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.

observed, but there was no sign of glomerular thrombotic microangiopathy (no thrombosis, mesangiolysis, or double contouring of the capillary wall). Immunofluorescence staining for IgG, IgA, IgM, C3, C1q, Kappa, and Lambda was negative.

Both clinical and biological findings were consistent with the diagnosis of scleroderma renal crisis revealing undiagnosed, preexisting diffuse cutaneous systemic sclerosis.

One week after the initiation of antihypertensive drugs, including angiotensin-converting enzyme (ACE) inhibitors, the patient was discharged with normal blood pressure, no sign of biological hemolysis, and stable renal function. Given this life-threatening complication, no second injection of mRNA vaccine was planned.

In this case, vaccination was temporally associated with hypertensive emergency and acute kidney injury leading to the diagnosis of biopsy-proven scleroderma renal crisis. Renal biopsy features were highly suggestive of this diagnosis, with thrombotic microangiopathy lesions predominating in medium-size vessels.[2]

According to current guidelines,[3] our patient had a typical presentation of scleroderma renal crisis, with hypertensive emergency, ophthalmologic and neurologic involvement, hemolytic anemia and thrombocytopenia, and compatible renal histopathologic changes. Moreover, no other cause of renal thrombotic microangiopathy was identified, including shiga-toxin–induced typical hemolytic uremic syndrome (HUS), other infectious agents (pneumococcal infection, HIV infection), antiphospholipid syndrome, or drug-induced HUS. Finally, the close temporal relationship (7 days) between the first administration of the BNT162b2 vaccine and the appearance of hypertensive symptoms emphasizes the potential role of immune response to SARS-CoV-2 mRNA vaccination as a trigger of scleroderma renal crisis.

Whether other diseases associated with HUS/thrombotic microangiopathy (such as thrombotic thrombocytopenic purpura, complement-mediated atypical HUS, chemotherapy-associated HUS, or organ transplant–associated HUS) can be triggered by mRNA vaccination remains to be determined.

Our case does not modify the favorable safety profile of mRNA vaccination in patients with systemic sclerosis, given the potential occurrence of severe COVID-19 forms in this population.[4] Growing experience from large cohorts of patients with systemic sclerosis may provide additional information and allow more robust conclusions to be drawn regarding the vaccination safety profile in this specific population.

Nevertheless, our observation underscores the need for close monitoring of vascular complications in patients with systemic sclerosis after vaccination against COVID-19.

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Relapse of class V lupus nephritis after vaccination with COVID-19 mRNA vaccine

To the editor: Several of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines use an mRNA lipid nanoparticle-encapsulated platform. In experimental models, the induced antibody titers are higher, and T- and B-cell responses are enhanced, compared to the level with traditional vaccines. Possibly, due to this higher efficacy, more and more kidney-specific side effects of mRNA vaccines related to immune-mediated glomerular disease are being reported.[1–3] Because of similar type I interferon and proinflammatory cytokine pathways in systemic lupus erythematodes and coronavirus disease 2019 (COVID-19), either potentiated or dysregulated immune responses to SARS-CoV-2 vaccines can be suspected to trigger disease activity in previously stable lupus.[4]

We present the case of a 42-year-old female patient who was diagnosed with lupus nephritis class V in 2016 on renal biopsy (Figure 1g and h) after she developed typical

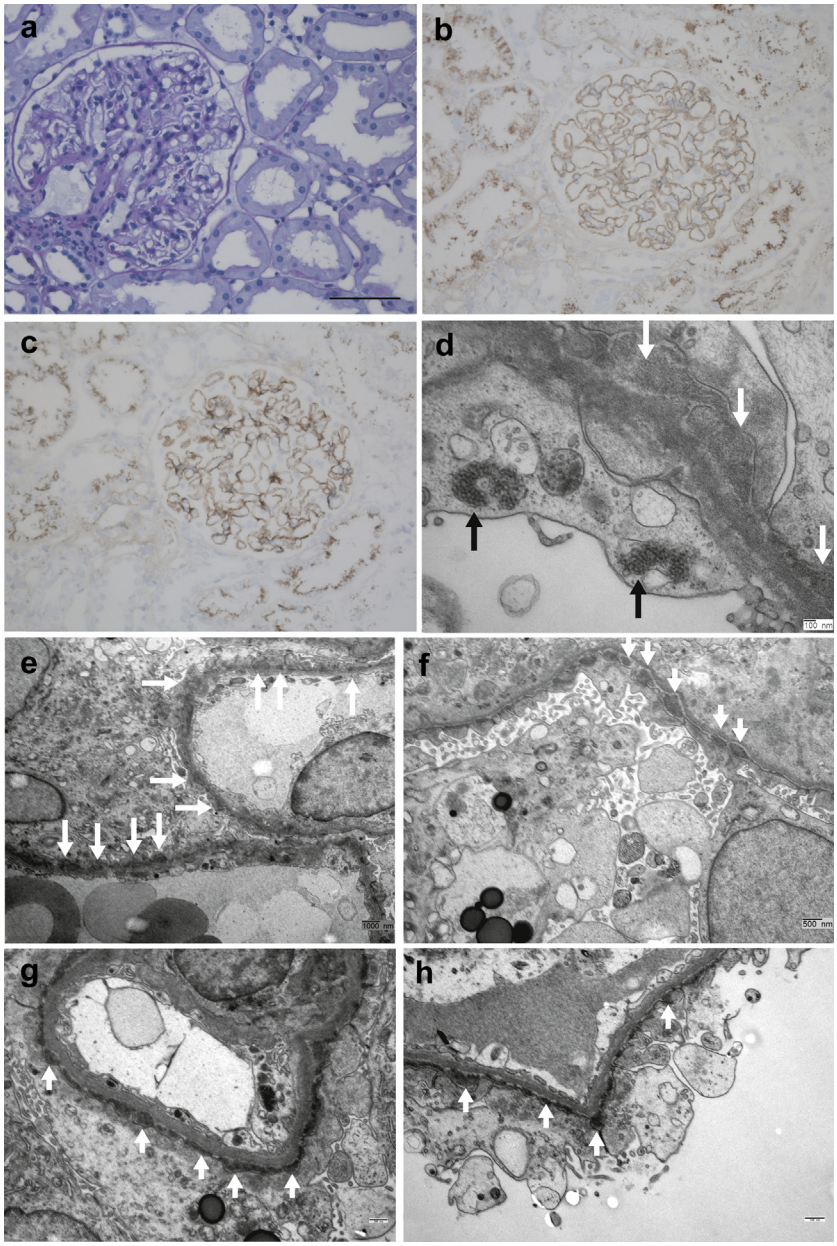

Figure 1 | Representative micrographs showing normal glomeruli by conventional histology (periodic acid–Schiff reaction) except for (a) slight focal and segmental mesangial hypercellularity and (b) granular immunoreactivity for IgG and (c) C3c along glomerular capillary walls and within the mesangium. (**d–h**) Ultrastructure (contrasted with osmium tetroxide and tannic acid) reveals endothelial tubuloreticular inclusions (black arrows) and global subepithelial electron-dense immune deposits (white arrows) amounting to >80% of all capillary loops as well as moderate (40%) loss of podocyte foot processes. (**g,h**) First biopsy from 2016, for comparison. (**a**) Periodic acid–Schiff reaction; (**b,c**) DAB immunohistochemistry. (**a–c**) Original magnification ×400. Bar = 50 μm. Ultrastructure: bars = (**d**) 100 nm, (**e,g**) 500 nm, and (**f,h**) 1000 nm. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

butterfly rash and nephrotic syndrome with proteinuria of 6 g/d (Figure 2a). At diagnosis, anti-dsDNA-IgG levels were 210 IU/ml, the antinuclear antibody (ANA) titer result was 1:640, and both complement C3 and C4 were slightly reduced (Figure 2b–d). Renal function was not impaired in 2016. She received induction treatment with cyclophosphamide and steroids and went into full remission (Figure 2a). Maintenance therapy consisted of hydroxychloroquine 200 mg qd until 2021. On April 21, 2021, she received the first dose of the COVID-19 mRNA vaccine BNT162b2, which she tolerated well. One week later, the proteinuria increased from 0.07 g/d to 6 g/d, and 5 weeks later it increased to 8.4 g/d (Figure 2a). She developed nephrotic syndrome with hyperlipoproteinemia and hypalbuminemia. Renal function was again not impaired. There were no other obvious

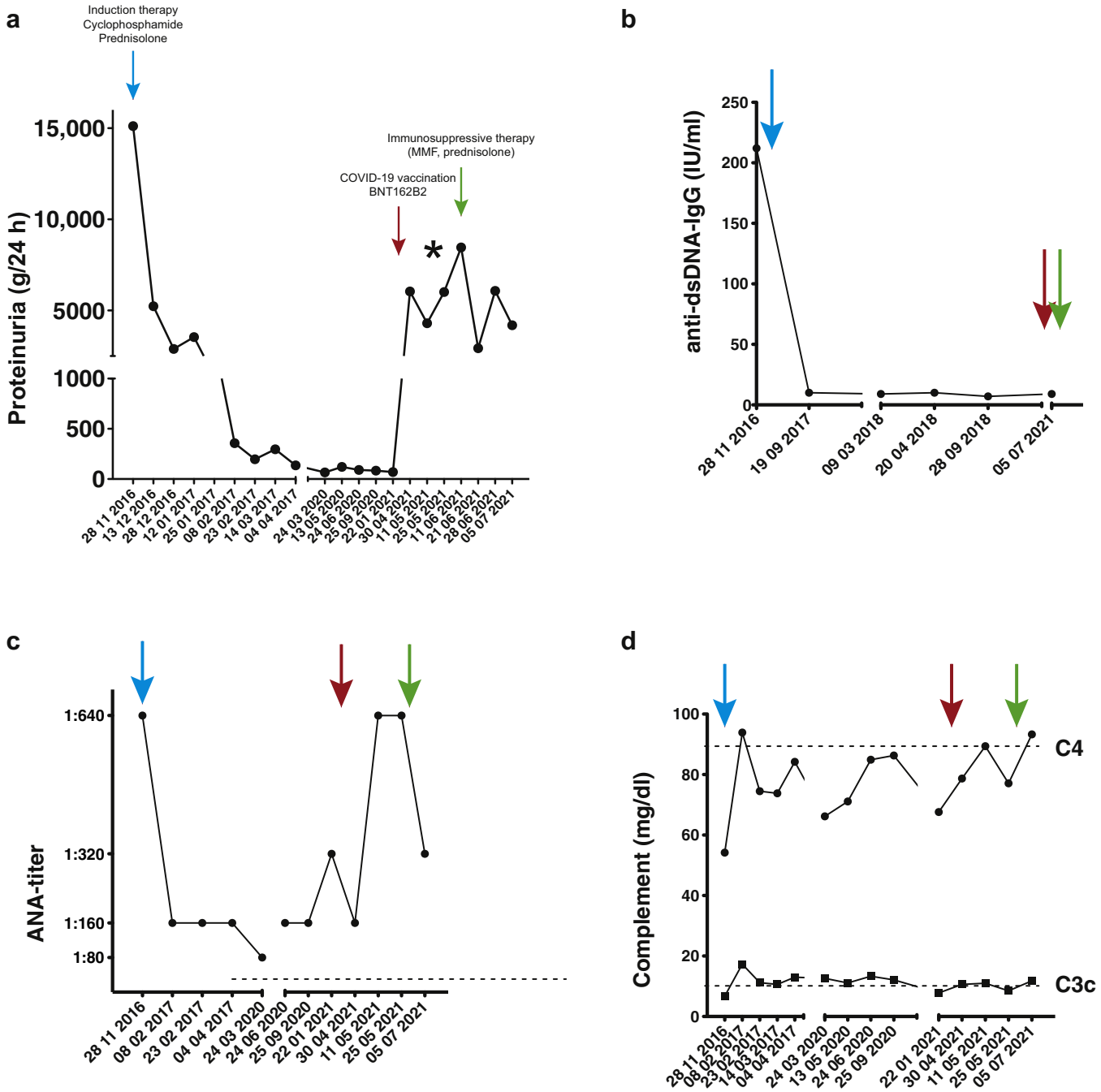

Figure 2 | (a) Time course of proteinuria with end of induction therapy (blue arrow), coronavirus disease 2019 (COVID-19) vaccination (red arrow), and start of immunosuppressive therapy (green arrow). *Time of biopsy and detection of spike-specific IgG antibody after the first vaccination with BNT162b2. Serological parameters (**b**) anti-dsDNA-IgG, (**c**) antinuclear antibody (ANA), and (**d**) complement C3c and C4 are plotted in relation to induction therapy, 2016 (blue); vaccination (red); and start of immunosuppression (green). Dotted lines mark normal limits. Note that the dates are different in the graphs because values were not obtained at each visit. MMF, mycophenolate mofetil.

triggers present. Complement was slightly below normal, as it had been in previous analyses (Figure 2d). ANA titers increased to 1:640, but there was no spike of anti-dsDNA-IgG (Figure 2b and c). Hematuria and skin abnormalities were absent, but she was feeling fatigued and complained about an unspecific weakness. Renal biopsy (Figure 1a–f) demonstrated lupus nephritis class V and II with slight focal and segmental mesangial hypercellularity (up to 5 cells per mesangial field) without any irregularities of the basement membranes

(no spikes or double contours). The modified activity score (International Society of Nephrology/Renal Pathology Society/National Institutes of Health [ISN/RPS/NIH]) was 0/24, and the chronicity score was 0/12.[5] Spontaneous remission did not occur in follow-up measurements, and as nephrotic proteinuria persisted for 7 weeks, we initiated immunosuppressive therapy with mycophenolate mofetil (1 g bid) and prednisolone (60 mg qd). As can be seen in Figure 2a, proteinuria declined initially, and the patient reported substantial improvement of her general well-being and the absence of foamy urine. Proteinuria increased again the following week, but with a tendency toward improvement of the absolute amount in the next measurements. ANA titers, which increased after vaccination, also declined after the start of therapy. Anti-DNA-antibody levels did not increase after the vaccination, and the slightly-below-normal C3c-levels increased (Figure 2b–d).

The patient had already developed an antibody response against the spike protein of SARS-CoV-2 (Figure 2); thus, we decided to postpone the second vaccination in light of declining incidence numbers. When to proceed with the second vaccination remains to be determined, as full remission of the proteinuria has not been achieved yet.

To our knowledge, our case report is the first to describe a biopsy-proven relapse of lupus nephritis class V and II. New-onset minimal change glomerulopathies[3,6] and other forms of glomerulonephritis (e.g., *de novo* IgAN,[2] relapse IgA nephropathy,[1] and even anti–glomerular basement membrane glomerulonephritis)[7] have been described as sequelae of mRNA COVID-19 vaccination. This case adds yet another piece of evidence that relapse in immune-mediated disease might be induced by COVID-19 mRNA vaccine. Although the mechanisms triggering these relapses are still elusive, stringent postvaccination surveillance for renal function, proteinuria, and serologic markers for immune disease is essential in this vulnerable patient population.

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Acute kidney injury with gross hematuria and IgA nephropathy after COVID-19 vaccination

To the editor: The mRNA coronavirus disease 2019 (COVID-19) vaccines induce an IgG response that prevents people from contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Interestingly, there are now at least 6 cases of gross hematuria reported in patients with a history of biopsy-proven IgA nephropathy (IgAN), involving both mRNA vaccines.[1–3] All of the previous patients were treated with supportive therapy with rapid resolution of hematuria and no acute kidney injury (AKI). It has been reported in preclinical trials that nasal shedding of SARS-CoV-2 still occurred after vaccination with both mRNA vaccines, suggesting a lack of a mucosal IgA response.[1,4] We also cared for 2 patients who had prior biopsy-proven IgAN, who developed gross hematuria after their second dose of the Pfizer vaccine, without a preceding COVID-19 infection. Table 1 outlines the clinical data. Our first patient presented 5 days after his second dose, with nonspecific myalgias, chills, headache, dysuria, and gross hematuria within 24 hours of initial symptoms. Previous IgAN flares in this patient were precipitated by upper respiratory infections and were limited to gross hematuria with no AKIs and no requirement for steroids in the past. His postvaccine workup was notable for AKI, with a serum creatinine level of 3.53 mg/dl and a urine protein–creatinine ratio of 3.0. He was empirically started on steroids with recovery to baseline renal function at 1 month and recovery to baseline proteinuria within 2 months. Our second patient developed gross hematuria within 24 hours of receiving his second dose. His hematuria resolved after 3 days with supportive therapy only. To our knowledge, we are the first to report an IgAN flare that has led to an AKI that resolved with steroid therapy. We agree that it is not clear how a nonmucosal immune challenge led to an IgAN