22, 2021, and was associated with recurrence of aseptic leukocyturia. Anti–SSA-52 levels increased from 4 to 17 UI/L. SARS-CoV-2 serology was positive for anti–spike protein at 177 UI/L (electrochemiluminescence immunoassay, Roche Elecsys). Steroid therapy was initiated at 0.5 mg/kg and associated with rituximab perfusion (500 mg), allowing a quick improvement of the general symptoms and resolution of acute kidney injury. Anti–SSA-52 levels also decreased to 12 UI/L by May 2021 (Figure 2).

Our report highlights the possibility of immune disease relapse following mRNA vaccine, a situation previously described by others. It is currently unknown if immune disease recurrence is linked to direct immune activation following vaccination, chronic immune activation following a paucisymptomatic allergic reaction, or both. Indeed, IgG4-RD pathogenesis has been linked to IgE production, as seen in late immune-mediated allergic reactions.[4] If the benefit-to-risk ratio indisputably favors vaccination of this at-risk

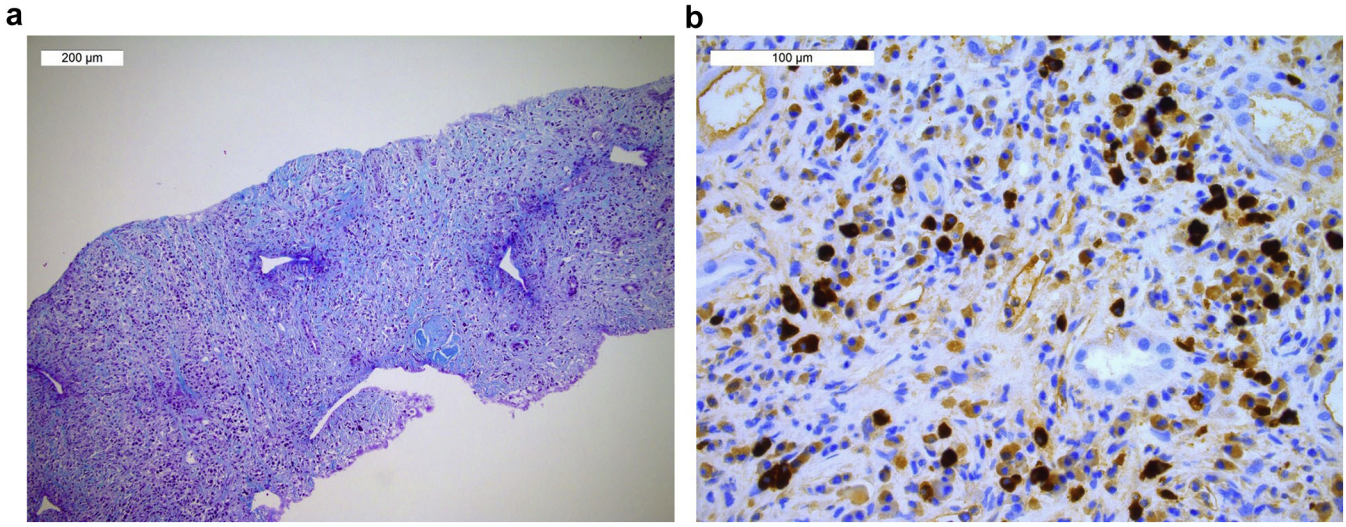

Figure 1 | (a) Destructive storiform interstitial fibrosis, representing >50% of the biopsy, with abundant plasma cell infiltrate (Masson trichrome stain, original magnification ×100). (**b**) Presence of >10 IgG4 plasma cells per large field at ×400 original magnification (immunohistochemistry with anti-IgG4 [clone ZSIGG4 Diagomics]), with a 40% IgG4-to-IgG ratio. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.