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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New-onset systemic lupus erythematosus beginning as class V lupus nephritis after COVID-19 vaccination

To the editor: We read the report by Tuschen *et al.* of a 42-year-old woman with a previous diagnosis of systemic lupus erythematosus (SLE) and class V lupus nephritis (LN) that developed a flare 1 week after vaccination with the mRNA coronavirus disease 2019 (COVID-19) vaccine BNT162b2 (Pfizer–BioNTech).[1] Here, we report a case of a 23-year-old woman who presented with nephrotic syndrome 1 week after vaccination with the first dose of the AZD1222 (ChAdOx1-S) nCoV-19 vaccine (AstraZeneca).

She had no previous medical history of disease and was taking no medications. She had not been previously infected by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Her family history was negative for autoimmune diseases. On July 21, 2021, she was vaccinated, without major adverse events. One week later, she developed abrupt eyelid edema and foamy urine that progressed to anasarca within days. She also experienced hair loss. Physical examination showed normal blood pressure and pitting edema up to the thighs. Her laboratory tests showed lymphopenia (1000 × 10^3/ml), a serum creatinine level of 0.8 mg/dl (estimated glomerular filtration rate of 104 ml/min per 1.73 m^2), a serum albumin level of 1.57 g/dl, a total cholesterol level of 351 mg/dl, proteinuria of 12.6 g/24 h (protein-to-creatinine ratio of 11.0 mg/mg), a complement C3 level of 85 mg/dl (reference, 87–200 mg/dl), and a C4 level of 12 mg/dl (reference, 19–52 mg/dl). Antinuclear antibody (ANA) titer was a 1:1280 homogeneous pattern; the anti-dsDNA-IgG level was 17.1 IU/ml; and antiphospholipid antibody panel was negative. Serology for SARS-CoV-2 demonstrated negative IgM and IgG antibodies to the nucleocapsid antigen (NCP), suggesting no previous infection by this virus. Anti–SARS-CoV-2–Spike IgG antibodies in response to vaccination were quantified at 32.8 UI/ml (reference, <1 UI/ml), suggesting an appropriate response to vaccination.

The kidney biopsy performed 1 week after the start of symptoms (2 weeks post-vaccination) demonstrated secondary membranous nephropathy, with diffuse thickening of the basement glomerular membrane and mild mesangial expansion. One of 13 glomeruli had sclerosis, and interstitial fibrosis was less than 10%, with no tubular atrophy, and normal vessels. Direct immunofluorescence revealed deposits of IgG, IgM, C1q, C3c, kappa, and lambda chains in the subepithelial and mesangial space. Electron microscopy showed mesangial and subepithelial electron-dense deposits (Figure 1). A diagnosis of SLE with class V LN was established. We started treatment with mycophenolate mofetil, high-dose glucocorticoids, hydroxychloroquine, and diuretics. After 3 weeks of follow-up, edema has improved and the patient continues follow-up.

Diverse glomerular diseases have been reported in association with COVID-19 vaccination, particularly podocytopathies, IgA nephropathy, and anti-neutrophil cytoplasmic antibody (ANCA) vasculitis.[2] For SLE, the Vaccination Against COVID in Systemic Lupus (VACOLUP) study[3] reported 2 renal flares (with no specification of the type of LN), and the report by Tuschen *et al.*[1] also corresponded to a class V LN flare. In animal models, the loss of the T-helper type 1 (Th1)/T-helper type 2 (Th2) balance is crucial for the development of LN, and may even determine the phenotype of the glomerulonephritis.[4] For example, the lack of the *WSX-1* gene in the MRL/lpr SLE mice model increases both the Th2 response, with increased interleukin-4, and the development of a disease resembling human membranous nephropathy with IgG1-dominant electro-dense deposits in the subepithelial space.[5] Moreover, the Th1 response has been associated with the development of LN proliferative variants.[6]

T cells are key to stimulating the immune response to vaccination. From phase 1 and 2 trials of the AZD1222 nCoV-19 vaccine, it has been shown that the spike-specific effector T-cell response presents early, from day 8 post-vaccination through day 56.[7] There is a robust Th1 response with an expansion of CD8+ T cells, with increases in cytokines such as tumor necrosis factor, interleukin-2, and interferon gamma. However, no Th2 response has been found after AZD1222 nCoV-19 vaccination.[8]

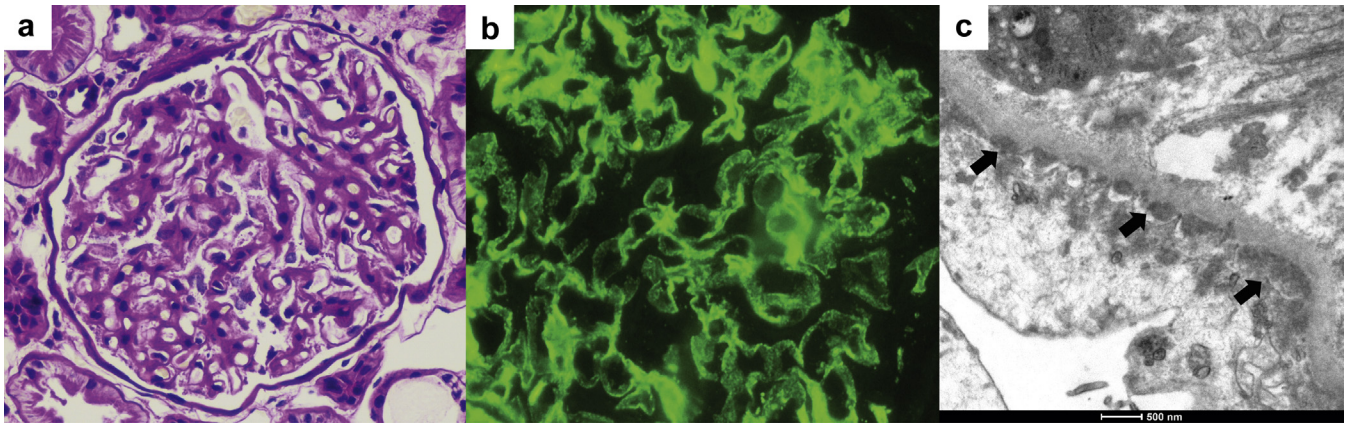

Figure 1 | Representative micrographs from the kidney biopsy. (**a**) Light microscopy showed diffuse thickening of the glomerular basement membrane with mild mesangial expansion (periodic acid–Schiff stain, original magnification ×40). (**b**) Direct immunofluorescence demonstrated IgG, IgM, C1q, kappa, lambda, and C3c deposits in a fine granular pattern along the glomerular basement membrane and mesangium (**b**, C3c deposits). (**c**) Electron microscopy showed mesangial and subepithelial (black arrows) electron-dense deposits. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

Until now, there are no mechanisms or triggers to support a direct causal relationship between COVID-19 vaccination and SLE flares.[9] In this case, it is plausible that the immune response elicited by vaccination elicited SLE emergence in an immunologically predisposed individual. Patients with SLE after vaccination need to be closely followed, and post-vaccination events need to be registered in multinational registries.[3]

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Antiresorptives in patients with chronic kidney disease with adynamic bone: Is absence of evidence of harm equal to no harm?

To the editor: We are impressed with the concept discussed by Haarhaus *et al.* of using antiresorptives in patients with chronic kidney disease (CKD) with adynamic bone (AB),[1] but we need to clarify some concerns. Clinical trials put all patients in 1 group, without stratifying them according to their bone turnover. The impressive response to antiresorptives in patients with high-turnover bone disease might mask their potential harm in patients with AB. Antiresorptives with mild AB might not be harmful, but what about in patients with severe hypoparathyroidism and profound AB? No studies have investigated the impact of antiresorptives specifically in patients with AB who have CKD.

The authors have emphasized the benefits of parathyroidectomy.[1] The evidence is based mainly on observational studies with inherent limitations. Moreover, these benefits could be attributed to the resolution of severe high-turnover bone disease, which would not occur with use of antiresorptives in CKD patients with AB. Prospective studies have shown safety concerns after parathyroidectomy.[2,3]

There are major differences between bisphosphonates and denosumab pharmacodynamics, especially in CKD.