



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Minimal change disease relapse following SARS-CoV-2 mRNA vaccine



To the editor: Although the pathogenesis of minimal change disease (MCD) has not yet been clearly elucidated, immune dysregulation is probable,¹ and the risk of relapse after the administration of various vaccines (especially meningococcal C conjugate vaccines) has been suggested.^{2,3} Here, we report a case of MCD relapse following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccination.

The patient was a 34-year-old woman with a recent history of nephrotic syndrome diagnosed as MCD. Steroids allowed complete remission, but she was corticoid-dependent, as 2 relapses occurred during steroid tapering (Figure 1). A second-line treatment (rituximab) was thus planned, after vaccination against SARS-CoV-2 with the BNT162b2 vaccine (Pfizer-BioNTech). Six weeks before the first injection, steroids had been increased (0.5 mg/kg) due to the onset of low-grade proteinuria, leading to remission. Ten days after the first vaccine injection (ongoing steroid dose 0.4 mg/kg), she presented with full-blown relapse

(edema; protein-to-creatinine ratio [PCR] of 2.4 g/g), leading to an increase of steroid dose to 0.5 mg/kg, achieving a decrease in proteinuria (PCR 1.2 g/g). She received the second injection (27 days after the first one), and a few days later, proteinuria increased again to a nephrotic range (PCR 3 g/g), leading to a new increase of steroid dose to 1 mg/kg that finally allowed complete remission. Response to the vaccine was satisfying, with a positive SARS-CoV-2 serology (anti-S protein antibodies assessed by electrochemiluminescence immunoassay [Roche Elecsys] before second injection at 55.2 U/ml), and no other immediate or delayed adverse event occurred following vaccination. This observation suggests that the BNT162b2 vaccine could favor MCD relapse, potentially through the stimulation of the immune response and the cytokine release it induces. Steroids seem efficient in achieving prompt remission.

1. Vivarelli M, Massella L, Ruggiero B, Emma F. Minimal change disease. *Clin J Am Soc Nephrol*. 2017;12:332–345.
2. Patel C, Shah HH. Vaccine-associated kidney diseases: a narrative review of the literature. *Saudi J Kidney Dis Transpl*. 2019;30:1002.
3. Abeyagunawardena A, Goldblatt D, Andrews N, Trompeter R. Risk of relapse after meningococcal C conjugate vaccine in nephrotic syndrome. *Lancet*. 2003;362:449–450.

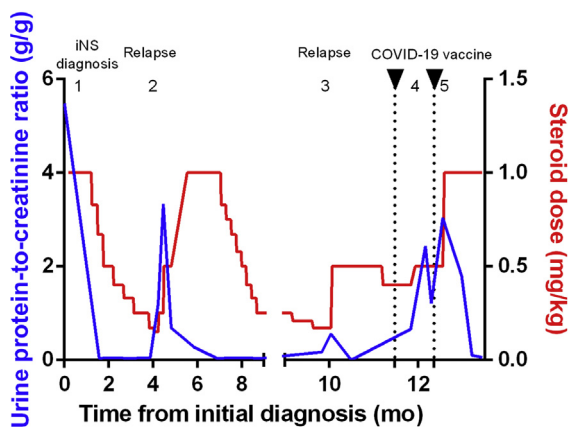


Figure 1 | Urine protein-to-creatinine ratio and steroid dose during follow-up. (1) Diagnosis of idiopathic nephrotic syndrome (iNS; minimal change disease diagnosed on kidney biopsy). (2) First relapse when tapering steroids from 10 mg to 9 mg; increase of steroid dose to 1 mg/kg (60 mg), leading to remission of NS. (3) Second relapse when tapering steroids from 12.5 mg to 10 mg; increase of steroid dose to 0.5 mg/kg, leading to remission. Coronavirus disease 2019 (COVID-19) mRNA vaccine was injected while the patient was treated with 0.4 mg/kg steroids (25 mg; ongoing tapering from last relapse occurring 6 weeks before first vaccine injection; no proteinuria on urine dipstick test at the time of vaccine injection). (4) Proteinuria after first mRNA COVID-19 vaccine injection; increase of steroid dose from 25 mg to 30 mg (0.5 mg/kg). (5) Proteinuria increase after second mRNA COVID-19 vaccine injection; increase of steroids to 60 mg (1 mg/kg), leading to remission.

Editor's Note

The RNA-platform COVID-19 vaccines strongly stimulate the immune system. Many of us who care for GN patients were concerned that these vaccines could cause disease flares in our patients. While this has not yet been studied systematically, it appears that most patients with GN who have been vaccinated have not had kidney disease exacerbations. Nonetheless, starting with one letter to the *Journal* describing gross hematuria in 2 patients with known IgA nephropathy after the second dose of a COVID-19 vaccine, *Kidney International* has received many similar reports. While IgA nephropathy seems to be the most frequently exacerbated GN, the following letters offer the experiences of our readers who have observed other types of glomerular disease worsened or uncovered after vaccination. Undoubtedly, these patients are trying to tell us something about the immunopathogenesis of their glomerular diseases.

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

Kidney International (2021) **100**, 457–458; <https://doi.org/10.1016/j.kint.2021.04.033>

Copyright © 2021, International Society of Nephrology. Published by Elsevier Inc. All rights reserved.

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

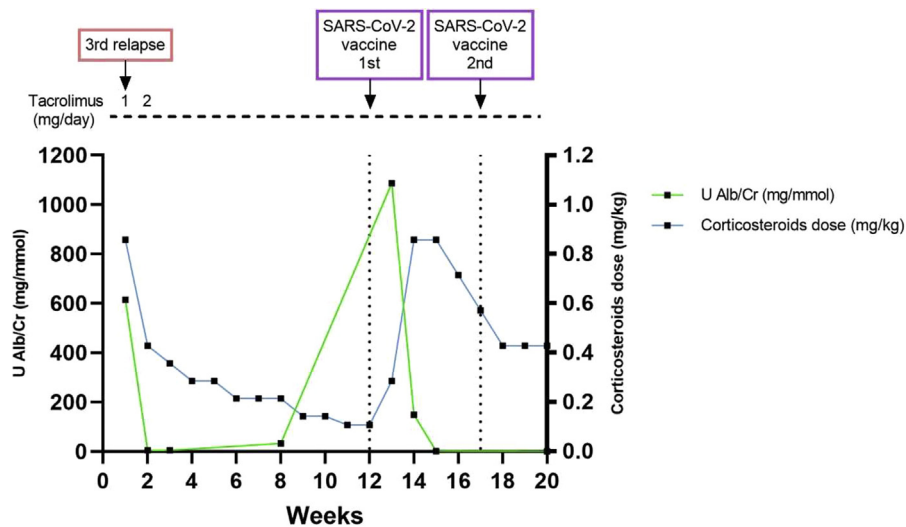


Figure 1 | Evolution over time of the idiopathic nephrotic syndrome in a 22-year-old male patient who experienced a relapse of his nephrotic syndrome following anti–coronavirus disease 2019 (COVID-19) mRNA vaccine. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; U Alb/Cr, urinary albumin/creatinine.