Clinical Kidney Journal, 2022, vol. 0, no. 0, 1–3

https://doi.org/10.1093/ckj/sfac222
Advance Access Publication Date: 19 October 2022
Exceptional Case

EXCEPTIONAL CASE

Development of crescentic membranoproliferative glomerulonephritis after COVID-19 vaccination

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ABSTRACT

Membranoproliferative glomerulonephritis (MPGN) comprises a histologic pattern of glomerular injury with different underlying diseases. Here we report on a 47-year-old female with rapidly progressive glomerulonephritis (RPGN) on top of a previously diagnosed idiopathic MPGN after receiving the first dose of the Pfizer-BioNTech coronavirus disease 2019 (COVID-19) mRNA vaccine. After aggressive immunosuppression her serum creatinine returned to normal values, along with reduction of proteinuria. Recently, numerous publications have reported an association of glomerular diseases with COVID-19 vaccination. Our case presents to the best of our knowledge the first occurrence of possible association of COVID-19 mRNA vaccination with a crescentic form of MPGN.

Keywords: AKI, COVID-19, membranoproliferative glomerulonephritis, nephrotic syndrome, vaccination

BACKGROUND

Since the beginning of vaccination during the coronavirus disease 2019 (COVID-19) pandemic, multiple case reports on the new onset or relapse of glomerular diseases related to COVID-19 vaccination have been published. mRNA vaccines, viral vector-based and inactivated vaccines have all been claimed to be associated with individual cases of glomerulonephritis (GN)—both newly diagnosed as well as relapsed forms of GN. The mRNA vaccines accomplish their effect by inducing cell-mediated and antibody-mediated immune responses. A possible underlying mechanism of induction of GNs related to mRNA COVID-19 vaccination is immune system activation, which comprises adaptive and innate immune cell activation by the vaccine [1–4].

CASE REPORT

A 47-year-old Caucasian female patient presented in our outpatient nephrology clinic with weakness and pain in multiple joints during the last month and claimed reduced urine volume for days before hospital admission.

She had a history of chronic MPGN, which was diagnosed in 2014. The first kidney biopsy showed an MPGN pattern of injury with diffuse mesangial expansion and mesangial and endocapillary hypercellularity without any crescents. The immunohistochemical staining revealed diffuse global IgG, IgM, C3 and C1q deposits. Electron microscopy with glomerular sclerosis and mesangial, subendothelial and sporadically subepithelial electron dense deposits and podocyte foot process effacement confirmed the diagnosis of an MPGN type proliferative immune

Received: 7.7.2022; Editorial decision: 28.9.2022

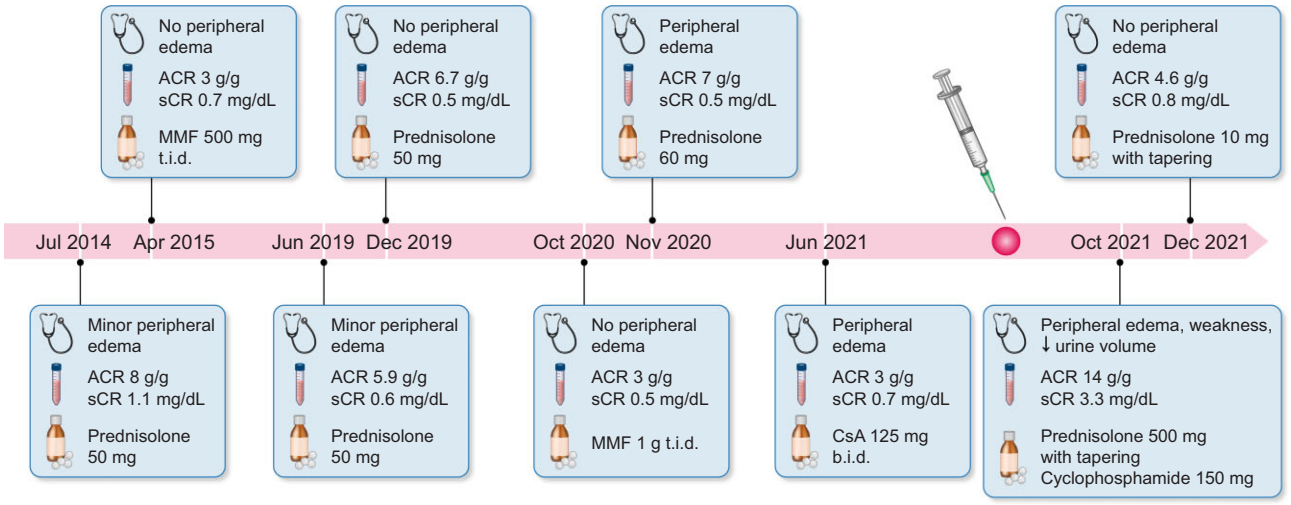

Figure 1: The timeline of the patient's medical history listing the clinical status and symptoms, ACR in the urine, serum creatinine (sCr) and the current immunosuppressive therapy.

complex-mediated GN. Comprehensive diagnostic workup ruled out underlying autoimmune and infectious diseases, as well as hematological disorders. Thus, MPGN was considered idiopathic. In the following years, the patient was treated with various immunosuppressive agents due to fluctuating clinical symptoms and persisting gross albuminuria of above 3 g/g creatinine, as shown in Fig. 1.

In September 2021 the COVID-19 mRNA vaccine BNT162b2 (Pfizer-BioNTech) was administered. In the weeks that followed, the patient suffered from the above-mentioned symptoms, which led her to seek medical help (Fig. 1).

Laboratory results were compatible with acute kidney disease (AKD) with an increased serum creatinine of 3.3 mg/dL (estimated glomerular filtration rate 15 mL/min/1.73 m^2). The patient displayed albuminuria with an albumin-to-creatinine ratio (ACR) of above 14 g/g and a serum albumin of 21.8 g/L. Cyclosporine A (CsA) levels were within therapeutic range since the change of immunosuppressive medication in June 2021 with 121 ng/mL before the vaccination and 114 ng/mL at the time of hospital admission.

Kidney biopsy revealed an active MPGN with segmental cellular crescents in 9 out of 17 glomeruli and more prominent chronic tubulointerstitial lesions in comparison with previous biopsies. Treatment of the patient was started with intravenous steroids (500 mg a day, 3 times), followed by a combination of oral cyclophosphamide (150 mg per day) and prednisolone (75 mg per day).

Five days after discharge from the hospital, serum creatinine values had dropped to 1.8 mg/dL and further declined to 1.0 and 0.7 mg/dL, respectively, after 2 and 4 weeks, while ACR decreased to 5.6 g/g.

DISCUSSION

Here we demonstrate a patient with chronic MPGN and stable kidney function parameters but persistent gross proteinuria under immunosuppression for years. Following COVID-19 vaccination, the patient developed AKD and a clinical picture of nephrotic syndrome. Kidney biopsy revealed a crescentic form of MPGN arousing suspicion of a triggering event.

Before vaccination, the patient did not experience any signs of systemic infection and she was on continuous calcineurin inhibitor therapy with CsA levels in the target range rendering it unlikely to initiate aggravation of her MPGN, leaving the COVID-19 vaccine the only new variation in her recent medical history.

The selected aggressive immunosuppressive regimen with high-dose glucocorticoids and cyclophosphamide seems to be highly effective as serum creatinine normalized and albuminuria decreased significantly. Another option, although less likely, for the improvement of kidney function is the withdrawal of CsA.

Reports on COVID-19 vaccine–related glomerular diseases are being published consistently but so far there is only one mention of a patient developing a membranoproliferative pattern following the second dose of mRNA-1273 (Moderna) vaccine [5]. However, our report is the first to describe a crescentic MPGN with nephrotic syndrome after first administration of the Pfizer-BioNTech mRNA vaccine. Further studies are necessary to confirm or reject a potential causal relationship between relapse or new onset of glomerular disease and mRNA vaccinations in patients with MPGN.

PATIENT CONSENT

The authors declare that they have obtained consent from the patient reported in this article for publication of the information about her that appears within this case report.

FUNDING

This case report was not funded by any companies.

DATA AVAILABILITY STATEMENT

The data used to support the findings are included within the article.

CONFLICT OF INTEREST STATEMENT

A.K. has received consulting and personal fees from Vifor Pharma, Alexion, Otsuka, UriSalt, Delta4 and Catalyst

Biosciences. A.K. is member of the *CKJ* editorial board. M.D.S. has received honoraria for consulting and lectures from AstraZeneca, Bayer, Boehringer-Ingelheim, Novartis, Otsuka and Vifor Pharma. The other authors declare that they have no relevant financial interests.

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