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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 administered, 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.<sup>2,3</sup> 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.

1. Gutierrez S, Dotto B, Petiti JP, et al. Minimal change disease following influenza vaccination and acute renal failure: just a coincidence? *Nefrologia*. 2012;32:414–415.
2. D'Agati VD, Kudose S, Bomback AS, et al. Minimal change disease and acute kidney injury following the Pfizer-BioNTech COVID-19 vaccine. *Kidney Int*. 2021;100:461–463.
3. Lebedev L, Sapojnikov M, Wechsler A, et al. Minimal change disease following the Pfizer-BioNTech COVID-19 vaccine. *Am J Kidney Dis*. 2021;78:142–145.

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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,

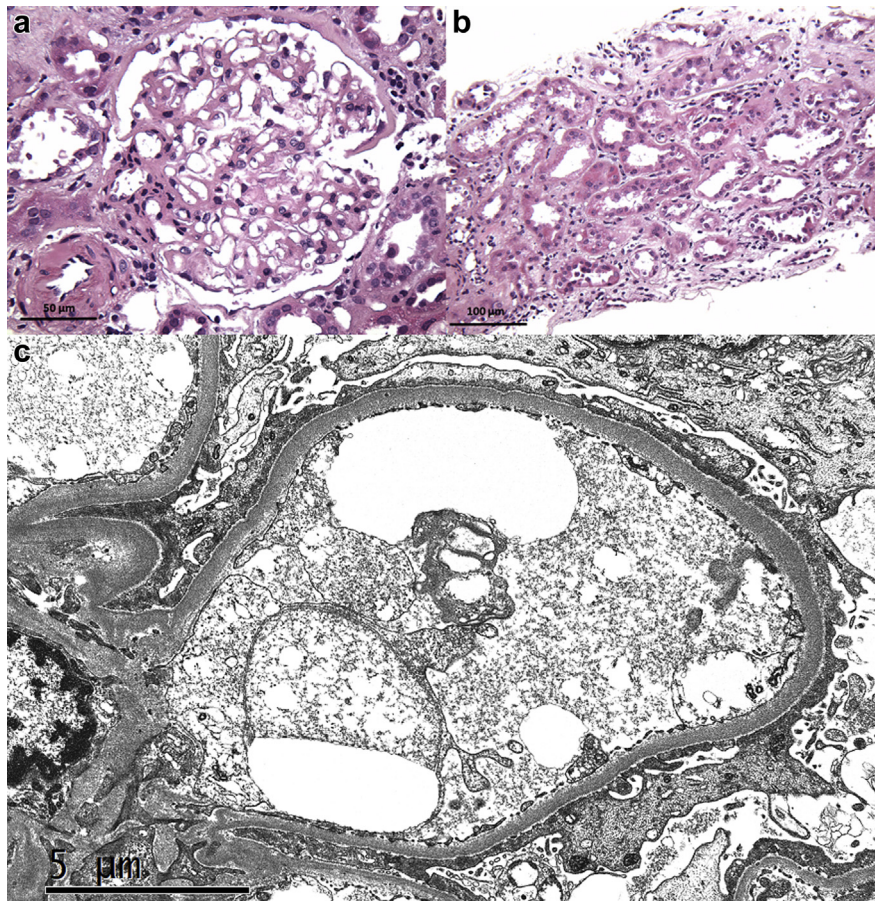
glipizide, losartan, metformin, and metoprolol. There was no history of nonsteroidal anti-inflammatory drug use. Seven days after vaccination, he presented to his local physician complaining of abrupt onset of lower-extremity edema. Laboratory testing revealed 4+ proteinuria by dipstick and serum albumin 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.

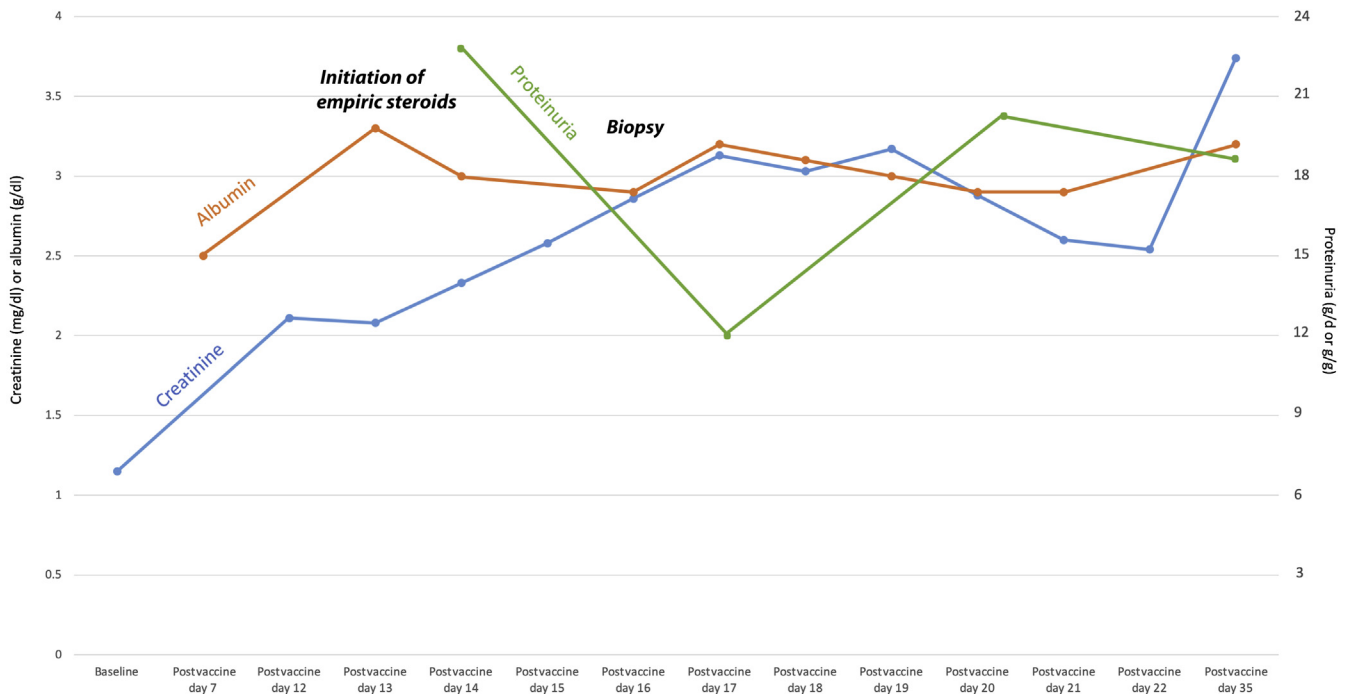
Empiric pulse methylprednisolone, 1 g daily for 3 days, was initiated on hospital admission, followed by oral prednisone, 60 mg daily, after biopsy. In the hospital, he required i.v. furosemide drip, 10 mg/h, transitioned to bumetanide, 0.25 mg/h, for 5 days for fluid overload. Creatinine peaked during 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.<sup>1</sup> He responded to steroid therapy with complete remission.<sup>1</sup>

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.<sup>2,3</sup> Although definitive causality is difficult to establish, greater awareness of this potential adverse effect of vaccination is needed to



**Figure 1 | (a) Light microscopy shows a histologically unremarkable glomerulus (hematoxylin and eosin, original magnification  $\times 400$ ). (b) A low-power view shows diffuse cortical acute tubular injury with focal shedding of degenerating epithelial cells into the lumen (hematoxylin and eosin, original magnification  $\times 200$ ). (c) Electron microscopy demonstrates complete podocyte foot process effacement (original magnification  $\times 8000$ ). To optimize viewing of this image, please see the online version of this article at [www.kidney-international.org](http://www.kidney-international.org).**



**Figure 2 | Temporal trends in serum creatinine (mg/dl), serum albumin (g/dl), and proteinuria (g/d if 24-hour sample, g/g if spot sample) are graphed over the first 5 weeks after vaccination.**

determine its frequency. With prompt renal biopsy and initiation of steroid therapy, complete remission of nephrotic syndrome and acute kidney injury can be achieved. It is uncertain if and when it is safe to administer a second dose of the Pfizer vaccine in these individuals.

1. Lebedev L, Sapojnikov M, Wechsler A, et al. Minimal change disease following the Pfizer-BioNTech COVID-19 vaccine. *Am J Kidney Dis.* 2021;78:142–145.
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3. Gutiérrez S, Dotto B, Petiti JP, et al. Minimal change disease following influenza vaccination and acute renal failure: just a co-incidence? *Nefrologia.* 2012;32:414–415.

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## Minimal change disease following the Moderna mRNA-1273 SARS-CoV-2 vaccine



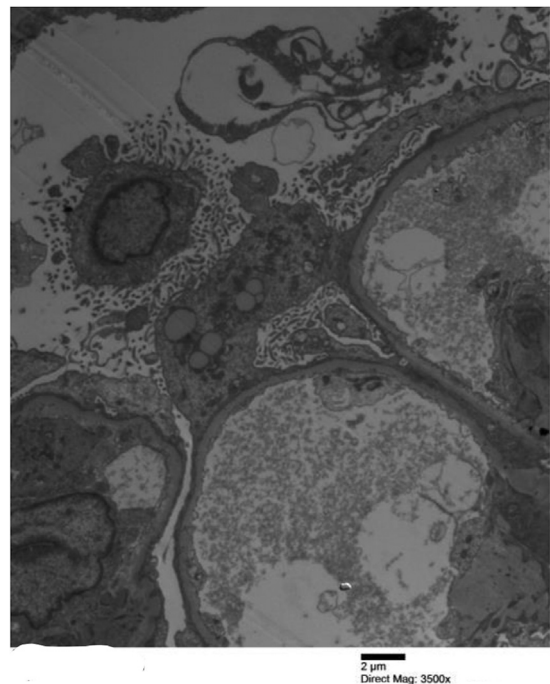
**To the editor:** The immunologic response following several varieties of vaccination has been described as a potential trigger for the development of both *de novo* as well as recurrent minimal change disease (MCD).<sup>1</sup> There have been emerging cases, including that described by D’Agati *et al.*, of MCD shortly after vaccination with the BNT162b2 vaccine (Pfizer-BioNTech).<sup>2,3</sup> We report, to the best of the authors’ knowledge, the first case of MCD presenting as nephrotic syndrome following the Moderna mRNA-1273 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine.

The patient, a 63-year-old woman, had a medical history that was significant only for hypertension and tobacco dependence. She had no prior history of renal disease. In April 2021, she presented to our hospital with a 4-week history of progressive anasarca, fatigue, periorbital edema, and dyspnea. The patient relayed that the edema and development of foamy urine appeared abruptly and occurred less than a week after having received the first (and only) dose of the Moderna mRNA-1273 SARS-CoV-2 vaccine (lot 006B21A). Vaccination was confirmed by cross-referencing

her outpatient pharmacy, which administered the dose. Unfortunately, anti-S protein antibody titer is not available to report.

Clinical and diagnostic evaluation also revealed newly uncontrolled hypertension (181/82 mm Hg) as well as mild acute kidney injury (serum creatinine 1.48 mg/dl; baseline was 0.7 mg/dl). Hypoalbuminemia (0.7 g/dl), urinalysis with 3+ proteinuria (without microscopic hematuria), and hyperlipidemia (triglycerides, 221 mg/dl; total cholesterol, 450 mg/dl) were noted. Nephrotic syndrome was confirmed as the 24-hour urine collection revealed 13.4 g proteinuria. Renal biopsy was promptly performed. Pathology confirmed MCD, with mild acute tubular injury, although a focal acute interstitial nephritis was also present. Four of 69 sampled glomeruli were globally sclerosed. There was 10% tubulointerstitial fibrosis. The sampled glomeruli were found to have 100% foot process effacement (Figure 1).

Treatment with conservative measures, including valsartan, 80 mg orally twice a day, for renin-angiotensin-aldosterone system inhibition was initiated along with a loop diuretic. She was also given pulse methyl-prednisolone, 500 mg i.v. for 3 days, followed by 1 mg/kg prednisone orally. On the basis of other case reports and our experience with MCD, we anticipate a prompt response to these measures.<sup>4</sup> We have recommended the patient forgo the second scheduled dose of the Moderna mRNA-1273 SARS-CoV-2 vaccine. In addition, the authors believe further rechallenges



**Figure 1 | Electron micrograph featuring glomerular capillary loop with diffuse podocyte effacement.** Bar = 2 μm. Original magnification ×3500. To optimize viewing of this image, please see the online version of this article at [www.kidney-international.org](http://www.kidney-international.org).