



### De novo vasculitis after mRNA-1273 (Moderna) vaccination

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3 **Letter to the Editor ::**  
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9 **De novo vasculitis after mRNA-1273 (Moderna) vaccination**  
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**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 SARS-Cov-2, the cause of the current Covid-19 pandemic. In a randomized, placebo-controlled phase 3 trial, the mRNA-1273 (Moderna) vaccine showed high efficacy at preventing Covid-19 illness. Aside from transient local and systemic reactions, no safety concerns were identified.<sup>1</sup>

Here we report two patients that 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 developed severe fever, flu-like symptoms and macrohematuria immediately after the second dose. Diagnostic workup showed acute kidney injury (AKI) with a nephritic syndrome. Repeat RT-PCR testing for SARS-CoV-2 from nasopharyngeal swabs was negative. Kidney biopsy revealed severe crescentic IgA-nephritis (Fig. 1 a-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 mRNA-1273 (Moderna) vaccine, he experienced sustained flu-like symptoms, which significantly worsened after the second dose. Laboratory workup showed AKI, proteinuria in the non-nephrotic range and an elevated proteinase 3 (PR3) antineutrophil cytoplasmic antibody (ANCA) Titer. A pulmonary CT-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, serological testing for SARS-CoV-2 showed positive anti-spike-IgG and negative anti-nucleocapsid-IgG. A kidney biopsy performed at day

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3 22 after the second vaccine dose showed severe pauci-immune crescentic glomerulonephritis  
4 with capillary necrosis and vasculitis present in renal vessel walls (Fig. 1 e-h). The patient was  
5 treated with high dose glucocorticoids, cyclophosphamide and plasmapheresis. Over the course  
6 of 3 weeks, the patient's symptoms disappeared and renal function improved, along with a  
7 significant decrease of PR3-ANCA and anti-spike IgG titer. Immunohistochemical staining for  
8 SARS-CoV-2 spike protein was negative in both patients.  
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11 Appearance of AKI concurrently with serious systemic symptoms shortly after the second dose  
12 strongly suggests a causal mechanism. Isolated cases of SARS-CoV-2-induced IgA-vasculitis  
13 and ANCA-associated vasculitis have been reported.<sup>2,3</sup> On the other hand, two patients with  
14 preexisting IgA nephropathy have been reported to experience gross hematuria after receiving  
15 the mRNA-1273 (Moderna) vaccine, with spontaneous resolution after 3 days.<sup>4</sup> Two cases of  
16 Minimal Change Nephropathy associated with the BNT162b2 mRNA (Pfizer–BioNTech)  
17 vaccine have also been described.<sup>5,6</sup>

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19 To the best of our knowledge, these are the first two cases of *de novo* vasculitis after vaccination  
20 with an mRNA-based vaccine.  
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23 The mechanism remains to be elucidated, but is likely due to aberrant immune response to spike  
24 protein or mRNA of SARS-Cov-2 in predisposed individuals.  
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27 We hope that this correspondence will prompt clinicians to consider vasculitis work-up in case  
28 of protracted systemic reactions, new onset macrohematuria or worsening kidney function after  
29 vaccination with mRNA-based SARS-CoV-2 vaccines. Given the massive scale-up of  
30 vaccination efforts worldwide, it is very likely that additional cases of vaccination-induced  
31 vasculitis will emerge. We strongly encourage additional reporting and communication for this  
32 rare, albeit severe side effect of the mRNA-1273 (Moderna) vaccine.  
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**Author contributions**

All authors contributed to the study design. MA, ML, CS and MM carried out the data analysis. UH and DF verified the data. All authors contributed to the data interpretation. MA 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 prior to submission.

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We declare no other competing interests.

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As there was no direct funding for the study, the funding bodies were not involved in the study design; in the collection, analysis, and interpretation of data; the writing of the report; or in the decision to submit the paper for publication.

**Ethics committee approval**

Not applicable.

## References

1. Baden LR, El Sahly HM, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med*. 2021;384(5):403-416.
2. Suso AS, Mon C, Onate Alonso I, et al. IgA Vasculitis With Nephritis (Henoch-Schonlein Purpura) in a COVID-19 Patient. *Kidney Int Rep*. 2020;5(11):2074-2078.
3. Uppal NN, Kello N, Shah HH, et al. De Novo ANCA-Associated Vasculitis With Glomerulonephritis in COVID-19. *Kidney Int Rep*. 2020;5(11):2079-2083.
4. Negrea L, Rovin BH. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. *Kidney Int*. 2021.
5. Lebedev L, Sapojnikov M, Wechsler A, et al. Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine. *Am J Kidney Dis*. 2021.
6. D'Agati VD, Kudose S, Bomback AS, Adamidis A, Tartini A. Minimal Change Disease and AKI following the Pfizer-BioNTech COVID-19 Vaccine. *Kidney International*.

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7 **Figure Legends:**

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9 **Figure 1:**

10 A-D show histopathological findings of patient 1 with crescentic IgA-nephritis (A, B) and  
11 mesangial IgA-deposition in immunofluorescence and electron microscopy (C, D).  
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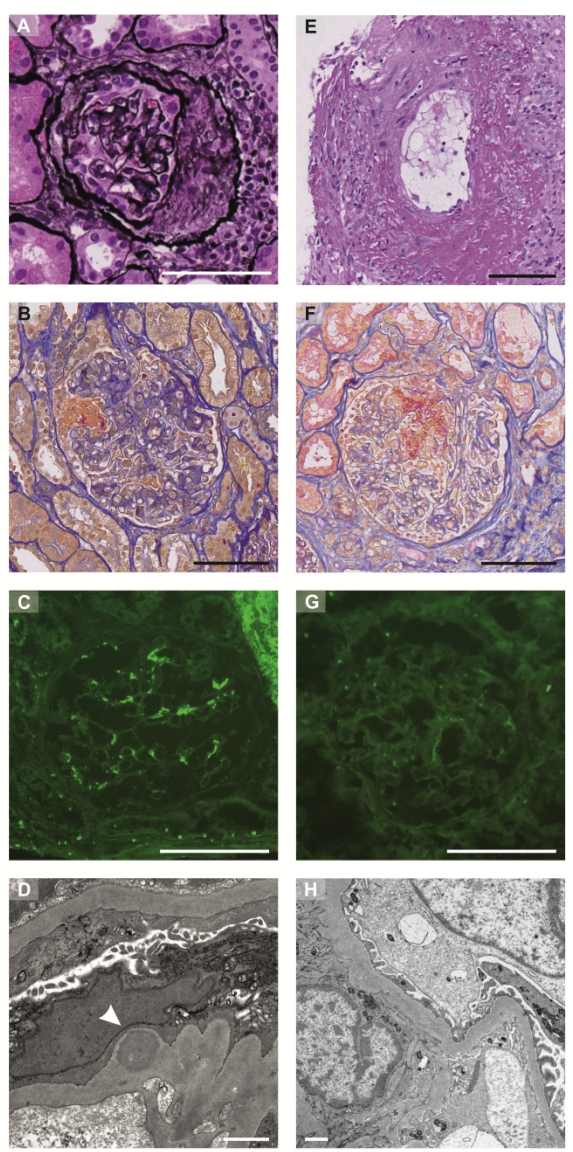
14 A: hematoxylin–eosin and silver staining (20x), B: acid fuchsin–orange G stain (20x), C:  
15 immunofluorescence against IgA (20x), D: transmission electron microscopy, arrowhead shows  
16 mesangial IgA depot.  
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22 E-H show histopathological findings of patient 2 with severe necrotizing vasculitis, without  
23 deposition of immunoglobulins in immunofluorescence and electron microscopy.  
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26 E) Periodic acid–Schiff's stain (20x), F) acid fuchsin–orange G stain (20x), G:  
27 immunofluorescence against IgA (20x), H: transmission electron microscopy.  
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31 Scale bar is 100  $\mu\text{m}$  for light microscopy and immunofluorescence and 1  $\mu\text{m}$  for electron  
32 microscopy.  
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Histopathology of the Two Patients Showing Crescentic IgA Nephritis and Necrotizing Vasculitis