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De novo vasculitis after mRNA-1273 (Moderna) vaccination

To the editor: The mRNA-1273 (Moderna) vaccine is a lipid nanoparticle–encapsulated mRNA-based vaccine that encodes the prefusion stabilized full-length spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of the current coronavirus disease 2019 (COVID-19) pandemic. In a randomized placebo-controlled phase 3 trial, the mRNA-1273 (Moderna) vaccine showed high efficacy at preventing COVID-19. Aside from transient local and systemic reactions, no safety concerns were identified.[1]

Here we report 2 patients who developed *de novo* vasculitis shortly after receiving the mRNA-1273 (Moderna) vaccine.

Patient 1 was a 39-year-old man with a history of treated arterial hypertension. After a well-tolerated first dose of mRNA-1273 (Moderna) vaccine, he had severe fever, flu-like symptoms, and macrohematuria immediately after the second dose. Diagnostic workup showed acute kidney injury (AKI) with nephritic syndrome. Repeat reverse transcription polymerase chain reaction (RT-PCR) testing for SARS-CoV-2 from nasopharyngeal swabs was negative. A kidney biopsy revealed severe crescentic IgA nephritis (Figure 1a–d). Treatment with high-dose glucocorticoids and cyclophosphamide was initiated. Over the following weeks, serum creatinine normalized and proteinuria significantly decreased, but microhematuria persisted.

Patient 2 was a healthy 81-year-old man. After the first dose of the mRNA-1273 (Moderna) vaccine, he had sustained flu-like symptoms, which significantly worsened after the second dose. Laboratory workup showed AKI, proteinuria in the nonnephrotic range, and an elevated proteinase 3 (PR3) anti–neutrophil cytoplasmic antibody (ANCA) titer. A pulmonary computed tomography scan demonstrated bilateral necrotic masses of the lung parenchyma and slight pleural effusion, without evidence of tumor or lymphadenopathy. Repeat RT-PCR testing for SARS-CoV-2 from nasopharyngeal swabs was negative; serologic testing for SARS-CoV-2 showed a positive anti-spike IgG and negative anti-nucleocapsid IgG. A kidney biopsy performed at day 22 after the second vaccine dose showed severe pauci-immune crescentic glomerulonephritis with capillary necrosis and vasculitis present in the renal vessel walls (Figure 1e–h). The patient was treated with high-dose glucocorticoids, cyclophosphamide, and plasmapheresis. Over the course of 3 weeks, the patient's symptoms disappeared, and renal function improved along with a significant decrease of PR3-ANCA and anti-spike IgG titer. Immunohistochemical staining for the SARS-CoV-2 spike protein was negative in both patients.

Appearance of AKI concurrently with serious systemic symptoms shortly after the second dose strongly suggests a causal mechanism. Isolated cases of SARS-CoV-2–induced IgA vasculitis and ANCA-associated vasculitis have been reported.[2,3] In contrast, 2 patients with preexisting IgA nephropathy have been reported to experience gross hematuria after receiving the mRNA-1273 (Moderna) vaccine, with spontaneous resolution after 3 days.[4] Two cases of minimal change nephropathy associated with the BNT162b2 mRNA (Pfizer-BioNTech) vaccine have also been described.[5,6]

To our knowledge, these are the first 2 cases of *de novo* vasculitis after vaccination with an mRNA-based vaccine.

The mechanism remains to be elucidated but is likely due to aberrant immune response to the spike protein or mRNA of SARS-CoV-2 in predisposed individuals.

We hope that this correspondence will prompt clinicians to consider vasculitis workup in the case of protracted systemic reactions, new-onset macrohematuria, or worsening kidney function after vaccination with mRNA-based SARS-CoV-2 vaccines. Given the massive scale-up of vaccination efforts worldwide, it is very likely that additional cases of vaccination-induced vasculitis will emerge. We strongly encourage additional reporting and communication for this rare, albeit severe, side effect of the mRNA-1273 (Moderna) vaccine.

DISCLOSURE

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AUTHOR CONTRIBUTIONS

All authors contributed to the study design. MAA, ML, CS, and MM performed the data analysis. UH-D and DGF verified the data. All authors contributed to the data interpretation. MAA and ML wrote the first draft of the manuscript, which was subsequently revised by the remaining authors. All authors approved the final version of the manuscript before submission.

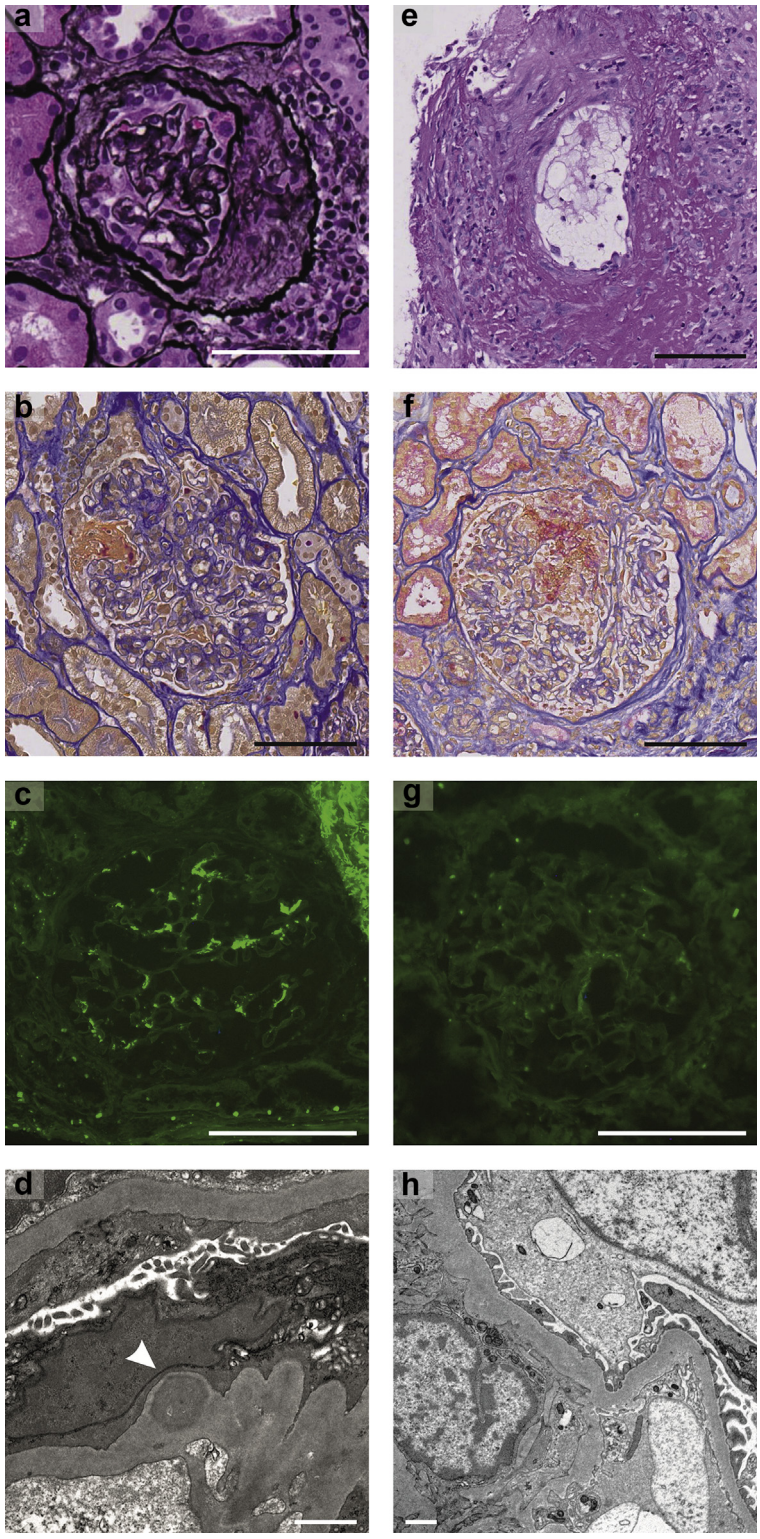

Figure 1 | (a–d) Histopathologic findings of patient 1 with (a,b) crescentic IgA nephritis and (c,d) mesangial IgA deposition on immunofluorescence and electron microscopy, and histopathologic findings of patient 2 with (e,f) severe necrotizing vasculitis, but (g,h) without deposition of Igs on immunofluorescence and electron microscopy. (**a**) Hematoxylin-eosin and silver staining (original magnification ×20). (**b**) Acid fuchsin–orange G stain (original magnification ×20). (**c**) Immunofluorescence against IgA (original magnification ×20). (**d**) Transmission electron microscopy. The arrowhead shows mesangial IgA depot. (**e**) Periodic acid–Schiff stain (original magnification ×20). (**f**) Acid fuchsin–orange G stain (original magnification ×20). (**g**) Immunofluorescence against IgA (original magnification ×20). (**h**) Transmission electron microscopy. Bar = 100 μm for light microscopy and immunofluorescence, and bar = 1 μm for electron microscopy. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

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Humoral response of the mRNA-1273 SARS-CoV-2 vaccine in peritoneal dialysis patients

To the editor: Patients with end-stage kidney disease on peritoneal dialysis are known to have an altered cellular and humoral immunity evidenced by the reduced response they have to several vaccines, such as the hepatitis B or influenza vaccine, albeit their response rate is slightly higher than that of patients on hemodialysis.[1]

Although patients on peritoneal dialysis have a reported lower prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection than patients on in-center hemodialysis, probably because of their ability to self-isolate appropriately, they still have higher mortality and longer hospital admissions than the general population.[2] Currently, there is a lack of data on this population's response to SARS-CoV-2 vaccines. As mRNA vaccines have data of higher potency in comparison to other types of vaccines, this class has been suggested as the preferred one until more data on their response are available.[3]

We evaluated the humoral response of 34 patients from our peritoneal dialysis unit at the Hospital Clínic of Barcelona. This population was immunized with 2 doses of the mRNA-1273 vaccine separated by a 28-day interval as specified by the manufacturer. Antibody titers were quantified with the Siemens Healthineers Atellica IM SARS-CoV-2 IgG assay, which detects IgG antibodies to the receptor-binding domain

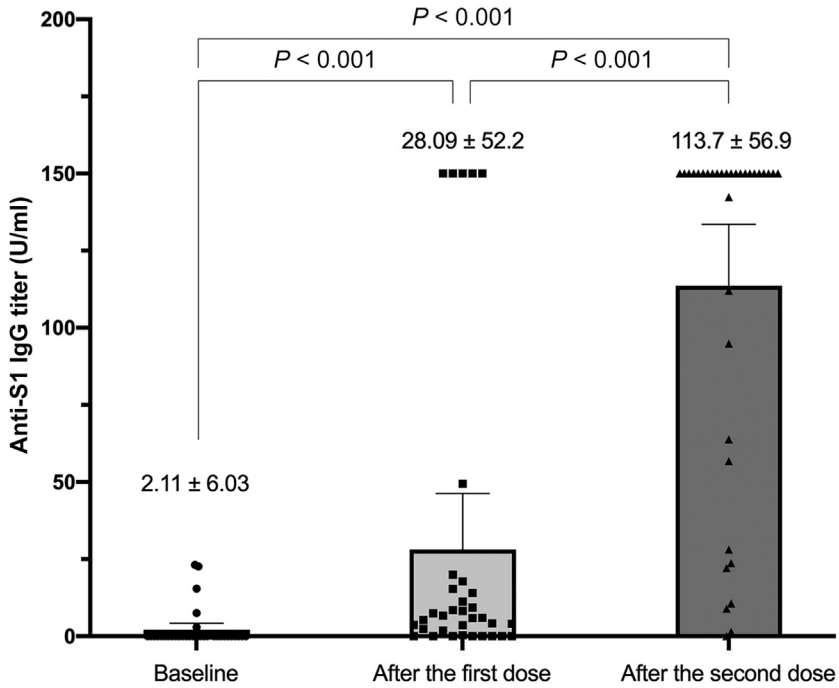

Figure 1 | IgG antibodies to the receptor-binding domain of the S1 spike antigen of severe acute respiratory syndrome coronavirus 2 (anti-S1 IgG) titer at baseline and after each dose of the mRNA-1273 vaccine.