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# IgA nephropathy presenting as macroscopic hematuria in 2 pediatric patients after receiving the Pfizer COVID-19 vaccine

**To the editor:** With great interest, we read the recent reports of IgA nephropathy (IgAN) flare-up presenting as macroscopic hematuria, following the second dose of coronavirus disease 2019 (COVID-19) vaccination in adult patients.[1–4] The US Food and Drug Administration granted an emergency use authorization for the Pfizer–BioNtech COVID-19 vaccination in December 2020 for individuals aged ≥16 years; the emergency use authorization was recently expanded to include children aged 12 to 15 years on May 10, 2021. Herein, we report 2 pediatric patients with IgAN presenting with macroscopic hematuria <24 hours after Pfizer COVID-19 vaccination. Neither patient had COVID-19 infection before vaccination nor any history of reactions to any vaccinations. See Table 1 for clinical information.

The first patient is a 13-year-old boy with a history of type 1 diabetes mellitus and known IgAN (Supplementary Figure S1). His initial IgAN diagnosis was made 6 months before this event during an evaluation for subnephrotic proteinuria and microscopic hematuria with normal renal function, and he was receiving treatment with lisinopril. Within 24 hours following the second dose of the COVID-19 vaccine, he developed new-onset gross hematuria and acute kidney injury. His gross hematuria self-resolved, and his kidney function recovered without intervention within 1 week.

The second patient is a previously healthy 17-year-old boy who presented with new-onset gross hematuria, proteinuria, and acute kidney injury <24 hours following the second dose of the vaccine. He had no family history of autoimmune disease, and he was not taking any medications. His gross hematuria self-resolved, but his kidney insufficiency persisted. Kidney biopsy performed 9 days later was consistent with IgAN with cellular glomerular crescents and moderate to severe tubulointerstitial scarring (Supplementary Figure S2), suggesting an acute exacerbation of preexisting IgAN. He received i.v. methylprednisolone pulses, and his follow-up serum creatinine level showed improvement.

The mechanism by which COVID-19 vaccination may be associated with IgAN flares is unclear. We concur with previous authors' statements that patients, including children, with IgAN should be monitored closely following COVID-19 vaccine, and COVID-19 vaccination may unmask previously undiagnosed glomerulonephritis in pediatric patients.[1–4]

## AUTHOR CONTRIBUTIONS

All authors contributed in drafting, reviewing, and revising this letter.

**Table 1 | Clinical characteristics of 2 pediatric patients with IgAN flare following COVID-19 vaccination**

| Patient no. | Age, yr | Race | Sex | Variables | Before COVID-19 vaccination | Following COVID-19 vaccination |
|---|---|---|---|---|---|---|
| 1 | 13 | White | Male | Clinical symptoms | Microscopic hematuria and subnephrotic proteinuria noted on routine urine screening for diabetes, leading to IgAN diagnosis | New-onset gross hematuria × 2 d, vomiting × 1 d |
| | | | | Serum creatinine, mg/dl | 0.54 | Day 2: 1.31<br>Day 6: 0.66 |
| | | | | Serum albumin, g/dl | 3.4 | Day 2: 3.8<br>Day 6: 3.0 |
| | | | | Urine protein-to-creatinine ratio, mg/mg | 1.6 | Day 2: 1.07<br>Day 6: 0.86 |
| | | | | Oxford MEST-C score | M0 E0 S0 T0 C0 | — |
| | | | | Treatment | Lisinopril, 10 mg/day | Stopped lisinopril on day 5 |
| 2 | 17 | White | Male | Clinical symptoms | Foamy urine for several months | New-onset macroscopic hematuria × 4 d and stage I hypertension |
| | | | | Serum creatinine, mg/dl | — | Day 6: 1.78<br>Day 9: 1.47<br>Day 22: 1.20 (following corticosteroid treatment) |
| | | | | Serum albumin, g/dl | — | Day 9: 3.8 |
| | | | | Urine protein-to-creatinine ratio, mg/mg | — | Day 9: 1.75 |
| | | | | Oxford MEST-C score | — | Day 9: M1 E1 S1 T1 C1 |
| | | | | Treatment | — | Day 9: 1 g i.v. methylprednisolone daily ×3, followed by oral prednisone |

COVID-19, coronavirus disease 2019; IgAN, IgA nephropathy; MEST-C, M = mesangial hypercellularity, E = endocapillary proliferation, S = segmental glomerulosclerosis, T = tubular atrophy/interstitial fibrosis, C = crescents.

**SUPPLEMENTARY MATERIAL**

Supplementary File (PDF)

**Figure S1.** IgAN with minor histomorphologic alterations on light microscopy. (**A**) Representative glomerulus showing mild mesangial matrix expansion without mesangial hypercellularity on periodic acid–Schiff stain, original magnification ×40. (**B**) Immunofluorescence microscopy with 3+ granular mesangial reactivity for IgA, original magnification ×10. Bar = 20 μm (**A**) and 50 μm (**B**).

**Figure S2.** IgAN with cellular glomerular crescents. (**A**) Moderate interstitial fibrosis is evident on the trichrome stain. (**B**) The glomerulus on the left shows a segmental cellular crescent, and the glomerulus on the right shows segmental mesangial hypercellularity with mild mesangial matrix expansion on periodic acid–Schiff stain. (**C**) Immunofluorescence staining shows 2+ granular mesangial staining for IgA. (**D**) Electron microscopy shows electron-dense deposits in mesangium. Bar = 600 μm (**A**), 60 μm (**B,C**), and 1 μm (**D**).


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Christian Hanna[1], Loren P. Herrera Hernandez[2], Lihong Bu[3], Sarah Kizilbash[4], Lydia Najera[4], Michelle N. Rheault[4], Jan Czyzyk[3] and Anne M. Kouri[4]

[1]*Division of Pediatric Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA;* [2]*Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota, USA;* [3]*Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota, USA; and* [4]*Division of Pediatric Nephrology, University of Minnesota, Minneapolis, Minnesota, USA*

**Correspondence:** *Anne M. Kouri, 2450 Riverside Ave, Corporate Bldg, Minneapolis, Minnesota 55454, USA. E-mail: akouri@umn.edu*



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# Granulomatous vasculitis after the AstraZeneca anti–SARS-CoV-2 vaccine

**To the editor:** Several reports of newly diagnosed or relapses of immune-mediated renal diseases following vaccination with anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA and AstraZeneca vaccines recently emerged in the litterature.[1,2]

We report the case of a 77-year-old man who developed an acute granulomatous nephritis associated with vasculitis after the first dose of the AstraZeneca vaccine. The patient had no significant medical history, and serum creatinine (SCr) was 1.2 mg/dl a month before vaccination with a protein-to-creatinine ratio at 0.07 g/g (N = 0.15) of creatinine. Four weeks after injection, the patient presented with fever, night sweating, and anorexia. He was not taking any medication. Laboratory tests revealed acute kidney injury (SCr, 2.7 mg/dl), normal proteinuria, no hematuria, and a C-reactive protein (CRP) level of 200 mg/L. Nasopharyngeal swab for SARS-CoV-2 was negative by polymerase chain reaction, as were anti–SARS-CoV-2 and anti-neutrophil cytoplasmic antibodies (repeated twice 15 days apart). Fluorine-18-fluorodeoxyglucose positron emission tomography scan showed diffuse hypermetabolism of medium vessels, suggesting vasculitis. The kidney biopsy revealed diffuse interstitial edema with noncaseating nonnecrotizing granulomas around small vessels (Figure 1); one showed fibrinoid necrosis. There were no immune deposits. Serum QuantiFERON for tuberculosis was negative, and there were no radiological or biological findings suggestive of sarcoidosis. The patient was started on methylprednisolone, with normalization of SCr and CRP levels within 4 weeks. Interestingly, the patient eventually mounted a humoral response 8 weeks after vaccination.

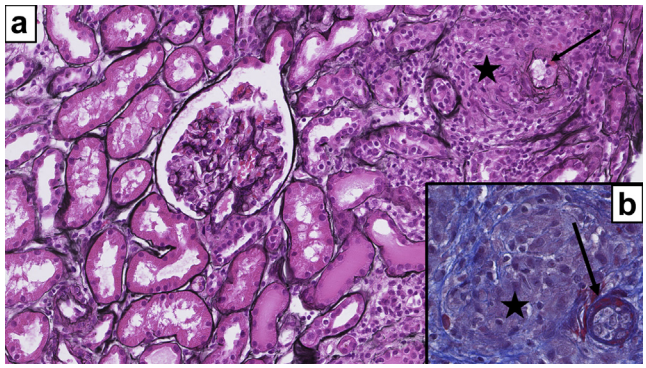


**Figure 1 | (a,b) On light microscopy, the renal parenchyma is infiltrated by chronic interstitial inflammatory cells and poorly formed granulomas (stars).** Some of these granulomas surrounded small vessels, which rarely showed segmental fibrinoid necrosis (arrows). Glomeruli are normal. (**a**) Jones silver stain, original magnification ×20; (**b**) Masson trichrome stain, original magnification ×40.

The association of vasculitis with *influenza* and *pertussis* vaccines has already been described but without granulomatous pattern.[3] Although causality between the renal lesions and the AstraZeneca vaccine cannot be definitively proven, the timing—and the absence of other causes—makes the link between the 2 plausible.[4]


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