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.

(no spikes or double contours). The modified activity score (International Society of Nephrology/Renal Pathology Society/National Institutes of Health [ISN/RPS/NIH]) was 0/24, and the chronicity score was 0/12.[5] Spontaneous remission did not occur in follow-up measurements, and as nephrotic proteinuria persisted for 7 weeks, we initiated immunosuppressive therapy with mycophenolate mofetil (1 g bid) and prednisolone (60 mg qd). As can be seen in Figure 2a, proteinuria declined initially, and the patient reported substantial improvement of her general well-being and the absence of foamy urine. Proteinuria increased again the following week, but with a tendency toward improvement of the absolute amount in the next measurements. ANA titers, which increased after vaccination, also declined after the start of therapy. Anti-DNA-antibody levels did not increase after the vaccination, and the slightly-below-normal C3c-levels increased (Figure 2b–d).

The patient had already developed an antibody response against the spike protein of SARS-CoV-2 (Figure 2); thus, we decided to postpone the second vaccination in light of declining incidence numbers. When to proceed with the second vaccination remains to be determined, as full remission of the proteinuria has not been achieved yet.

To our knowledge, our case report is the first to describe a biopsy-proven relapse of lupus nephritis class V and II. New-onset minimal change glomerulopathies[3,6] and other forms of glomerulonephritis (e.g., *de novo* IgAN,[2] relapse IgA nephropathy,[1] and even anti–glomerular basement membrane glomerulonephritis)[7] have been described as sequelae of mRNA COVID-19 vaccination. This case adds yet another piece of evidence that relapse in immune-mediated disease might be induced by COVID-19 mRNA vaccine. Although the mechanisms triggering these relapses are still elusive, stringent postvaccination surveillance for renal function, proteinuria, and serologic markers for immune disease is essential in this vulnerable patient population.

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Acute kidney injury with gross hematuria and IgA nephropathy after COVID-19 vaccination

To the editor: The mRNA coronavirus disease 2019 (COVID-19) vaccines induce an IgG response that prevents people from contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Interestingly, there are now at least 6 cases of gross hematuria reported in patients with a history of biopsy-proven IgA nephropathy (IgAN), involving both mRNA vaccines.[1–3] All of the previous patients were treated with supportive therapy with rapid resolution of hematuria and no acute kidney injury (AKI). It has been reported in preclinical trials that nasal shedding of SARS-CoV-2 still occurred after vaccination with both mRNA vaccines, suggesting a lack of a mucosal IgA response.[1,4] We also cared for 2 patients who had prior biopsy-proven IgAN, who developed gross hematuria after their second dose of the Pfizer vaccine, without a preceding COVID-19 infection. Table 1 outlines the clinical data. Our first patient presented 5 days after his second dose, with nonspecific myalgias, chills, headache, dysuria, and gross hematuria within 24 hours of initial symptoms. Previous IgAN flares in this patient were precipitated by upper respiratory infections and were limited to gross hematuria with no AKIs and no requirement for steroids in the past. His postvaccine workup was notable for AKI, with a serum creatinine level of 3.53 mg/dl and a urine protein–creatinine ratio of 3.0. He was empirically started on steroids with recovery to baseline renal function at 1 month and recovery to baseline proteinuria within 2 months. Our second patient developed gross hematuria within 24 hours of receiving his second dose. His hematuria resolved after 3 days with supportive therapy only. To our knowledge, we are the first to report an IgAN flare that has led to an AKI that resolved with steroid therapy. We agree that it is not clear how a nonmucosal immune challenge led to an IgAN

Table 1 | Patient characteristics, treatment, and symptoms

Patient characteristics	Patient 1	Patient 2
Year of IgAN diagnosis	2018	2020
Exacerbations since diagnosis	1. February 2019: UPCR 3.2 after URI; 2. February 2020: UPCR 2.6 after URI	None
Current treatment	Lisinopril and prednisone	Lisinopril
Baseline serum creatinine level, mg/dl	0.8	1.0
Peak serum creatinine level after COVID-19 vaccine, mg/dl	3.53	1.16
Last UPCR (gm/g) before COVID-19 vaccine	1.56	0.61
Last UACR (mg/g) before COVID-19 vaccine	NA	341
Gross hematuria	Yes	Yes
Other symptoms	Fevers, chills, body aches, dysuria	Body aches
UPCR (gm/g) after COVID-19 vaccine	4.97	0.92
UACR (mg/g) after COVID-19 vaccine	3160	320
Hematuria 5 days after COVID-19 vaccine	Present	Resolved

COVID-19, coronavirus disease 2019; IgAN, IgA nephropathy; NA, not applicable; UACR, urine albumin–creatinine ratio; UPCR, urine protein–creatinine ratio; URI, upper respiratory infection.

exacerbation; however, the delayed-type hypersensitivity reactions seen in our patients suggest a cell-mediated immune response, not an antibody response. We offer further evidence that patients with IgAN warrant close monitoring after receiving their second mRNA vaccine dose.

DISCLOSURE

The views expressed in this chapter are those of the authors and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or US government. The authors are military service members. This work was prepared as part of their official duties. Title 17 U.S.C. 105 provides that "Copyright protection under this title is not available for any work of the United States Government." Title 17 U.S.C. 101 defines a United States Government work as a work prepared by a military service member or employee of the United States Government as part of that person's official duties.

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Immune checkpoint inhibitor–associated electrolyte disorders: query of the Food and Drug Administration Adverse Event Reporting System

To the editor: Immune checkpoint inhibitor (ICI)–associated adverse events, such as hyponatremia and other electrolyte abnormalities, in patients receiving ICIs have not been well characterized.[1–4]

We performed a query of the Food and Drug Administration Adverse Event Reporting System (FAERS) database with a more detailed look at electrolyte disorders only (search terms: hyponatremia, hypernatremia, hypokalemia, hyperkalemia, hypercalcemia, hypocalcemia, hypophosphatemia, hypomagnesemia, acidosis, hyperphosphatemia, and renal tubular acidosis) from 2011 to 2021. The specific agents reviewed were atezolizumab, avelumab, durvalumab, ipilimumab, nivolumab, and pembrolizumab. Goodness-of-fit tests (χ^2 tests) were used to complete statistical analysis. Results for continuous variables are reported as mean ± SD. Statistical significance was determined to be a P value of <0.05.

A total of 2556 cases of electrolyte disorders were reported to the FAERS. The most commonly reported abnormality is hyponatremia (53.7%), followed by hypokalemia (18.71%), hypercalcemia (9.65%), hyperkalemia (5.56%), and hypocalcemia (4.68%). Hyperphosphatemia was the least reported abnormality (Table 1). In all 3 classes of the agents (cytotoxic T-lymphocyte–associated protein 4 [CTLA4] inhibitors, programmed cell death protein 1 [PD1], and programmed cell death ligand 1 [PD-L1] inhibitors), the trend remained similar. Among reported events, proportions of events in males were statistically more significant ($P < 0.01$) than in females in all 3 drug groups (Supplementary Tables S1 and S2). Nivolumab (n = 1130) and ipilimumab (n = 684) had the highest number of patients reported with electrolyte