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.

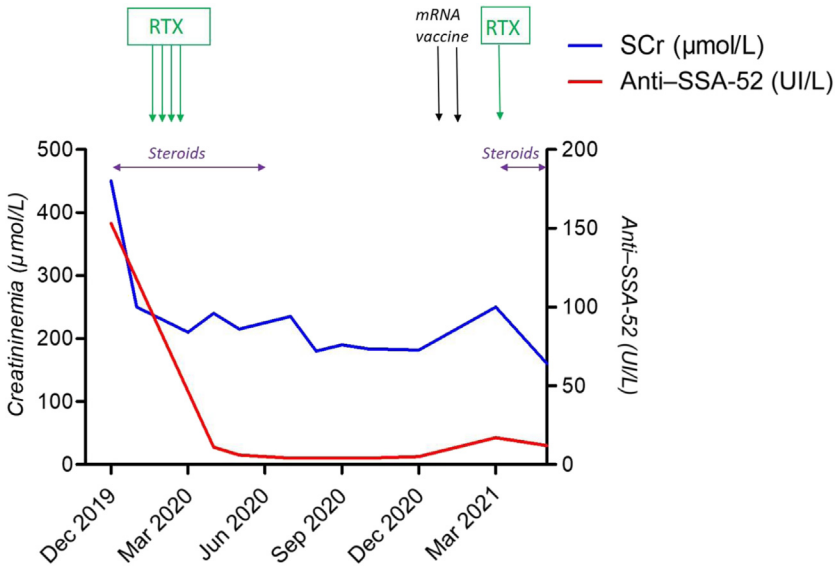

Figure 2| Evolution of sera creatininemia (SCr) and anti–SSA-52 antibodies, reflecting the activity of IgG4-related disease, from the diagnosis in December 2019 to the relapse in March 2021 following mRNA coronavirus disease 2019 (COVID-19) vaccine. RTX, rituximab.

population, physicians should be aware of the possibility of immune disease recurrence to provide close monitoring of these patients and fast treatment of relapses to avoid long-term consequences and progression to end-stage renal disease.

1. Kervella D, Jacquemont L, Chapelet-Debout A, et al. Minimal change disease relapse following SARS-CoV2 mRNA vaccine. *Kidney Int.* 2021;100:457–458.
2. Aydın MF, Yıldız A, Oruç A, et al. Relapse of primary membranous nephropathy after inactivated SARS-CoV-2 virus vaccination. *Kidney Int.* 2021;100:464–465.
3. Ebbo M, Grados A, Samson M, et al. Long-term efficacy and safety of rituximab in IgG4-related disease: data from a French nationwide study of thirty-three patients. *PLoS One.* 2017;12:e0183844.
4. Perugino CA, Stone JH. IgG4-related disease: an update on pathophysiology and implications for clinical care. *Nat Rev Rheumatol.* 2020;16:702–714.

Christophe Masset[1,2], Delphine Kervella[1,2], Christine Kandel-Aznar[3], Aurélie Fantou[2,4], Gilles Blancho[1,2] and Mohamed Hamidou[2,5]

[1]Institut de Transplantation Urologie Néphrologie, Centre Hospitalier Universitaire Nantes, Nantes, France; [2]Centre de Recherche en Transplantation et Immunologie UMR 1064, INSERM, Université de Nantes, Nantes, France; [3]Laboratoire d'Anatomie et Cytologie Pathologique, Centre Hospitalier Universitaire de Nantes, Nantes, France; [4]Laboratoire d'Immunologie, Centre Hospitalier Universitaire de Nantes, Nantes, France; and [5]Service de Médecine Interne, Centre Hospitalier Universitaire de Nantes, Nantes, France

Correspondence: *Christophe Masset, 30 Blvd Jean Monnet, 44093 Nantes Cedex 01, France. E-mail: christophe.masset@chu-nantes.fr*

Kidney International (2021) **100,** 465–466; https://doi.org/10.1016/j.kint.2021.06.002

Gross hematuria following SARS-CoV-2 vaccination in patients with IgA nephropathy

To the editor: After the publication of the 2 letters by Negrea and Rovin[1] and Rahim *et al.*,[2] we herein describe 3 additional patients with IgA nephropathy (IgAN) who developed gross hematuria after receiving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA-based vaccines. The clinical data of our cases are summarized in Table 1. In line with the 3 previously reported cases, patient 1 had normal kidney function. However, patients 2 and 3 were treated with kidney transplantation (KT) and hemodialysis, respectively. Notably, gross hematuria developed as early as after the first vaccine dose in patients 1 and 2. Additionally, gross hematuria in patient 1 relapsed after the second vaccine dose. Gross hematuria was sporadically accompanied by increased proteinuria, arthralgia, abdominal pain, and urticaria. Serum creatinine also transiently increased in patient 2. Symptoms spontaneously regressed in all the 3 cases. The apparent exacerbation of IgAN in patient 2 occurred in the absence of an anti–SARS-CoV-2 antibody response. Out of a total of 726 KT recipients, we examined the tolerability of 2 doses of the Moderna vaccine in 80 recipients with IgAN. No additional cases of gross hematuria were identified. Seventy patients had available data on anti–SARS-CoV-2 antibodies 1 month after the second dose, and positive serology was identified in 32 cases (45.7%). This finding is in accordance with our previous data.[3]

In summary, gross hematuria can occur even after the first vaccine dose and it can also affect—albeit rarely—KT

Table 1 | Patient demographics and clinical characteristics

Patient no.	Age, yr	Sex	Year of biopsy-proven IgAN diagnosis	Treatment	GFR (ml/min per 1.73 m^2) or renal treatment	Episodes of gross hematuria during the disease course	Persistent microscopic hematuria	Proteinuria in 2020, UPR, g/g	Vaccine name	Timing of gross hematuria occurrence after vaccination	Associated symptoms	Proteinuria after the first dose, g/g	GFR 1 mo after the second dose, ml/min per 1.73 m^2	Proteinuria 1 mo after the second dose	Anti-spike IgG antibody titers (AU/ml) measured 1 mo after the injection
1	22	M	2019 (IgA vasculitis)	Steroids for 6 mo followed by RAASi	89	No	Yes	0.20	mRNA-1273 (Moderna)	D2 and D25 after the first dose, D2 after the second dose	Arthralgia, transient proteinuria (3 g/g)	0.34	107	0.40	NA
2	41	F	2005	Tac, MPA, and steroids for KT	KT as of 2013	Yes	Yes	0	BNT162b2 (Pfizer)	D2 after the first dose (the patient refused the second dose)	Marked leukocytosis	0.47	57	0.41	14.9[a]
3	27	F	2020	Steroid for 1 mo followed by RAASi	HD since 1 yr	No	No	20	BNT162b2 (Pfizer)	D2 after the second dose	Abdominal pain, urticaria at D5, moderate pancytopenia	1.9	NA	1.2	>250[b]

AU, arbitrary unit; D, day; GFR, glomerular filtration rate; HD, hemodialysis; IgAN, IgA nephropathy; KT, kidney transplantation; MPA, mycophenolic acid; NA, not available; RAASi, renin-angiotensin-aldosterone system inhibitor; Tac, tacrolimus; UPR, urine protein-to-creatinine ratio.

[a]Serology assessment performed 1 mo after the first vaccine dose using the ARCHITECT IgG II Quant test (Abbott). Titers >50 AU/ml were considered positive (detection range, 6.8–80,000 AU/ml).

[b]Serology assessment performed 1 mo after the second vaccine dose using the Elecsys Anti-SARS-CoV-2 S (Roche). Titers >0.8 U/ml were considered positive (detection range, 0.8–250 U/ml).

recipients with IgAN. This event seems unrelated to the anti-SARS-CoV-2 antibody response. Patients with IgAN should be thoroughly followed up to shed more light on this potential adverse event.

1. Negrea L, Rovin BH. Gross hematuria following vaccination for severe acute respiratory syndrome coronavirus 2 in 2 patients with IgA nephropathy. *Kidney Int*. 2021;99:1487.
2. Rahim SEG, Lin JT, Wang JC. A case of gross hematuria and IgA nephropathy flare-up following SARS-CoV-2 vaccination. *Kidney Int*. 2021;100:238.
3. Benotmane I, Gautier-Vargas G, Cognard N, et al. Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine. *Kidney Int*. 2021;99:1498–1500.

Peggy Perrin[1,2,3], Xavier Bassand[4], Ilies Benotmane[1,2,3] and Nicolas Bouvier[5,6]

[1]Department of Nephrology and Transplantation, University Hospital, Strasbourg, France; [2]Fédération de Médecine Translationnelle (FMTS), Strasbourg, France; [3]INSERM U1109, LabEx TRANSPLANTEX Strasbourg, France; [4]Department of Nephrology, Hopital Pasteur, Colmar, France; [5]Department of Nephrology, Dialysis, Transplantation, University Hospital, Caen, France; and [6]Caen University, Caen, France

Correspondence: *Peggy Perrin, Néphrologie-Transplantation, Hôpitaux Universitaires de Strasbourg, 1 Place de l'Hopital, Strasbourg, Alsace 67091, France. E-mail: peggy.perrin@chru-strasbourg.fr*

Kidney International (2021) **100,** 466–468; https://doi.org/10.1016/j.kint.2021.05.022

Histologic correlates of gross hematuria following Moderna COVID-19 vaccine in patients with IgA nephropathy

To the editor: We read with interest the recent reports of gross hematuria occurring in 4 patients with IgA nephropathy shortly following the second dose of mRNA vaccine for coronavirus disease 2019 (COVID-19).[1–3] These include 2 cases following the Moderna vaccine[1] and 2 following the Pfizer BioNTech vaccine.[2,3] As only 1 of these patients had a postvaccination biopsy performed,[3] we report the biopsy findings in 2 additional patients who underwent their first kidney biopsy due to the development of gross hematuria shortly following the second dose of the Moderna vaccine for COVID-19.

A 50-year-old White woman with hypertension since age 18 years, obesity, and anti–phospholipid syndrome presented with gross hematuria 2 days after the second dose of the Moderna vaccine for COVID-19, accompanied by low-grade fever and generalized body aches. After the first dose, the patient had experienced only generalized weakness and decreased appetite for several days. Medications included amlodipine, furosemide, and olmesartan, with the more recent addition of warfarin and enoxaparin 3 months prior to presentation. There was no past history of gross hematuria. Laboratory evaluation revealed a serum creatinine of 1.7 mg/dl and a urine protein-creatinine ratio of 2 g/g (increased from baseline values of 1.3 mg/dl and 1.3 g/g, respectively, 7 months prior to presentation). Urinalysis demonstrated >50 red blood cells per high-power field (increased from baseline 10–20 red blood cells 7 months prior to presentation). Serologies included negative or normal anti-nuclear antibody, anti-neutrophil cytoplasmic autoantibody, hepatitis B surface antigen, hepatitis C virus antibody, PLA2R antibody, C3, and C4. The biopsy, performed 19 days after the onset of macrohematuria, demonstrated IgA nephropathy (Figure 1a and b). Among 12 glomeruli sampled, 3 were globally sclerotic and 1 contained a segmental scar. The remainder had mild diffuse mesangial hypercellularity, and 1 glomerulus displayed active segmental fibrinoid necrosis with mild leukocyte infiltration, rupture of glomerular basement membrane, and an overlying segmental cellular crescent. There was 30% tubulointerstitial scarring and moderate arterio- and arteriolosclerosis. Immunofluorescence revealed global granular mesangial staining for IgA (3+), C3 (1+), kappa (2-3+), and lambda (3+). The Oxford MEST-C score (where M is mesangial hypercellularity; E is endocapillary hypercellularity; S is segmental sclerosis; T is tubular atrophy and interstitial fibrosis >25%; C is active cellular or fibrocellular crescent) was M1E0S1T1C1. The gross hematuria resolved within 5 days.

A 19-year-old White man with a 6-month history of microhematuria presented with gross hematuria 2 days after receiving the second dose of the Moderna vaccine. The patient had no prior history of gross hematuria, was on no medications, and had no family history of kidney disease. Serum creatinine was 1.2 mg/dl (Chronic Kidney Disease Epidemiology Collaboration glomerular filtration rate, 87 ml/min per 1.73 m^2), and urinalysis revealed numerous red blood cells and no proteinuria. Kidney biopsy, performed 18 days later, demonstrated IgA nephropathy (Figure 1c and d). Among 25 glomeruli sampled, 1 was globally sclerotic. There was mild to moderate, diffuse and global, mesangial hypercellularity. Two glomeruli had segmental endocapillary hypercellularity including infiltrating monocytes and neutrophils. One glomerulus with an incipient segmental scar contained an overlying segmental fibrous crescent. Mild tubular atrophy and interstitial fibrosis involved approximately 10% of the cortex. Immunofluorescence revealed 1 to 2+ granular global mesangial staining for IgA, C3, kappa, and lambda. The Oxford MEST-C score was M1E1S1T0C0. The gross hematuria resolved within 2 days.

Our 2 patients were diagnosed, for the first time, with active IgA nephropathy, including focal endocapillary hypercellularity, fibrinoid necrosis, and crescents, following a second dose of the Moderna COVID-19 vaccine. Anticoagulation with warfarin in 1 case may have potentiated the development of gross hematuria. The history of prior microhematuria, as noted in other reported cases,[1–3] and the presence of focal glomerular and tubulointerstitial scarring in both biopsies support the