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.

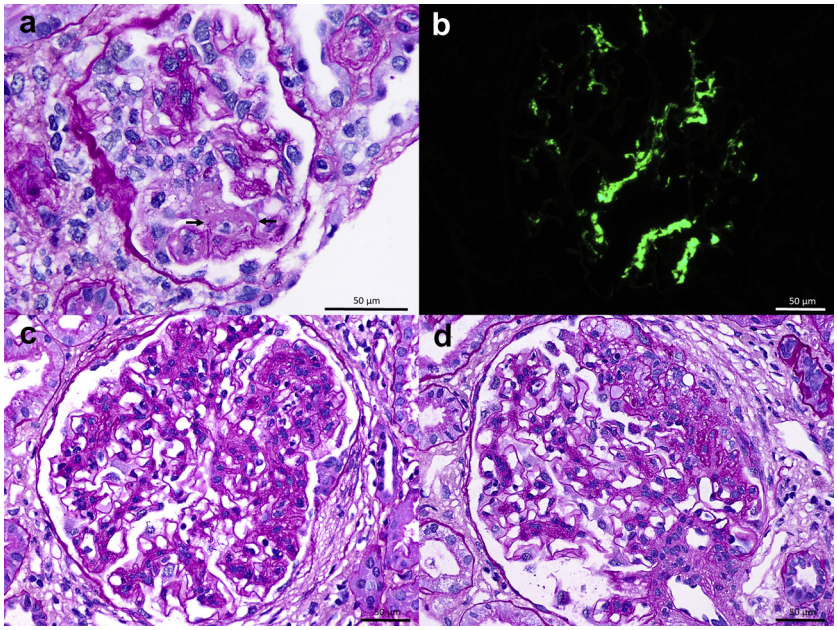

Figure 1 | (a) Light microscopy from patient 1 shows a glomerulus with fibrinoid necrosis associated with rupture of the glomerular basement membranes (arrows), and a small cellular crescent (periodic acid–Schiff). Original magnification ×1000. (**b**) Immunofluorescence demonstrates 3+ granular global mesangial staining for IgA. Original magnification ×600. (**c**) Light microscopy from patient 2 shows a glomerulus with segmental endocapillary hypercellularity including infiltrating neutrophils on a background of mesangial hypercellularity (periodic acid–Schiff). Original magnification ×600. (**d**) A glomerulus with a segmental scar contains an overlying segmental fibrous crescent with rupture of Bowman's capsule (periodic acid–Schiff). Original magnification ×600. (**a–d**) Bars = 50 μm. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

notion that immune response to vaccination exacerbated a preexisting IgA nephropathy. The rapid development of gross hematuria within several days of the second vaccination implicates a systemic cytokine-mediated flare, possibly via induction of heightened IgA1 anti-glycan immune responses. These reports are analogous to our previous observation that infection with severe acute respiratory syndrome coronavirus 2 itself can be associated with flares of underlying autoimmune glomerular diseases.[4] It remains unclear how the postvaccination setting should be factored into the design of optimal therapy for these active glomerular lesions.

1. Negrea L, Rovin BH. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. *Kidney Int*. 2021;99:1487.
2. Rahim SEG, Lin JT, Wang JC. A case of gross hematuria and IgA nephropathy flare-up following SARS-CoV-2 vaccination. *Kidney Int*. 2021;100:238.
3. Tan HZ, Tan RY, Choo JCJ, et al. Is COVID-19 vaccination unmasking glomerulonephritis? *Kidney Int*. 2021;100:469–471.
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Satoru Kudose[1], Paul Friedmann[2], Oltjon Albajrami[3] and Vivette D. D'Agati[1]

[1]Department of Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, USA; [2]Renal Care Associates, Rockville Center, New York, New York, USA; and [3]Nephrology and Hypertension Associates, Middlebury, Connecticut, USA

Correspondence: *Vivette D. D'Agati, Department of Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York 10032, USA. E-mail: vdd1@cumc.columbia.edu*

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Is COVID-19 vaccination unmasking glomerulonephritis?

To the editor: We read with great interest the reports of macroscopic hematuria occurring hours following coronavirus disease 2019 (COVID-19) vaccination in patients with known IgA nephropathy (IgAN).[1,2] We report 2 previously healthy individuals who presented with macroscopic hematuria shortly after COVID-19 vaccination and were diagnosed with IgAN and crescentic glomerulonephritis, respectively.

A 41-year-old woman presented with headache, generalized myalgia, and new-onset macroscopic hematuria 1 day after the second dose of tozinameran (Pfizer-BioNtech COVID-19 vaccine). Her medical history was unremarkable except for gestational diabetes. She had no prior history of macroscopic or synpharyngitic hematuria, and urine analysis during pregnancy did not show any proteinuria. She

Table 1 | Patient demographics and clinical characteristics

	Patient 1	Patient 2	Reference range
Clinical presentation			
Age, yr/race/sex	41/Chinese/female	60/Malay/female	
Medical history	Gestational diabetes mellitus	Hyperlipidemia	
Date of vaccination			
First dose	March 3, 2021	January 29, 2021	
Second dose	March 26, 2021	February 19, 2021	
Date of hematuria	March 27, 2021	February 20, 2021	
Date of presentation to nephrology	March 28, 2021	March 31, 2021	
Blood pressure at presentation, mm Hg	153/99	188/95	
Significant laboratory results[a]			
Serum creatinine, μmol/L	153	541	
Urine dysmorphic red blood cells/μl	>200	>200	
Urine protein-to-creatinine ratio, g/g	2.03	7.58	
Serum Ig			
Serum IgG, g/L	12.90	9.95	5.49–17.11
Serum IgA, g/L	6.40	1.62	0.47–3.59
Serum IgM, g/L	1.10	0.35	0.15–2.59
Complement C3, g/L	0.83	1.11	0.90–1.80
Complement C4, g/L	0.20	0.24	0.10–0.40
Anti-nuclear antibody	1:320; Homogeneous	Negative	
Anti-GBM antibody (ELISA)	<1.5	10.0	<7 U/ml = negative; 7–10 U/ml = indeterminate; >10 U/ml = positive
Anti-GBM antibody (IF)	Not done	Positive	
Histopathology report			
Glomeruli	36 Glomeruli; 5 globally sclerosed. Focal proliferative glomerulonephritis with focal segment glomerulosclerosis; 6% cellular and 8% fibrocellular crescents	22 Glomeruli; 6 segmentally sclerosed. Diffuse crescentic glomerulonephritis with segmental sclerosis; 59% cellular, 14% fibrocellular, and 5% fibrous crescents	
Tubules and interstitium	Mild tubulointerstitial inflammation. Mild tubular atrophy and interstitial fibrosis	Acute tubular injury Mild tubular atrophy	
Vessels	Mild hyalinosis. No vasculitis or thrombotic microangiopathy	Mild intimal fibrosis	
IF	Dominant glomerular IgA staining	Trace to 1+ linear IgG staining of glomerular basement membrane	
Electron microscopy	Electron-dense deposits mostly in mesangial and paramesangial locations	No electron-dense deposits	
Treatment	Pulse methylprednisolone, followed by oral prednisolone; i.v. cyclophosphamide	Pulse methylprednisolone, followed by oral prednisolone; oral cyclophosphamide; plasma exchange	

ELISA, enzyme-linked immunosorbent assay; GBM, glomerular basement membrane; IF, immunofluorescence.
[a]Other autoantibodies, such as anti–streptomycin O titer (ASOT), anti–double-stranded DNA (anti-dsDNA), anti–neutrophil cytoplasmic antibody (ANCA) by IF, anti-myeloperoxidase, and anti–proteinase 3 antibodies, were not detected.

was found to have subnephrotic range proteinuria, hypertension, and elevated serum creatinine on admission (Table 1). Renal biopsy performed showed IgAN with fibrocellular and fibrous crescents (Supplementary Figure S1). The chronic features on histopathology suggest preexisting undiagnosed IgAN that may have been unmasked after the vaccination.

A 60-year-old woman developed macroscopic hematuria 1 day after receiving the second dose of tozinameran. She was treated empirically for urinary tract infection, but presented 6 weeks later with persistent macroscopic hematuria, nephrotic-range proteinuria, hypertension, and acute kidney injury (Table 1). She had been well before her vaccination and did not have any respiratory, gastrointestinal, or constitutional symptoms, such as fever, chills, or myalgia, before and after vaccination. Kidney biopsy revealed crescentic glomerulonephritis with features consistent with anti–glomerular basement membrane nephritis (Supplementary Figure S2). Chest radiography showed no pulmonary involvement. Both patients did not have COVID-19 infection before vaccination, and the community transmission and infection rates were low during the time of vaccination. Seroconversion after vaccination was not evaluated in both patients.

Although there is insufficient evidence to postulate causality as it may be coincidental that COVID-19 vaccination closely preceded macroscopic hematuria, these cases emphasize the need for pharmacovigilance. Vigilance should be exercised in patients presenting with new-onset urinary abnormalities and hypertension following COVID-19 vaccination. Besides urinary tract infection and urological causes, glomerulonephritis should be considered in patients with unresolving macroscopic hematuria. Meanwhile, these isolated reports should not lead to vaccine hesitation during this pandemic as the benefits of vaccination strongly outweigh potential risks.

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AUTHOR CONTRIBUTIONS

All authors contributed significantly in drafting and revising the letter.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. (**A**–**D**) Renal biopsy shows IgAN with fibrocellular and fibrous crescents. (**A**) Glomerulus showing endocapillary hypercellularity. Periodic acid–Schiff, original magnification ×400. (**B**) Fibrous crescent with >75% fibrous matrix. Note disrupted Bowman's capsule. Combined Masson-silver stain, original magnification ×400. (**C**) Immunofluorescence microscopy with moderate to intense (2+ to 3+) mesangial/paramesangial staining for IgA. Anti-IgA FITC, original magnification ×200. (**D**) Electron microscopy demonstrating mesangial electron-dense deposits. Uranyl acetate and lead citrate were used.

Figure S2. (**A**–**G**) Renal biopsy shows crescentic glomerulonephritis, with predominantly cellular crescents. (**A**) All 3 glomeruli show crescents, with a circumferential cellular crescent in the central glomerulus (PAS). (**B**) High magnification of the compressed glomerular tuft amid a cellular crescent, with part of the glomerulus displaying segmental sclerosis (arrows) (PAS). (**C**) Masson-trichrome stain shows a segmentally sclerotic portion of the glomerulus juxtaposed to proliferating cells of a cellular crescent. (**D,E**) Immunofluorescence for IgG (**D**) and lambda light chain (**E**) shows trace to 1+ linear staining of the glomerular capillary walls. (**F,G**) Electron micrographs show between 20% and 60% effacement of podocyte foot processes, without any ultrastructural electron-dense deposits. Subendothelial widening with interpositioned mesangial cytoplasm is seen (**F**, arrow), whereas fibrin tactoids are noted in the urinary space (**G**, arrow).

1. Rahim SEG, Lin JT, Wang JC, et al. A case of gross hematuria and IgA nephropathy flare-up following SARS-CoV-2 vaccination. *Kidney Int*. 2021;100:238.
2. Negrea L, Rovin BH. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. *Kidney Int*. 2021;99:1487.

Hui Zhuan Tan[1], Ru Yu Tan[1], Jason Chon Jun Choo[1], Cynthia Ciwei Lim[1], Chieh Suai Tan[1], Alwin Hwai Liang Loh[2], Carolyn Shan-Yeu Tien[1], Puay Hoon Tan[2] and Keng Thye Woo[1]

[1]*Department of Renal Medicine, Singapore General Hospital, Singapore; and* [2]*Department of Anatomical Pathology, Singapore General Hospital, Singapore*

Correspondence: *Hui Zhuan Tan, Department of Renal Medicine, Singapore General Hospital, Academia Level 3, 20 College Rd, Singapore 169856. E-mail: tan.hui.zhuan@singhealth.com.sg*

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Anti-GBM nephritis with mesangial IgA deposits after SARS-CoV-2 mRNA vaccination

To the editor: We read with interest recent reports of minimal change disease and glomerulonephritis following receipt of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine, including 1 case of anti–glomerular basement membrane (anti-GBM) antibody disease.[1]

We would like to report another case of anti-GBM disease, which had coexistent mesangial IgA deposits. The patient is an older woman with previously normal renal function and no significant past medical history, prior coronavirus disease 2019 (COVID-19) infection, or medication use, who developed fevers, anorexia, nausea, and gross hematuria 2 weeks after receiving the second