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.

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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

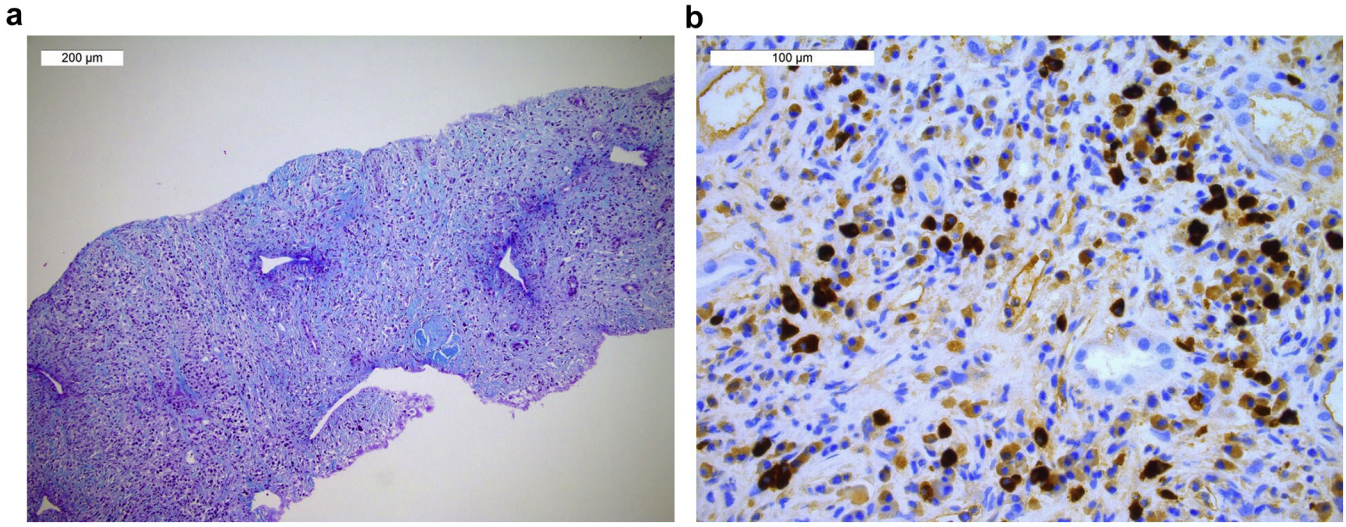

Figure 1 | (a) Destructive storiform interstitial fibrosis, representing >50% of the biopsy, with abundant plasma cell infiltrate (Masson trichrome stain, original magnification ×100). (**b**) Presence of >10 IgG4 plasma cells per large field at ×400 original magnification (immunohistochemistry with 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.

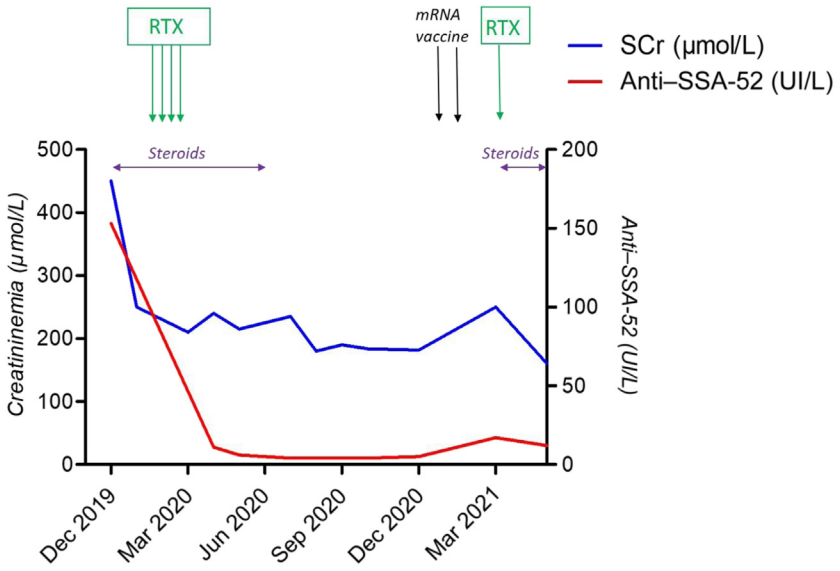

Figure 2| Evolution of sera creatininemia (SCr) and anti–SSA-52 antibodies, reflecting the activity of IgG4-related disease, from the diagnosis in December 2019 to the relapse in March 2021 following mRNA coronavirus disease 2019 (COVID-19) vaccine. RTX, rituximab.

population, physicians should be aware of the possibility of immune disease recurrence to provide close monitoring of these patients and fast treatment of relapses to avoid long-term consequences and progression to end-stage renal disease.

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Gross hematuria following SARS-CoV-2 vaccination in patients with IgA nephropathy

To the editor: After the publication of the 2 letters by Negrea and Rovin[1] and Rahim *et al.*,[2] we herein describe 3 additional patients with IgA nephropathy (IgAN) who developed gross hematuria after receiving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA-based vaccines. The clinical data of our cases are summarized in Table 1. In line with the 3 previously reported cases, patient 1 had normal kidney function. However, patients 2 and 3 were treated with kidney transplantation (KT) and hemodialysis, respectively. Notably, gross hematuria developed as early as after the first vaccine dose in patients 1 and 2. Additionally, gross hematuria in patient 1 relapsed after the second vaccine dose. Gross hematuria was sporadically accompanied by increased proteinuria, arthralgia, abdominal pain, and urticaria. Serum creatinine also transiently increased in patient 2. Symptoms spontaneously regressed in all the 3 cases. The apparent exacerbation of IgAN in patient 2 occurred in the absence of an anti–SARS-CoV-2 antibody response. Out of a total of 726 KT recipients, we examined the tolerability of 2 doses of the Moderna vaccine in 80 recipients with IgAN. No additional cases of gross hematuria were identified. Seventy patients had available data on anti–SARS-CoV-2 antibodies 1 month after the second dose, and positive serology was identified in 32 cases (45.7%). This finding is in accordance with our previous data.[3]

In summary, gross hematuria can occur even after the first vaccine dose and it can also affect—albeit rarely—KT