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.

immunosuppression. Nevertheless, as with other vaccinations, the benefit of immune protection, most probably, outweighs the risk of relapse.

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Relapse of minimal change disease following the AstraZeneca COVID-19 vaccine

To the editor: Anecdotal reports linking minimal change disease (MCD) to vaccinations possibly due to immune dysregulation,[1] including influenza vaccine,[2] pneumococcal,[3] meningococcal C vaccines,[4] and BNT162b2 coronavirus disease 2019 (COVID-19) vaccine (Pfizer-BioNTech)[5,6] have been published. We report 2 cases of biopsy-proven MCD relapsing within 2 days of receiving an AstraZeneca COVID-19 vaccine.

A 30-year-old man had received 1 g of rituximab in August 2020, having experienced annual relapses on tacrolimus. His prednisolone had been weaned to 1 mg/day by January and discontinued altogether by February 2021. Two days after his COVID-19 vaccine, he developed a headache and frothy urine. Urine protein-to-creatinine ratio 1 week later was 213 mg/mmol; albumin was preserved at 47 g/l; creatinine was stable at 82 μmol/l. At that time, lymphocyte subsets showed complete B-cell depletion; CD19 was 0.00. He did not seek medical attention until 2 months after receiving the vaccine when his urine protein-to-creatinine ratio was 142 mg/mmol. Repeat lymphocyte subsets then revealed B-cell return; CD19 was 0.06. Complete remission was achieved with 10 days of starting prednisolone 20 mg daily.

A 40-year-old woman was maintained on prednisolone 5 mg daily and tacrolimus (Adoport); trough level was 4.6 μg/l before vaccination. One day after receiving her first COVID-19 vaccine, she developed a headache, frothy urine, and ankle swelling. After 1 week, her general practitioner recorded 3+ dipstick proteinuria. Unfortunately, no laboratory samples were sent. Prednisolone was increased to 30 mg daily, and complete remission was achieved within 2 weeks. Creatinine was unchanged at 105 μmol/l.

The association with various vaccines has been described, occurring between 4 days to several weeks later.[1,5,6,7] The timing of COVID-19 vaccination and the very early development of relapse of MCD in our cases raises questions as to the mechanisms involved. At 2 days after vaccination, one would assume the vaccine triggered a more generalized cytokine-mediated response.[7] Others have postulated that symptoms after 4 days represent a rapid T cell–mediated response to viral mRNA.[2,5,6]

We administered the second dose of a different COVID vaccine, and neither patient suffered an adverse effect. However, both patients were taking 15 mg prednisolone daily at the time. This may prove a useful strategy in similar cases.

We await further reports to evaluate the true incidence.

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Post-vaccinal minimal change disease

To the editor: Previous reports have described the onset of minimal change disease after the administration of certain vaccines.[1]

Recently a 61-year-old woman was admitted to our hospital 8 days after her first coronavirus disease 2019 (COVID-19) vaccination (BioNTech/Pfizer SARS-CoV-2 COMIRNATY) because of edema and weight gain (6 kg). Medical

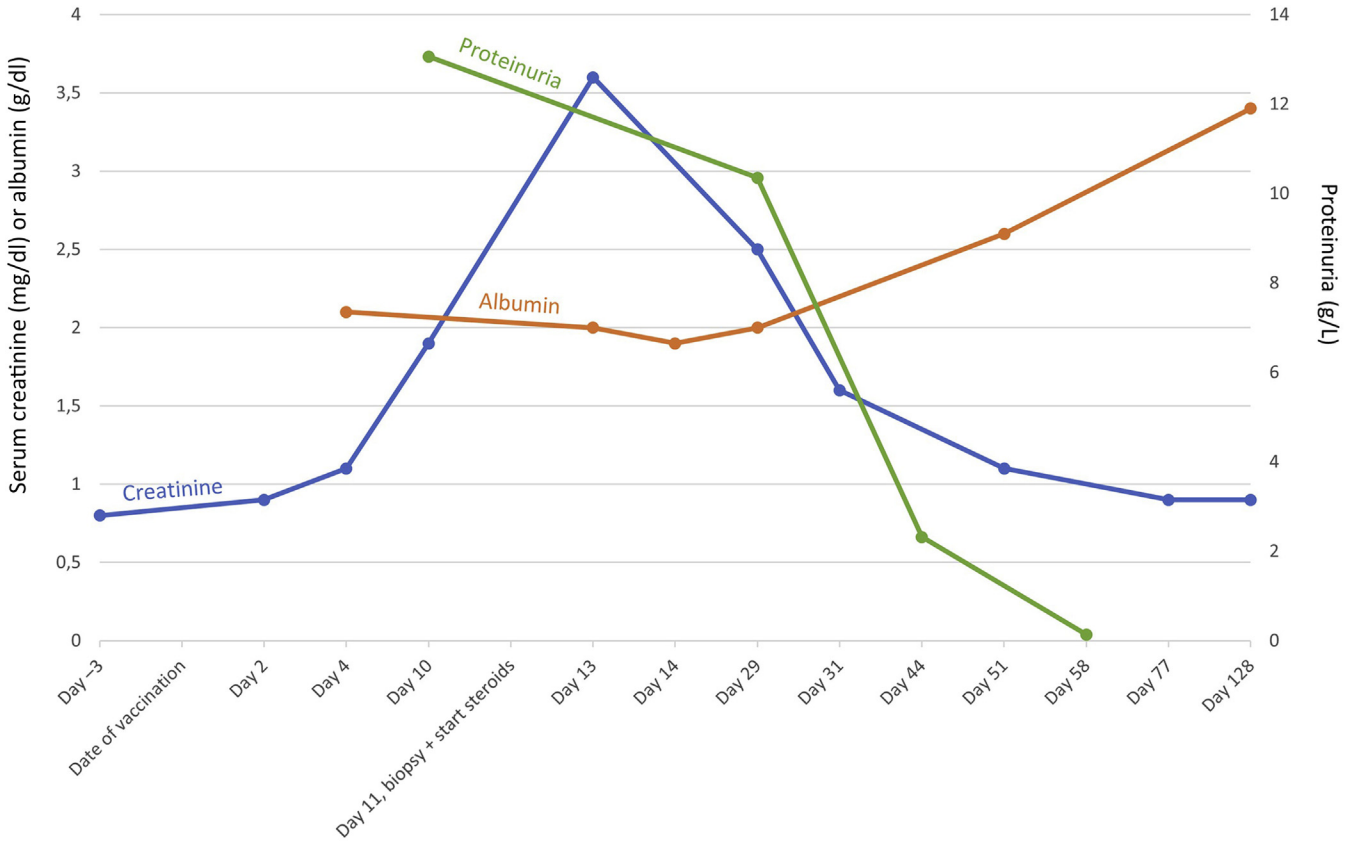

Figure 1 | The course of serum creatinine (blue), albumin (orange), and proteinuria (green), from 3 days prior to vaccination to 128 days after vaccination.

history included autoimmune hepatitis and hypothyroidism, for which she used tioguanine (20 mg), prednisone (2.5 mg), and levothyroxine (50 μg). Her kidney function and urine sediment had always been normal. Symptoms, consisting of edema in the lower extremities, dyspnea, and oliguria, started 1 day after vaccination. Physical examination revealed edema in the lower extremities without further abnormalities. Laboratory findings showed hypoalbuminemia (21 g/l), an elevated creatinine level (1.47 mg/dl), and nephrotic range proteinuria (12 g/l; Figure 1). Urine analysis showed no glomerular erythrocyturia. Diagnostic workup, consisting of anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, anti-PLA2R, protein spectrum, free light chains, C3/C4 levels, hepatitis B surface antigen, and hepatitis C virus,

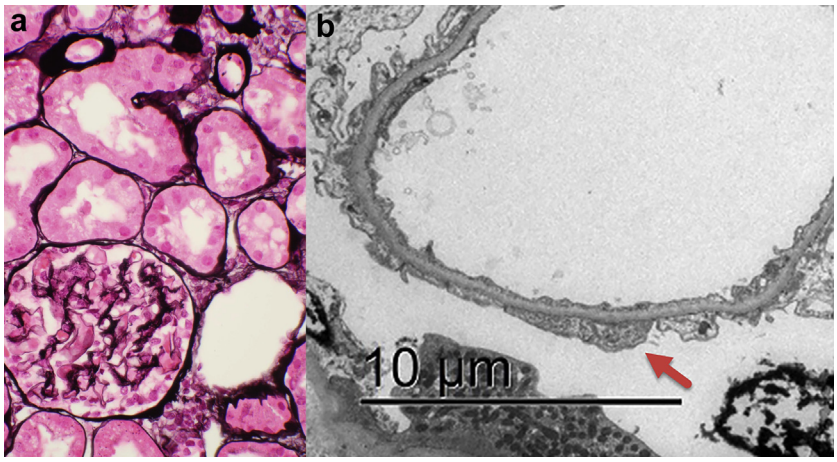

Figure 2 | Kidney biopsy findings. (**a**) Light microscopy with Jones stain shows no glomerular or tubular abnormalities. Original magnification ×400. (**b**) Electron microscopy. Red arrow indicates extensive podocyte foot process effacement. Original magnification ×6000. Bar = 10 μm. To optimize viewing of this image, please see the online version of this article at www.kidney-international.org.

was negative. A diagnostic kidney biopsy was performed. Serum creatinine rose to 3.6 mg/dl, and renal replacement therapy was started because of anuria and diuretic resistant fluid overload with pleural effusion and dyspnea. Steroids (1 mg/kg) were administrated, pending biopsy results. Light microscopy did not show significant glomerular nor tubular abnormalities, immunofluorescence was negative, and electron microscopy showed extensive foot process effacement (Figure 2), most of which are compatible with minimal change disease. Kidney function gradually recovered with decreasing proteinuria (2.3 g/l). After 3 weeks, hemodialysis could be stopped.

This case adds to other reports of new-onset nephrotic syndrome after COVID-19 vaccination.[2,3] If new-onset nephrotic syndrome incidence rises after this type of vaccination, reporting nephrotic syndrome as a side effect in patient information should be considered.

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Minimal change disease and acute kidney injury following the Pfizer-BioNTech COVID-19 vaccine

To the editor: As mass vaccinations for coronavirus disease 2019 (COVID-19) are being administered worldwide, rare reports of adverse events are emerging. We report a case of minimal change disease presenting with nephrotic syndrome 1 week after a first injection of the COVID-19 vaccine (Pfizer-BioNTech).

A 77-year-old white male with a 15-year history of type 2 diabetes mellitus without retinopathy received a first dose of the Pfizer-BioNTech vaccine on March 17, 2021. Medical history included obesity, prior smoking, and coronary artery disease. Baseline serum creatinine ranged from 1.0 to 1.3 mg/dl, with no proteinuria over the previous year. Outpatient medications included atorvastatin, aspirin, dulaglutide, empagliflozin, glipizide, losartan, metformin, and metoprolol. There was no history of nonsteroidal anti-inflammatory drug use. Seven days after vaccination, he presented to his local physician complaining of abrupt onset of lower-extremity edema. Laboratory testing revealed 4+ proteinuria by dipstick and serum albumin of 2.5 g/dl. Nephrology consultation 12 days after vaccination found anasarca with 13.6-kg weight gain due to edema, elevated blood pressure (152/81 mm Hg), and 4+ proteinuria on urinalysis with inactive urine sediment, prompting hospital admission. Laboratory evaluation by 14 days after vaccination showed 24-hour urine protein of 23.2 g/d, serum creatinine of 2.33 mg/dl, and serum albumin of 3.0 g/dl. Complete blood cell count was normal, and hemoglobin A1c was 7.5%. Serologies included elevated C3 and C4 and negative hepatitis B surface antigen and hepatitis C antibody.

A kidney biopsy was performed 16 days after vaccination (Figure 1). Among 7 glomeruli sampled for light microscopy, 4 were globally sclerotic and 3 were histologically unremarkable. There was 25% tubular atrophy and interstitial fibrosis with moderate arteriosclerosis. Cortical tubules displayed diffuse acute epithelial injury. No immune deposits were identified by immunofluorescence (2 glomeruli) or electron microscopy (2 glomeruli). Electron microscopy revealed 100% podocyte foot process effacement, leading to a diagnosis of minimal change disease with acute tubular injury. The ultrastructural findings of minimal segmental mesangial sclerosis and glomerular basement membrane thickening (mean, 460 nm) suggested underlying mild diabetic changes.

Empiric pulse methylprednisolone, 1 g daily for 3 days, was initiated on hospital admission, followed by oral prednisone, 60 mg daily, after biopsy. In the hospital, he required i.v. furosemide drip, 10 mg/h, transitioned to bumetanide, 0.25 mg/h, for 5 days for fluid overload. Creatinine peaked during the hospitalization at 3.17 mg/dl at 19 days after vaccination. The patient was discharged 3 days later with 19.8 g/g proteinuria by spot ratio, serum albumin of 2.9 g/dl, and serum creatinine of 2.54 mg/dl. At the most recent follow-up, approximately 3 weeks after initiation of corticosteroids, creatinine remained elevated at 3.74 mg/dl, with 24-hour urine protein of 18.8 g/d (Figure 2).

This is the second report of the onset of minimal change disease occurring within a week of an initial dose of the Pfizer-BioNTech vaccine. The first report was of a 50-year-old healthy man who developed lower-extremity edema 4 days after injection, followed rapidly by anasarca and acute kidney injury, with serum creatinine of 2.3 mg/dl and urine protein of 6.9 g/d on admission.[1] He responded to steroid therapy with complete remission.[1]

The strong temporal association with vaccination in both cases suggests a rapid T cell–mediated immune response to viral mRNA as a possible trigger for podocytopathy. Acute onset of minimal change disease has also been reported in a 65-year-old woman and a 44-year-old man at 4 and 18 days, respectively, following the influenza vaccine.[2,3] Although definitive causality is difficult to establish, greater awareness of this potential adverse effect of vaccination is needed to