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A case of ANCA-associated vasculitis after AZD1222 (Oxford–AstraZeneca) SARS-CoV-2 vaccination: casualty or causality?



To the editor: Two cases of anti-neutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination have been reported to date, and both appeared after Moderna (mRNA) vaccination.^{1,2}

We report a case of a 63-year-old man with a nonrelevant medical background, previously normal kidney function, and no previous adverse reactions to vaccination. He was admitted to the hospital after noting 3 episodes of hemoptysis 7 days after his first dose of the AZD1222 vaccine. He had taken acetaminophen and acetylsalicylic acid for a flu-like syndrome, which appeared 48 hours after vaccination. Diagnostic workup showed creatinine 257.2 $\mu\text{mol/l}$ with proteinuria ++ and mild hematuria. Chest X-ray showed infiltration in the left lower lung field. Diagnostic tests for SARS-CoV-2 were negative. Anti-myeloperoxidase antibodies (pANCA) were positive (12 UI/ml). Treatment for ANCA-associated vasculitis was initiated (high-dose i.v. glucocorticoids, followed by a tapering course of oral prednisone reduction [60 mg/d for 1 month followed by a decrease of 10 mg every 2 weeks], and

oral cyclophosphamide). Plasma exchange was not instituted as the hemoptysis was self-limited without anemia or hemodynamic instability. Kidney biopsy showed focal extracapillary proliferation and crescent formation, resulting in a diagnosis of a focal class of ANCA-associated pauci-immune glomerulonephritis according to the Berden classification (Figure 1). Hemoptysis disappeared during admission, and progressive recovery of kidney function was observed. Creatinine improved initially with high-dose glucocorticoids to 247.5 $\mu\text{mol/l}$ at 5 days after admission, creatinine was 252 $\mu\text{mol/l}$ at discharge after 18 days of admission, and the last creatinine was 184.8 $\mu\text{mol/l}$ after 6 weeks of treatment. Our patient had not developed an antibody response to the SARS-CoV-2 spike protein 2 months after the first AZD1222 vaccine.

To our knowledge, no cases of ANCA vasculitis have been reported after viral vector coronavirus disease 2019 vaccines, but they have been described after influenza vaccination.³ To our knowledge, this is the first case of ANCA vasculitis after the AZD1222 vaccine so far.⁴ In our patient, causality is based on temporal association, although we cannot demonstrate a direct link with vaccination.

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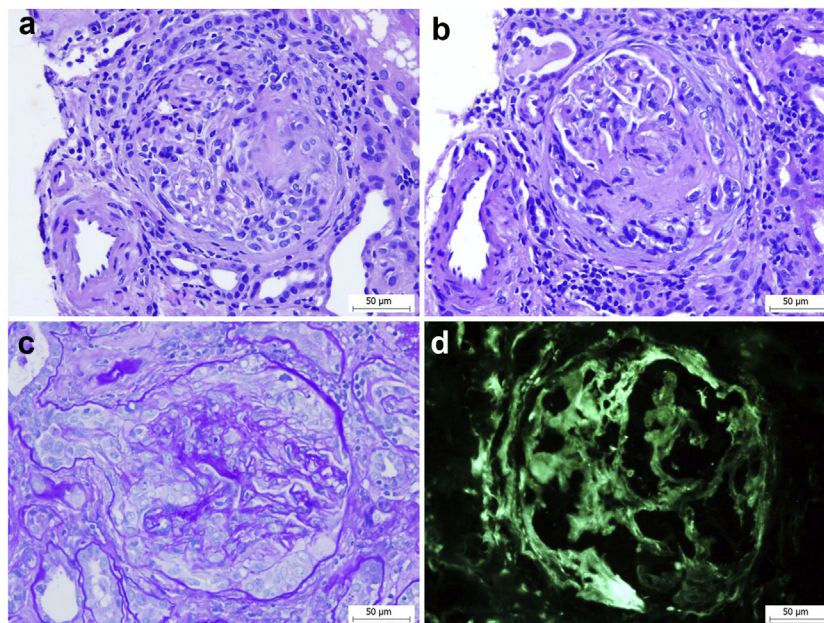


Figure 1 | Kidney biopsy showing extracapillary proliferation images with fibrocellular (a), fibrous (b), and cellular crescents (c), and with the presence of fibrinogen deposits in the context of fibrinoid necrosis with extracapillary proliferation (d). Bars = 50 μm . (a,b) Hematoxylin and eosin, original magnification $\times 20$. (c) Periodic acid–Schiff, original magnification $\times 20$. (d) Direct immunofluorescence, original magnification $\times 20$. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

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A case of membranous nephropathy following Pfizer–BioNTech mRNA vaccination against COVID-19



To the editor: We read a recent report describing the relapse of membranous nephropathy (MN) following the administration of inactivated vaccine against coronavirus disease 2019 (COVID-19).¹ Here, we describe a case of new-onset MN following vaccination with the Pfizer–BioNTech mRNA-based COVID-19 vaccine.

A 70-year-old man with no significant past medical history was referred to our institution for generalized edema, which occurred a week after his first dose of the Pfizer–BioNTech vaccine and got worse a day after the second dose, which was given 3 weeks after the first dose. He denied other symptoms. On examination, his blood pressure was 155/86 mm Hg, and he

had bilateral pitting edema up to his thighs. Laboratory tests revealed a serum creatinine level of 114 $\mu\text{mol/l}$, an albumin level of 17 g/l, a total cholesterol level of 9.24 mmol/l, 17 red blood cells/ μl in urine analysis, and a 24-hour total urine protein level of 4.4 grams. Secondary causes, including drugs and infections (hepatitis B, hepatitis C, HIV), were excluded. He was found to have IgM kappa monoclonal gammopathy of undetermined significance. A thorough malignancy screening, including enhanced computed tomography of the thorax, abdomen, and pelvis, gastroscopy plus colonoscopy, and prostate-specific antigen testing yielded no significant results.

A percutaneous kidney biopsy was performed, and diagnosis of MN was confirmed. The results are shown in Figure 1.

Serum anti-phospholipase A2 receptor (PLA2R) was negative, and a kidney biopsy stained negative for PLA2R antigen as well. Serum thrombospondin type-1 domain-containing 7A (THSD7A) antibody was positive by indirect immunofluorescence assay. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein antibody was 147.0 U/ml 3 months after his second dose of vaccine. The patient is currently being managed with irbesartan, frusemide, and warfarin. There are no signs of spontaneous remission after 2 months.

Our observation, together with other case reports of MN development post–COVID-19 infection,^{2,3} and MN relapse post–COVID-19 vaccine administration,¹ supports a possible immune dysregulation process causing loss of tolerance to certain podocyte antigens. Elucidation of this possibility requires further studies.

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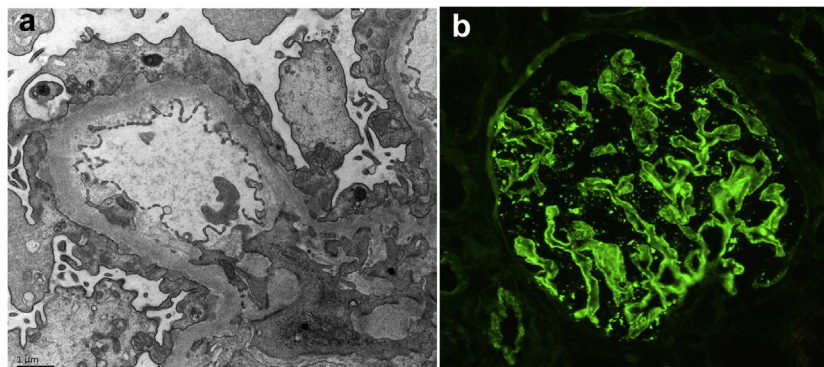


Figure 1 | (a) Electron microscopy. Glomerular capillary loops showed numerous small subepithelial electron-dense deposits. The overlying podocytes showed extensive foot process effacement. **(b) IgG immunofluorescence** showed diffuse 2+ finely granular capillary loop staining. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.