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Delphine Kervella^{1,2}, Lola Jacquemont¹,
Agnès Chapelet-Debout¹, Clément Deltombe¹
and Simon Ville^{1,2}

¹CHU de Nantes, Nantes Université, Néphrologie et Immunologie clinique, Nantes, France; and ²CHU de Nantes, Université de Nantes, Inserm, Centre de Recherche en Transplantation et Immunologie, UMR 1064, ITUN, Nantes, France

Correspondence: Delphine Kervella, Néphrologie et Immunologie Clinique, CHU de Nantes, 30 Bd Jean Monnet—Immeuble Jean Monnet, 44093 Nantes cedex 01, France. E-mail: delphine.kervella@univ-nantes.fr

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Letter regarding “Minimal change disease relapse following SARS-CoV-2 mRNA vaccine”



To the editor: We read with interest the report by Kervella *et al.*¹ on a patient with minimal change disease who experienced a relapse of her nephrotic syndrome following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine.

We would like to report a similar observation. A 22-year-old adult male patient has been followed up in our department since 2019 for an idiopathic nephrotic syndrome due to minimal change disease. His disease proved to be corticosteroid dependent, and he had 3 relapses of his nephrotic syndrome, requiring prolonged corticosteroid treatment and tacrolimus administration. He experienced his third relapse in December 2020

(Figure 1) while receiving no corticosteroids, and during a phase of progressive tacrolimus withdrawal. Complete remission was achieved with increased corticosteroid dosage and tacrolimus reintroduction. Treatment with rituximab was decided but was delayed to allow anti–coronavirus disease 2019 (COVID-19) vaccination. The patient was advised to monitor proteinuria, using urinary dipsticks, more closely after vaccination.

Three days after receiving SARS-CoV-2 mRNA vaccine (BNT162b2; Pfizer), he presented with a severe nephrotic syndrome relapse (serum albumin, 23 g/L) and persistently normal kidney function (creatinine, 71 μmol/L) (Figure 1). He reported having experienced chills and low-grade fever in the 48 hours following vaccination and positive proteinuria (2+/3+) on dipsticks as early as 36 hours after the injection. Prednisone dosage was increased to 20 mg/d and subsequently to 60 mg/d, tacrolimus was maintained at 1 mg twice daily, but remission was not obtained until 17 days after treatment regimen modification. Subsequently, corticosteroid dosage was progressively decreased to 30 mg/d, and tacrolimus dosage was unchanged. The patient received his second vaccine dose 6 weeks after the first one, while still on immunosuppressive treatment. His urinary dipsticks became transiently faintly positive (+), but no nephrotic syndrome relapse occurred. The patient responded well to vaccination, with a positive SARS-CoV-2 serology (IgG, 95.5 U/ml) documented 7 weeks after the first vaccine injection.

Vaccination (notably, hepatitis B, influenza, measles, and rubella) is a recognized trigger for the relapse of idiopathic nephrotic syndrome,² and SARS-CoV-2 mRNA vaccine is probably to be added to the list of at-risk vaccines. Close monitoring using urinary dipsticks is mandatory after a SARS-CoV-2 mRNA vaccination in patients with idiopathic nephrotic syndrome for an early detection of relapse that may occur despite

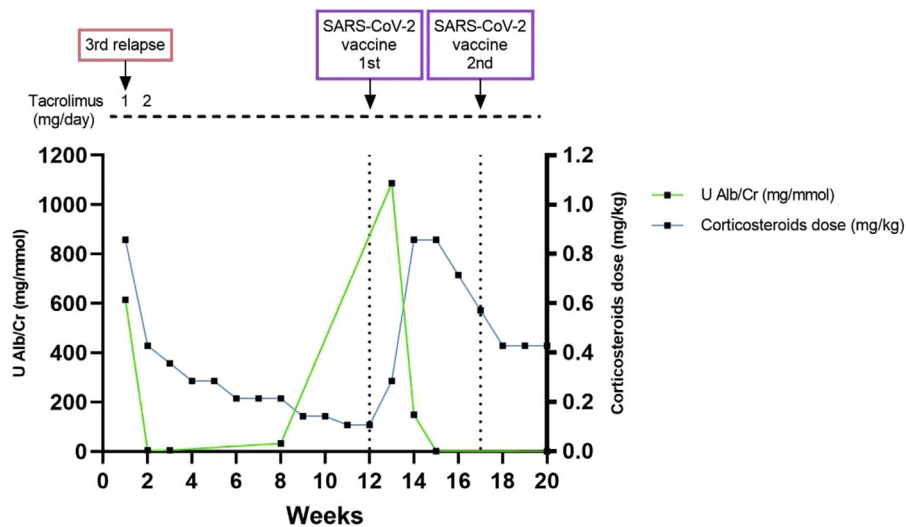


Figure 1 | Evolution over time of the idiopathic nephrotic syndrome in a 22-year-old male patient who experienced a relapse of his nephrotic syndrome following anti–coronavirus disease 2019 (COVID-19) mRNA vaccine. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; U Alb/Cr, urinary albumin/creatinine.

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

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Nora Schwotzer¹, Sébastien Kissling¹ and Fadi Fakhouri¹

¹Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland

Correspondence: Nora Schwotzer, Service of Nephrology and Hypertension, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland. E-mail: nora.schwotzer@chuv.ch

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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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Clare Morlidge¹, Sally El-Kateb², Praveen Jeevaratnam² and Barbara Thompson²

¹Pharmacy Department, Lister Hospital, Stevenage, Hertfordshire, UK; and ²Renal Department, Lister Hospital, Stevenage, Hertfordshire, UK

Correspondence: Clare Morlidge, Pharmacy Department, East and North Hertfordshire NHS Trust, Coreys Mill Lane, Stevenage, Hertfordshire, SG1 4AB, UK. E-mail: claremorlidge@nhs.net

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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 COM-IRNATY) because of edema and weight gain (6 kg). Medical