COVID-19 Vaccination and Glomerulonephritis

Nattawat Klomjit1,2, Mariam Priya Alexander3, Fernando C. Fervenza1, Ziad Zoghby1, Arvind Garg1, Marie C. Hogan1, Samih H. Nasr3, Marwan Abu Minshar4 and Ladan Zand1

1Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; 2Division of Nephrology and Hypertension, University of Minnesota, Minneapolis, Minnesota, USA; 3Department of Pathology and Laboratory Medicine, Mayo Clinic, Rochester, Minnesota, USA; and 4Division of Nephrology and Hypertension, Essentia Health, Fargo, North Dakota, USA

Introduction: mRNA COVID-19 vaccine is more effective than traditional vaccines owing to superior immune activation. Nevertheless, the impact of mRNA COVID-19 vaccine on triggering de novo/relapsing glomerulonephritis (GN) is limited. We report a case series of patients who developed new or relapsing GN postvaccination.

Methods: We evaluated baseline characteristics, vaccine type, and clinical outcomes of 13 patients from our institution who had a new diagnosis or relapse of their GN post–mRNA COVID-19 vaccination.

Results: Of 13 patients, 8 patients were newly diagnosed with having GN and 5 patients had relapse. Median age was 62 years (range 19–83 years). Autoimmune disease (38%) was the most prevalent underlying disease followed by cancer (23%). Most patients were White males. IgA nephropathy (IgAN) was the most common GN in our series (5 patients, 38%) followed by membranous nephropathy (MN) (3 patients, 23%). There was 1 patient with IgAN who had evidence of IgA deposits before vaccination suggesting the immune activation after vaccination triggered a flare of the disease. Our case series also included the first case report of tip-variant focal segmental glomerulosclerosis (FSGS), NELL-1–associated MN, and atypical anti–glomerular basement membrane (GBM) nephritis. A total of 77% developed acute kidney injury (AKI) with most being Kidney Disease: Improving Global Outcomes stage 1 (67%). Outcomes are favorable with 80% responding to therapy.

Conclusion: New cases and relapse of GN can present shortly after mRNA COVID-19 vaccination. New cases of IgAN may result from unmasking of undiagnosed IgAN owing to robust immune activation rather than development of new deposits.

Kidney Int Rep (2021) 6, 2969–2978; https://doi.org/10.1016/j.ekir.2021.09.008

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GN cases thus far. We also provide evidence in 1 case of “new” IgAN wherein the deposits were present previously. We also report on 3 new diagnoses after COVID-19 vaccination, including a case of NELL-1–associated MN, a case of primary FSGS, and a case of atypical anti-GBM nephritis.

**METHOD**

**Patient Selection**

Patients who were either newly diagnosed or had a relapse of their GN after vaccination are reported in this case series. All patients had their kidney pathology results reviewed at the Mayo Clinic, Rochester, Minnesota. Clinical data and baseline characteristics, vaccine type, onset of symptoms, laboratories on presentation, treatments, and outcomes are based on review of medical records.

**Literature Review**

We searched all literature since the inception that reported newly diagnosed or relapse of GN after any type of COVID-19 vaccines through PubMed. We then extracted baseline characteristics, laboratories on presentation, treatments, and outcomes.

**Statistical Analysis**

We report continuous data with median and range. Categorical data are found with number and percentage. We used descriptive statistics in this report as the sample size is quite small and no analytical statistics were implemented.

**RESULTS**

**Baseline Demographic and Clinical Characteristics of Newly Diagnosed and Relapsed GNs**

There were 13 patients reported in this case series. Of these, 8 of 13 cases (62%) were newly diagnosed with having GN whereas 5 of 13 cases (38%) were relapses. The median age was 62 (19–83) years. Most patients were White (12 of 13, 92%) and male (9 of 13, 69%). Autoimmune disease (38%) was the most common comorbidity in our series followed by cancer (23%). The autoimmune diseases included diabetes mellitus type 1, Crohn’s disease, ulcerative colitis, primary sclerosing cholangitis, and psoriatic arthritis. IgAN was the most common GN in our case series (5 of 13, 38%). The second most common GNs were MN (3 of 13, 23%) and primary podocytopathy (2 cases of minimal change disease [MCD] and 1 case of primary FSGS) (3 of 13, 23%). In addition, 54% of our patients received mRNA-1273 (Moderna) and the other 46% received BNT162b2 (Pfizer) vaccine. Most patients presented after the second dose (10 of 13, 77%). The median time of onset varied. Median time of onset in those newly diagnosed with having GN was 1 week after the first dose and 4 weeks after the second dose. In contrast, all of our relapse cases occurred after the second dose with median onset of 3 weeks. AKI, edema, and macroscopic hematuria were common presentations. Median serum creatinine level was 1.6 (0.6–2.5) mg/dl. Baseline clinical characteristics of each patient are found in Table 1.

**Clinical Characteristics of Patients With Newly Diagnosed GNs**

Of newly diagnosed cases (8 patients), there were 4 cases of IgAN, 1 case of MCD, 1 case of NELL-1–associated MN, 1 case of myeloperoxidase-antineutrophilic cytoplasmic Ab (ANCA) crescentic GN, and 1 case of atypical anti-GBM nephritis. The clinical characteristics of these patients are found in Table 1. There were 5 patients who presented after the second dose of the vaccine (range 2–6 weeks) and 3 patients who presented after the first dose (range 1–2 weeks). The main presenting symptom in patients with new diagnosis of IgAN included AKI and gross hematuria. Furthermore, 1 patient had a symptom of pericarditis in addition to gross hematuria at the time of presentation. There was also 1 patient who had a history of inflammatory bowel disease which raised possibility that he may have had IgA deposits in the kidney before undergoing vaccination and likely had asymptomatic IgAN. This patient also had history of renal cell carcinoma and had undergone partial nephrectomy 7 years before his vaccination. Results of his serum creatinine and urine studies had been normal at the time and in follow-up (last value from 1 year before vaccination). To evaluate for the presence of IgA deposits before vaccination, the nephrectomy sample was retrieved for further evaluation. Glomeruli were unremarkable on light microscopy. Immunofluorescence on pronase-digested, paraffin tissue was performed and revealed segmental mesangial staining of IgA, kappa, and lambda. Electron microscopy revealed presence of mesangial deposits. Therefore, the partial nephrectomy sample revealed evidence of subclinical IgAN. In addition, we had 1 case of atypical anti-GBM nephritis, characterized by bright diffuse linear GBM staining for IgG, kappa, and lambda on immunofluorescence and mesangial proliferation and basement membrane duplication on light microscopy, without the necrotizing and crescentic phenotype typically found in classic anti-GBM nephritis.16
Clinical Characteristics of Patients With Relapse of GN

Of the 5 patients who had a relapse, 2 patients had underlying phospholipase A2 receptor (PLA2R)-associated MN, 1 patient had relapse of MCD, and 1 patient originally had diagnosis of MCD but underwent a repeat kidney biopsy on relapse which revealed tip-variant lesion of primary FSGS, and 1 patient had underlying IgAN. All cases of relapse occurred after the second dose with onset ranging from 1 to 4 weeks. Detailed clinical characteristics of each patient are found in Table 1.

There was 1 patient with PLA2R-associated MN who was in complete remission with negative PLA2R Ab titer result and on no immunosuppression for 18 months before relapse. On relapse, the patient developed sudden-onset nephrotic syndrome and PLA2R Ab was elevated at 28 IU/ml. Another patient with PLA2R-associated MN who was in remission for 8 months presented with nephrotic syndrome, and PLA2R Ab titer result was positive at 3 IU/ml on enzyme-linked immunosorbert assay and positive by indirect immunofluorescence (they were both previously negative). The patient with primary FSGS was in complete remission and off immunosuppression for 24 months before relapse and presented with nephrotic syndrome. The patient with MCD was originally diagnosed with having MCD 3 months before vaccination. She went into complete remission within 4 weeks of starting therapy with high-dose steroids with proteinuria down to 200 mg per 24 hours. As a result, prednisone was tapered to 5 mg daily at which point she received her first dose of the vaccine. Nevertheless, 3 weeks after her second dose, she presented with worsening edema and was noted to have 19 g of protein in 24 hours. The patient with IgAN on last evaluation (2 months before vaccination) had serum creatinine level of 0.96 mg/dl, and urinalysis results revealed 50 to 100 red blood cells per high-powered field with 431 mg of protein per 24 hours. The patient also developed gross hematuria 24 hours after the second dose of COVID-19 vaccination.

Treatment and Clinical Follow-Up

Of 13 patients, 9 (69%) received immunosuppression (5 of 8 [63%] had new diagnosis and 4 of 5 [80%] were recurrence). The other 4 patients were treated conservatively. There were 10 patients who have available follow-up data ranging from 1 to 5 months. Of these, 8 patients responded to the treatments (6 treated with immunosuppression and 2 treated conservatively with angiotensin-converting enzyme inhibitor). Patient number 3 who responded to therapy had developed symptoms after the first dose and had further elevation in creatinine after the second dose (peak creatinine 2.2 mg/dl) which then subsequently improved to 1.4 mg/dl. One patient with IgAN and acute interstitial nephritis and the patient with atypical anti-GBM nephritis were both treated with immunosuppressive therapy with high-dose steroids with proteinuria down to 200 mg per 24 hours. As a result, prednisone was tapered to 5 mg daily at which point she received her first dose of the vaccine. Nevertheless, 3 weeks after her second dose, she presented with worsening edema and was noted to have 19 g of protein in 24 hours. The patient with IgAN on last evaluation (2 months before vaccination) had serum creatinine level of 0.96 mg/dl, and urinalysis results revealed 50 to 100 red blood cells per high-powered field with 431 mg of protein per 24 hours. The patient also developed gross hematuria 24 hours after the second dose of COVID-19 vaccination. He had a similar reaction after influenza vaccination a year before.

Table 1. Characteristics of initial presentation of patients with newly diagnosed and relapsed glomerulonephritis post-COVID-19 vaccination

| Case | Age | Sex | Race | Diagnosis                  | Vaccine | Onset after which dose | Onset time (wk) | Presenting symptoms | Baseline SCR (mg/dl) | SCR (gd/l) | Urine RBC (HPF) | Urine protein (gd/l) | SAbl (gd/l) |
|------|-----|-----|-----|---------------------------|---------|------------------------|-----------------|---------------------|---------------------|------------|-----------------|---------------------|------------|
| 1    | 38  | M   | W   | IgAN                      | Pfizer  | 2nd                    | 2               | Gross hematuria     | 1.3                 | 1.6        | 51–100          | 0.32                | NA         |
| 2    | 44  | M   | W   | IgAN + acute interstitial nephritis | Moderna | 1st                    | 2               | AKI                 | 1.1                 | 2.5        | 21–30           | 14                  | 3.7        |
| 3    | 66  | M   | W   | IgAN                      | Moderna | 1st                    | 2               | Gross hematuria     | 1.1                 | 1.5<   | 51–100          | 1.2                 | 4.1        |
| 4    | 62  | M   | W   | IgAN                      | Pfizer  | 2nd                    | 6               | AKI                 | 1                   | 2.2        | 31–40           | 0.9                  | 4.2        |
| 5    | 77  | M   | W   | Atypical anti-GBM nephritis | Pfizer  | 1st                    | 1               | Hypertension        | 1                   | 1.8        | 51–100          | 1.6                  | NA         |
| 6    | 83  | M   | W   | MCD + ATN                 | Moderna | 2nd                    | 4               | AKI                 | 1.19                | 2.19       | <3             | 18                  | 2.0        |
| 7    | 50  | F   | W   | NELL-1 MN                 | Pfizer  | 2nd                    | 4               | Joint pain and proteinuria | 0.84                | 0.7        | 3–10            | 6.5                  | 3.5        |
| 8    | 82  | F   | W   | MPO-ANCA                  | Moderna | 2nd                    | 4               | AKI, hematuria, proteinuria | 0.8                 | 2.5<   | 3–10            | 1.2                  | NA         |

A, Asian; AKI, acute kidney injury; ATN, acute tubular necrosis; F, female; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; HPF, high-powered field; IgAN, IgA nephropathy; M, male; MCD, minimal change disease; MN, membranous nephropathy; MPO-ANCA, myeloperoxidase-antineutrophilic cytoplasmic antibody; NA, unavailable; PLA2R, phospholipase A2 receptor; RBC, red blood cell; SAbl, serum albumin; SCR, serum creatinine; W, White.

*Serum creatinine peaked at 2.2 mg/dl.

*Serum creatinine peaked at 3.1 mg/dl.
therapy but have not yet responded and have had progression of their kidney disease. Both of these patients developed symptoms after the first dose of the vaccine but proceeded to receive the second dose. Additional treatment details and outcomes are outlined in Table 2.

Clinical Characteristics of Patients From Published Literatures

We found a total of 20 articles related to COVID-19 vaccines and GN published since inception until July 25, 2021. There were 27 cases including 13 cases of newly diagnosed GNs (48%) and 14 cases of relapse (52%) (Table 3). IgAN was the most common pathology (11 cases [41%]: 4 new and 7 relapse) followed by MCD (10 cases [37%]: 4 new and 6 relapse). Other pathologies include 2 cases of anti-GBM (7%) (both new cases), 2 cases of ANCA vasculitis (7%) (both new cases, 1 case of myeloperoxidase-ANCA and 1 case of proteinase 3-ANCA), 1 case of ANCA-negative granulomatous vasculitis (4%) (relapse), and 1 case of PLA2R-associated MN (4%) (relapse). Median age was 41 years, and 48% were male. Nevertheless, patients tended to be younger in the relapse group (median age 38 years) compared with the newly diagnosed group (median age 56 years) (Table 4).

Of 27 patients, 15 patients (56%) developed symptoms after the first dose whereas the remaining (12 patients, 44%) developed symptoms after the second dose. Nevertheless, patients newly diagnosed with having GN tended to develop symptoms after the second dose (7 of 13 patients, 54%) and those with relapses tended to develop symptoms after the first dose (9 of 14 patients, 64%) (Table 4).

Clinical Characteristics and Follow-Up of Patients by Disease

IgA Nephropathy

In our case series, there were 5 cases of IgAN (4 new and 1 relapse). In the literatures, there were 11 cases of IgAN reported (4 new and 7 relapse). Gross hematuria was the most common presentation followed by AKI. Nevertheless, in most patients, gross hematuria was often self-limited and seldom required immunosuppression. Of the total of 16 patients, only 3 patients received immunosuppression and 1 patient had superimposed acute interstitial nephritis as well. All cases of relapsed IgA improved spontaneously within 1 to 2 weeks.

Primary Podocytopathy

In our case series, there were 2 cases of MCD (1 new and 1 relapse) and 1 case that was previously MCD but on repeat biopsy revealed a tip-variant FSGS lesion. In the literatures, there were 10 cases (4 new and 6 relapse). All cases in our series developed symptoms after the second dose, whereas all MCD cases in the literature developed symptoms after the first dose. All patients received immunosuppression. One patient with new MCD responded rapidly to therapy. One
Table 3. Summary of published cases of newly diagnosed and relapsed glomerulonephritis

| Authors          | Case | Age | Sex | Underlying disease | Vaccine (Manufacturer) | Symptoms | Onset after which dose | Onset | Diagnosis  | Treatments | Outcomes                      |
|------------------|------|-----|-----|--------------------|------------------------|----------|------------------------|-------|------------|------------|--------------------------------|
| Lebedev et al.  | 1    | 50  | M   | No                 | mRNA (Pfizer)          | Nephrotic syndrome, AKI, HTN | 1st | D 10       | MCD        | High-dose steroid | Proteinuria and AKI significantly improved at 2 wks |
| D’Agati et al.  | 2    | 77  | M   | DM type 2          | mRNA (Pfizer)          | Nephrotic syndrome, AKI, HTN | 1st | 1 wk       | MCD        | High-dose steroid | Proteinuria and SD not improved at 3 wks |
| Holzworth et al.| 3    | 63  | F   | HTN, tobacco dependence | mRNA (Moderna) | Nephrotic syndrome, uncontrolled HTN | 1st | <1 wk      | MCD        | High-dose steroid | NA |
| Maas et al.     | 4    | 80  | F   | NA                 | mRNA (Pfizer)          | Nephrotic syndrome, HTN | 1st | 1 wk       | MCD        | High-dose steroid | Proteinuria reduced from 15 g/d to >0.7 g/d at d 10 |
| Sekar et al.    | 5    | 52  | M   | HTN                | mRNA (Moderna)        | Headache, AKI, hematuria | 2nd | 2 wks      | PR3-ANCA vasculitis | RTX (side effects) and then i.v. CyC + steroid was started | Dialysis was started. 2nd dose of i.v. CyC was planned |
| Shaker et al.   | 6    | 78  | F   | DM type 2          | mRNA (Pfizer)          | AKI, hematuria, proteinuria | 1st | 2 wks      | MPO-ANCA vasculitis | High-dose steroid and RTX | SCR improved from 3.5 to 2.3 mg/dL |
| Gillion et al.  | 7    | 77  | M   | No                 | Adenovirus vector (AstraZeneca) | Fever, night sweat, and AKI | 1st | 4 wks      | ANCA-negative granulomatous vasculitis | High-dose steroid | SCR was normalized at 4 wks |
| Kudose et al.   | 8    | 50  | F   | HTN, APS           | mRNA (Moderna)        | Gross hematuria | 2nd | D 2        | IgAN       | Conservative | Hematuria resolved in 5 d |
| Tan et al.      | 9    | 19  | M   | Microscopic hematuria | mRNA (Moderna) | Gross hematuria | 2nd | D 2        | IgAN       | Conservative | Hematuria resolved in 2 d |
| Tan et al.      | 10   | 41  | F   | GDM                | mRNA (Pfizer)          | Gross hematuria | 2nd | D 1        | IgAN       | Anti-GBM     | High-dose steroid + IV CyC and oral CyC + PLEX | NA |
| Hanna et al.    | 11   | 60  | M   | Hyperlipidemia     | mRNA (Pfizer)          | Gross hematuria, AKI, proteinuria | 2nd | <24 h      | IgAN       | High-dose steroid | SCR improved (duration not reported) |
| Sacker et al.   | 12   | 17  | M   | No                 | mRNA (Moderna)        | AKI, hematuria, proteinuria | 2nd | 2 wks      | Anti-GBM   | High-dose steroid, CyC, PLEX | Remained dialysis dependent |
| Negrea et al.   | 13   | —   | F   | IgAN in remission  | mRNA (Moderna)        | Macroscopic hematuria | 2nd | 8-24 h     | IgAN       | Conservative | Spontaneously resolved |
| Perrin et al.   | 1     | 38  | F   | IgAN in remission  | mRNA (Moderna)        | Macroscopic hematuria | 2nd | 8-24 h     | IgAN       | Conservative | Spontaneously resolved |
| Perkins et al.  | 2     | 38  | F   | IgAN in remission  | mRNA (Moderna)        | Macroscopic hematuria | 2nd | D 2        | IgAN       | Conservative | Spontaneously resolved |
| Hann et al.     | 3     | 22  | M   | IgA vasculitis     | mRNA (Moderna)        | Macroscopic hematuria | 1st | D 2        | IgAN       | Conservative | Spontaneously resolved |
| Kervella et al. | 4     | 41  | F   | Kidney transplant  | mRNA (Pfizer)          | Macroscopic hematuria | 1st | D 2        | IgAN       | Conservative | Spontaneously resolved |
| Rahman et al.   | 5     | 27  | F   | On hemodialysis    | mRNA (Pfizer)          | Macroscopic hematuria | 2nd | D 2        | IgAN       | Conservative | Hematuria and AKI resolved within 1 wk |
| Schwitzer et al. | 6     | 13  | M   | DM type 1          | mRNA (Pfizer)          | Gross hematuria, AKI | 2nd | <24 h      | IgAN       | Conservative | Hematuria resolved within 1 wk |
| Schwitzer et al. | 7     | 52  | F   | IgAN treated with ACEi | mRNA (Pfizer) | Gross hematuria, worsening proteinuria | 2nd | <24 h      | IgAN       | Conservative | Hematuria resolved within 1 wk |
| Kombo et al.    | 8     | 22  | M   | Steroid-dependent MCD | mRNA (Pfizer) | Nephrotic syndrome | 1st | D 3        | MCD        | High-dose steroid + TAC | Remission was achieved at d 17 after treatment |
| Kerella et al.  | 9     | 34  | F   | Steroid-dependent MCD | mRNA (Pfizer) | Nephrotic syndrome | 1st | D 10       | MCD        | High-dose steroid | Remission was achieved shortly after treatment |
| Kombo et al.    | 10    | 65  | M   | MCD in remission   | mRNA (Pfizer)          | Nephrotic syndrome | 1st | D 19       | MCD        | High-dose steroid + cyclosporine | Remission was achieved at 2 wks |

(Continued on following page)
patient with relapse of MCD did not respond to high-dose steroids and received rituximab to which the patient responded. The patient with primary FSGS had partial response to prednisone in combination with tacrolimus.

Membranous Nephropathy
In our case series, there were 3 cases of MN in which 2 cases were associated with PLA2R (relapse) and 1 case with NELL-1 (new). The patient with NELL-1–associated MN had age-appropriate cancer screening completed with negative results. On the basis of literature review, there has been 1 case of PLA2R-associated MN after inactivated vaccine. All patients in our series developed nephrotic syndrome after the second dose. The patient with NELL-1–associated MN significantly improved after conservative management. Proteinuria improved from 6.5 g/d to 0.4 g/d within 3 months after angiotensin-converting enzyme inhibitor initiation. Of 2 patients with PLA2R-associated MN, only 1 patient from our series has follow-up data. The patient was restarted on tacrolimus. At 1 month, proteinuria and serum albumin improved from 8.7 g/d to 5.7 g/d and 2.0 g/dl to 2.9 g/dl, respectively.

Anti-GBM and ANCA–Associated Vasculitis
In our case series, there was 1 case of atypical anti-GBM nephritis. In the literatures, there have been 2 cases of classic anti-GBM nephritis. The patient from our series presented 1 week after the first dose with symptom of uncontrolled hypertension (systolic blood pressure level >200 mm Hg), whereas the other 2 cases from literatures presented within 2 weeks after the second dose. Outcome data were available in 2 patients (one from our series and another from the literature). Our patient did not respond to mycophenolate and high-dose steroid, and his serum creatinine level continued to rise. He has now been initiated on cyclophosphamide, but it is too early to know the response. Another patient received cyclophosphamide, plasmapheresis, and high-dose steroid, but the patient did not respond and has remained on dialysis.

We had 1 patient with myeloperoxidase-ANCA–associated vasculitis, and in the literature, there were 2 cases of ANCA–associated vasculitis, one associated with myeloperoxidase and another with proteinase 3. In addition, there was a single case report of ANCA-negative granulomatous vasculitis post adenoviral vector vaccine. Our patient presented with shortness of breath and fatigue 4 weeks after the second dose. The patient was found to have AKI, serum creatinine level of 2.5, with microscopic hematuria and subnephrotic range proteinuria. Subsequently, serum creatinine level increased to 3.1, and a kidney biopsy was done which revealed pauci-immune crescentic GN. The patient was
treated with rituximab and high-dose prednisone, and serum creatinine level 1 month post-treatment improved at 2.3 mg/dl. From the literature, patients with myeloperoxidase-ANCA and ANCA-negative granulomatous vasculitis responded to therapy with improvement in serum creatinine. In contrast, the patient with proteinase 3-ANCA–associated vasculitis required initiation of dialysis.

**DISCUSSION**

Our case series is the largest series to report on both newly diagnosed and relapsed cases of GN post–COVID-19 vaccination. All patients in our series received mRNA vaccines. The BNT162b (Pfizer) and mRNA-1273 (Moderna) are the 2 most widely used vaccines in the United States after their use was approved under emergency use authorization by the US Food and Drug Administration. Most patients in our series developed kidney-related symptoms after the second dose, but the onset of symptoms varied from 1 week after the first dose to 6 weeks after the second dose. Taking into account cases reported in the literature, the onset of symptoms has been reported as early as few hours after the first dose.17–19 It is possible that some patients in our series may have had signs of kidney injury (e.g., elevated creatinine, proteinuria, or microscopic hematuria) between the first and second

### Table 4. Clinical characteristics of patients with GN post–COVID-19 vaccine from previously published literatures and current case series

| Characteristics | Current case series (n = 13) | Literatures (n = 27) | Total (n = 40) |
|-----------------|-----------------------------|----------------------|---------------|
| Age (yr)        | 62 (19–83)                  | 41 (13–80)           | 50 (13–83)    |
| Male sex, n (%) | 9 (69)                      | 13 (48)              | 22 (55)       |
| Underlying disease, n (%) |                       |                      |               |
| - Autoimmune disease | 5 (38)                    | NA                   | NA            |
| - Diabetes | 2 (15)                      | NA                   | NA            |
| - Cancer | 3 (23)                      | NA                   | NA            |
| New vs. recurrent disease, n (%) |                       |                      |               |
| - New | 8 (62)                      | 13 (48)              | 21 (53)       |
| - Recurrent | 5 (38)                     | 14 (52)              | 19 (47)       |
| Diagnosis, n (%) |                        |                      |               |
| - IgA nephropathy | 5 (38)                    | 11 (41)              | 16 (40)       |
| - Minimal change disease | 2 (15)                    | 10 (37)              | 12 (30)       |
| - Membranous nephropathy | 3 (23)                  | 1 (4)                | 4 (10)        |
| - Anti-GBM disease | 1 (8)                      | 2 (7)                | 3 (7)         |
| - ANCA vasculitis | 1 (8)                      | 2 (7)                | 3 (7)         |
| - Focal segmental glomerulosclerosis | 1 (8)                   | —                    | 1 (3)         |
| - ANCA-negative granulomatous vasculitis | —                      | 1 (4)                | 1 (3)         |
| Vaccine type, n (%) |                        |                      |               |
| - BNT162b2 (Pfizer) | 6 (46)                     | 15 (55)              | 21 (53)       |
| - mRNA-1273 (Moderna) | 7 (54)                      | 8 (30)               | 15 (37)       |
| - Adenovirus vector (AstraZeneca) | —                        | 5 (11)               | 3 (7)         |
| - Inactivated vaccine (CoronaVac by Sinovac) | —                        | 1 (4)                | 1 (3)         |
| Symptoms occur after 1st or 2nd dose, n (%) |                      |                      |               |
| - 1st dose | 3 (23)                      | 15 (56)              | 18 (45)       |
| - 2nd dose | 10 (77)                     | 12 (44)              | 22 (55)       |
| Onset |                        |                      |               |
| - New case s/p 1st dose | 1 (1, 2)                   | 1 (1, 4)             | 1 (1, 4)      |
| - New case s/p 2nd dose | 4 (2, 6)                   | 1 (1, 2)             | 2 (1, 6)      |
| - Relapse case s/p 1st dose | —                        | 1 (1, 2)             | 1 (1, 2)      |
| - Relapse case s/p 2nd dose | 3 (1, 4)                   | 1 (1, 1)             | 1 (1, 4)      |
| Laboratory on presentation |                      |                      |               |
| - Serum creatinine (mg/dl) | 1.6 (0.6, 2.5)             | 1.7 (0.7, 8.4)       | 1.7 (0.6, 8.4) |
| - Serum albumin (g/dl) | 3.1 (2.0, 4.6)             | 2.7 (0.7, 4.7)       | 2.9 (0.7, 4.7) |
| - Hematuria, n (%) | 9 (75)                      | 15 (58)              | 24 (63)       |
| - Urine protein (g/dl) | 6.5 (0.3, 19)              | 2.0 (0.3, 23.2)      | 2.2 (0.3, 23.2) |
| Treatment, n (%) |                        |                      |               |
| - Conservative management | 4 (31)                     | 9 (33)               | 13 (32)       |
| - Immunosuppression | 9 (69)                      | 18 (67)              | 27 (68)       |
| Outcome, n (%) |                        |                      |               |
| - Response | 8 (60)                      | 21 (91)              | 29 (88)       |
| - Not response | 2 (20)                     | 2 (9)                | 4 (12)        |

ANCA, antineutrophil cytoplasmic antibodies; GBM, glomerular basement membrane; GN, glomerulonephritis; NA, nonavailable; s/p, status post. 
*There were only 10 patients in our case series and 23 patients from the literatures with follow-up outcome.
It is noteworthy that many of the reported GNs in association with COVID-19 vaccination have also been noted with the COVID-19 infection itself. Podocytopenathy and collapsing glomerulopathy in addition to cases of anti-GBM disease and ANCA–associated vasculitis have all been reported.26–29 The pathophysiology of GNs in association with COVID-19 infection is complex and may include direct cytotoxicity to the podocytes in addition to immune dysregulation.27,28 It is possible that the immune response to COVID-19 vaccine mimics what happens in response to natural infection thus resulting in GN in susceptible patients.

Relapse of GN after vaccination when there is up-regulation of both cell-mediated (e.g., in cases of relapse of MCD)30 and Ab-mediated immunity (e.g., relapse of PLA2R-associated MN) is conceivable. But why do some patients develop new GN? One possibility is that they have underlying immune dysregulation which in turn makes them predisposed to development of GN. As noted previously, 38% of the individuals in our series had altered autoimmunity at baseline. Another possibility is that the disease perhaps was present before the vaccination, but patient was clinically asymptomatic. This may be the case in patients with new IgAN. We were able to reveal for the first time that in at least 1 patient with “new” diagnosis of IgAN, the IgA deposits were indeed present before the vaccination. This patient had a previous partial nephrectomy sample available from 7 years before, and review of this sample confirmed IgA deposits. This case provides proof that in some individuals, the vaccine only results in a “flare” of the already present disease rather than development of new IgA antibodies that are deposited in the kidney. Although we cannot confirm this finding in other cases of IgAN owing to lack of prevaccination kidney specimen, it is likely that cases with earlier onset of symptoms postvaccination have already had IgA deposits. IgAN was the most often noted GN post–COVID-19 vaccination both in our series and based on review of the literature. This finding might be explained by the fact that IgA comprises the major Ab response early after mRNA COVID-19 vaccination.31

The development of GN (e.g., IgAN and MCD) after vaccination is not new and has been reported in humans and animal models.32–34 It is likely that the mRNA vaccine results in a more potent immune response and therefore associated with a higher rate of GN compared with other types of vaccine (inactivated virus). It is important to also note that this unwanted immune activation occurs in only a very small percentage of vaccinated patients. The exact incidence is unknown as some cases may not have been reported in the literature or may not have been recognized. The
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rarity of GNs post–COVID-19 vaccine may be similar to the cases of myocarditis in association with the mRNA vaccines, and thus far, the Centers for Disease Control and Prevention endorses continuation of COVID-19 vaccination owing to benefits over risk profile.5

At this point in time, outcome of newly diagnosed and relapsed GNs post–COVID-19 vaccine seems favorable in patients with nephrotic syndrome and IgAN. Most IgAN cases who presented with gross hematuria spontaneously remitted without specific intervention. Approximately 69% of the patients in our case series developed AKI, but most of them developed AKI stage 1. Of the 10 patients with available follow-up data, 8 have responded to therapy (conservative and immunosuppression). One case of IgAN has had a progressive course. This patient, however, also had features of acute interstitial nephritis on his kidney biopsy results which may have contributed to progression of the disease. In contrast, patients with anti-GBM and ANCA–associated vasculitis particularly seem to have fewer desirable outcomes. One patient with atypical anti-GBM nephritis has had progressive disease after treatment with high-dose steroids and mycophenolate mofetil. His treatment has been changed to cyclophosphamide, and additional follow-up at this point is not available. None of the patient from our case series required dialysis. Nevertheless, there were 2 patients from the literature including anti-GBM and proteinase 3-ANCA vasculitis who did not respond to therapy and thus required dialysis initiation. Taken together, of 40 reported cases, only 2 patients (5%) have been reported to require dialysis. Longer term follow-up is needed to better understand the trajectory and kidney outcome of these patients.

Our case series has limitations. Even though it is the largest series reported thus far, the sample size is still limited. This is likely in part due to the fact that the incidence is low, but we cannot exclude the possibility that some cases may have been missed. Another limitation is lack of long-term data on these patients. Even though in short-term outcomes seem favorable we need longer term follow-up of these patients. Finally, we cannot prove with certainty that the vaccine resulted in development of new or relapse of the GN, but certainly the temporal association is compelling.

In summary, this case series in combination with cases published thus far in the literature provides data on 40 patients with new and relapsed GN post–mRNA COVID-19 vaccine. As mass vaccination efforts continue, and recognizing the overwhelming benefits of vaccination for individuals with chronic kidney disease who are at increased risk of devastating COVID-19 complications (including death, dialysis, long COVID-19 infection), nephrologists and other physicians should be aware of this association and remain vigilant when evaluating patients postvaccination especially when there are symptoms of kidney-related injury present.

DISCLOSURE

All the authors declared no competing interests.

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