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Relapse of Minimal Change Disease Following the Pfizer-BioNTech COVID-19 Vaccine

To the Editor:

We read with interest the recent reports[1,2] describing the development of minimal change disease (MCD) following the first injection of the BNT162b2 vaccine (Pfizer-BioNTech) against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[3] Here, we report a case of nephrotic syndrome relapse in a patient with known MCD following the first injection of the Pfizer-BioNTech coronavirus 19 (COVID-19) vaccine.

A man in his mid-sixties was followed up at our division for MCD, which was diagnosed by kidney biopsy when he developed nephrotic syndrome at the age of 40. He had been treated with prednisolone and cyclosporine; after long-term remission, the medications were tapered and discontinued 4 and 2 years prior, respectively. Recently, 8 days after receiving the first injection of the Pfizer-BioNTech vaccine, he noticed frothy urine. On the 19th day after vaccination, he visited our clinic, where laboratory tests revealed stable kidney function (serum creatinine 0.99 mg/dL), hypoalbuminemia (2.8 g/dL), and massive proteinuria (urinary protein-creatinine ratio, 11.48 g/g) with high selectivity (selectivity index 0.096), making a relapse of MCD the most likely diagnosis. As measured by the Elecsys immunoassay (Roche Diagnostics), the level of serum antibodies to the SARS-CoV-2 spike protein was markedly elevated (196 U/mL), indicating an immune response to vaccination. Prednisolone (20 mg/d) and cyclosporine (100 mg/d) were restarted, and his proteinuria resolved within 2 weeks (Fig 1).

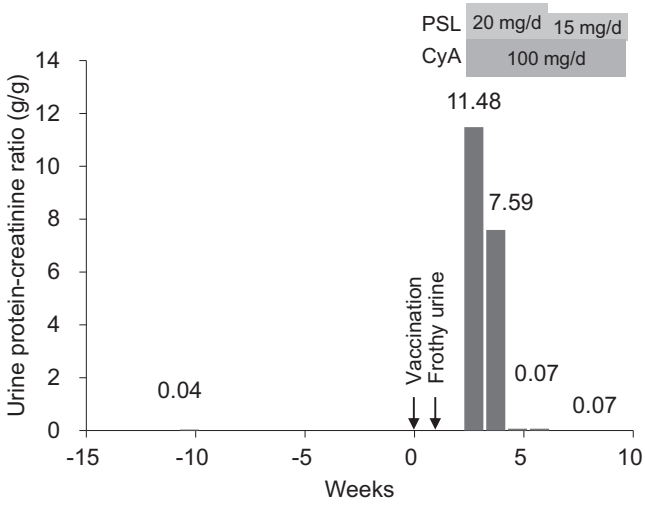

Figure 1. Clinical course of the patient. Abbreviations: CyA, cyclosporine; PSL, prednisolone.

The Pfizer-BioNTech vaccine is reported to induce robust T-cell activation and cytokine release along with strong antibody responses,[4] which might have contributed to MCD relapse in our patient. However, whether SARS-CoV-2 vaccines could trigger a relapse of MCD or other forms of nephrotic syndrome is currently unclear. Additional case reports and studies are required to address this important question.

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RESEARCH LETTER

Association of Baclofen With Falls and Fractures in Patients With CKD

To the Editor:

Baclofen is a popular muscle relaxant that is eliminated primarily unchanged in the urine.[1] We recently reported a higher risk of encephalopathy in a cohort of 15,942 older adults with chronic kidney disease (CKD) who started baclofen at ≥20 versus <20 mg/d; a higher risk was also observed in all baclofen users versus nonusers.[2] In another study of patients receiving dialysis, 1 in 14 were hospitalized with encephalopathy within 3 days of starting baclofen.[3]

In the present study, we analyzed the same cohort of 15,942 older adults with CKD not receiving dialysis,[2] and examined the 30-day risk of a hospital encounter with a fall, a fracture, or hypotension in patients newly prescribed baclofen at ≥20 versus <20 mg/d. The data source, design, and methods were the same as in our prior report[2] and are described in Table S1.

Briefly, we analyzed linked administrative health care data housed at ICES in Ontario, Canada, where all residents aged ≥65 years have universal prescription drug coverage. The primary cohort included adults aged ≥66 (to ensure at least 1 year of drug coverage) who had an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 and who were newly dispensed oral baclofen from an outpatient pharmacy between January 1, 2007, and March 1, 2018. Patients with evidence of baclofen use in the 180-day period before the prescription start date were excluded (this period was extended to 5 years in a sensitivity analysis).

The primary exposure was baclofen ≥ 20 mg/d (20 mg/d is the median dose reported in cases of baclofen toxicity, and the median dose prescribed during the study period [Table S2]).[2] To reduce the potential for indication bias, the prespecified reference group was baclofen < 20 mg/d.

In a secondary analysis, study outcomes in each group of baclofen users (≥20 and <20 mg/d) were compared separately to nonusers (ie, patients with CKD not taking baclofen). Nonusers were randomly assigned a simulated baclofen start date that followed the same distribution of start dates as baclofen users.

Inverse probability of treatment weighting on the propensity score was used to balance comparison groups on 164 indicators of baseline health, including indications for

Table 1. Baseline Characteristics of Older Adults With CKD Newly Prescribed Baclofen in Ontario, Canada (2007-2018)

	Observed Data (N = 15,942)			Weighted Data (N = 19,387)[a]		
	Baclofen Dose			Baclofen Dose		
	≥20 mg/d (n = 9,707)	<20 mg/d (n = 6,235)	Std Diff[b]	≥20 mg/d (n = 9,707)	<20 mg/d (n = 9,680)	Std Diff[b]
Demographics						
Women	5,719 (58.9%)	3,980 (63.8%)	10%	5,719 (58.9%)	5,702 (58.9%)	2%
Men	3,988 (41.1%)	2,255 (36.2%)	10%	3,988 (41.1%)	3,978 (41.1%)	0%
Age, y	76.5 ± 6.9	78.0 ± 7.4	21%	76.5 ± 6.9	76.5 ± 8.8	0%
Residence						
Urban	8,870 (91.4%)	5,800 (93.0%)	6%	8,870 (91.4%)	8,845 (91.4%)	0%
Rural	837 (8.6%)	435 (7.0%)	6%	837 (8.6%)	835 (8.6%)	0%
Long-term care	210 (2.2%)	379 (6.1%)	20%	210 (2.2%)	217 (2.2%)	0%
Income quintile[c]						
1 (lowest)	2,313 (23.8%)	1,508 (24.2%)	1%	2,313 (23.8%)	2,309 (23.9%)	0%
2	2,098 (21.6%)	1,345 (21.6%)	0%	2,098 (21.6%)	2,121 (21.9%)	1%
3 (middle)	2,010 (20.7%)	1,280 (20.5%)	0%	2,010 (20.7%)	1,988 (20.5%)	0%
4	1,893 (19.5%)	1,145 (18.4%)	3%	1,893 (19.5%)	1,871 (19.3%)	1%
5 (highest)	1,393 (14.4%)	957 (15.3%)	3%	1,393 (14.4%)	1,389 (14.4%)	0%

(Continued)