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Letter

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LETTER TO THE EDITOR

Hematuria after COVID-19 vaccination: A case report

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Sir, – Due to the worldwide spreading of coronavirus disease 2019 (COVID-19), an unprecedented amount of resources were located in the development of vaccines and by the end of 2020. At least four of them (BNT162b2, Pfizer-BioNTech; mRNA-1273, Moderna; ChAdOx1 nCoV-19, Astra-Zeneca; Gam-COVID-Vac, Sputnik V) have been shown to be effective and safe [1, 2, 3, 4].

After vaccination started, many side effects have been reported, but only 2 cases of hematuria in patients with previous diagnosis of IgA nephropathy have been described [5]. Here, we present the first case of a 29-year-old woman with two episodes of de novo hematuria temporally coincident with each single dose of the BNT162b2 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine.

Our patient is a woman from Venezuela with a personal history of hypercholesterolemia without medical treatment, who developed a mild symptomatic COVID-19 infection without respiratory compromise in March 2020. There was no family history of renal disease. She works as a healthcare professional. Following Spanish National Recommendations, she received the first dose of the BNT162b2 vaccine on January 12, 2021, and reported fever and myalgia as side effects in the first 24 hours. Two days after this first dose, the patient developed macroscopic hematuria and presented to the Nephrology outpatient clinic (Figure 1A).

Complementary test revealed preserved renal function (serum creatinine 0.78 mg/dL and estimated glomerular filtration rate by CKD-EPI 103.06 mL/min/1.73m^2), with 5 – 10 red blood cells per high-power field, the majority being dysmorphic erythrocytes. Urine albumin-to-creatinine ratio (UCAR) was 58.2 mg/g. Immunological study showed serum immunoglobulin A (IgA) 536 mg/dL, with normal values of complement C3 and C4, antinuclear antibodies (ANA), and antineutrophil cytoplasmic antibodies (ANCA). Renal and urinary tract echography showed no structural alterations or signs of lithia-

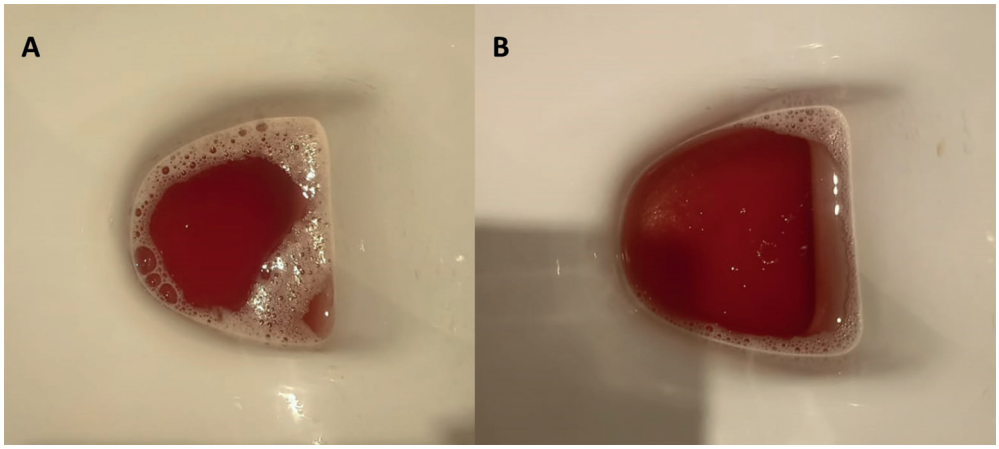

Figure 1. Photos taken by the patient during the first (A) and second (B) episode of hematuria after each single dose of the COVID-19 vaccine.

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citation

Table 1. Renal adverse events registered in the pivotal phase III COVID-19 vaccine trials [6, 7, 8, 9].

	BNT162b2 (Pfizer-BioNTech) N = 21,720	mRNA-1273 (Moderna) N = 15,185	ChAdOx1 nCoV-19 (Astra-Zeneca) N = 12,021	Gam-COVID-Vac (Sputnik V) N = 16,427
Acute kidney injury	0	1 (< 0.1%)	1 (< 0.1%)	0
Urethral calculi	0	0	0	0
Urinary calculus	0	0	1 (< 0.1%)	0
Nephrolithiasis	0	3 (< 0.1%)	0	0
Renal colic	0	0	2 (< 0.1%)	1 (< 0.1%)
Renal abscess	0	0	0	1 (< 0.1%)
Hematuria	0	0	0	0

sis. Urine culture and cytology were negative. Assuming the clinical diagnosis of IgA nephropathy, without risk of progression at that moment, no specific treatment was prescribed and kidney biopsy was not indicated. Hematuria disappeared spontaneously after 48 hours. Being asymptomatic, the patient received the second dose of the BNT162b2 vaccine 3 weeks later. As with the first dose, the patient developed fever and myalgia in the first 24 hours, and a new episode of hematuria, which also disappeared after 48 hours (Figure 1B). The patient has remained asymptomatic, and a new follow-up visit to our outpatient clinic was arranged for the following 3 months.

We describe a case of an isolated, transient hematuria in a healthy adult, with no personal or family history of kidney disease, after the administration of the first and second dose of the BNT162b2 vaccine. Both episodes were self-limited, and the patient has maintained preserved renal function.

Although we decided not to biopsy this patient, all diagnoses other than IgA nephropathy were reasonably ruled out. The patient denied moderate or intense physical activity, and no data of concomitant infections were noted. Physical examination and blood pressure were normal. Immunological study was performed in the context of dysmorphic hematuria, showing elevated titers of IgA, with normal levels of complement, ANA, and ANCA. In addition, no alterations or signs of nephrolithiasis were revealed in renal echography. The lack of family history of hematuria or kidney disease make diagnosis such as Alport syndrome or thin basement membrane nephropathy less likely. Unaltered levels of C3 exclude C3 glomerulopathy, and normal ANA and ANCA levels with preserved renal function and no systemic symptoms argue against the diagnosis of pauci-immune glomerulonephritis and lupus nephritis. Taking all these data together, IgA nephropathy was the most probable diagnosis option.

As part of the not fully understood pathogenesis of IgA nephropathy, it is believed that certain factors (such as viral or bacterial infections and environmental stimuli) could increase the serum level of poorly galactosylated IgA1 [6]. However, it is unknown how COVID-19 vaccine-driven immunity could enhance the production of defective IgA, and consequently in patients with an IgA nephropathy could produce direct mesangial injury.

In the published clinical trials, the only renal and urinary tract adverse events reported were acute kidney injury, urinary calculi, nephrolithiasis, renal colic, and renal abscess, and each one of them accounted for less than 0.1% of the studied population (Table 1) [1, 2, 3, 4]. However, hematuria was not reported as an adverse effect in any of the COVID-19 vaccine phase III clinical trials, probably because less than 1% of the included population had chronic kidney disease. Recently, two cases of hematuria in the context of a previous IgA nephropathy have been recently published, supporting our hypothesis [7].

In conclusion, the described case leads us to think that the immune response produced by the SARS-CoV-2 vaccine is capable of acting as a trigger to produce outbreaks of IgA nephropathy. This is of special interest not only in those patients who may have subclinical forms of the disease, but also in those with more severe forms of it. Until the scientific community can confirm our findings in clinical studies, we recommend closer follow-up of these patients after the administration COVID-19 vaccines.

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Conflict of interest

No conflict of interest.

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