

Glomerulopathies after vaccination against COVID-19. Four cases with three different vaccines in Argentina

Glomerulopatías después de la vacunación frente a COVID-19. Cuatro casos con tres vacunas diferentes en Argentina

Dear Editor,

After reading some recent reports on the appearance or de novo recurrence of different glomerulopathies after the application of vaccines against COVID-19^{1–10} we would like to contribute our experience.

Four patients (P) previously asymptomatic began with asthenia (P1, P2), foamy urine (all) and edema (P2, P3) within 2 weeks after the first dose of the COVID-19 vaccine (P1: Sinopharm, P2: Oxford-AstraZeneca, P3 and P4: Gamaleya). All presented hypertension and microscopic hematuria. The first three patients also presented with acute kidney injury, nephrotic range proteinuria, hypoalbuminemia and

dyslipidemia. The P4 increased his proteinuria significantly. Renal biopsies performed showed two IgA nephropathy with crescent (Supplementary Fig. S1, A–F) and recurrence of proliferative glomerulonephritis (Supplementary Fig. S2, A and B). P4 did not undergo a new biopsy since she had a previous diagnosis in 2020 of minimal change disease (Supplementary Fig. S2, C and D) and it was interpreted as the beginning of a recurrence of her disease. All received corticosteroids and P1 and P2 also received cyclophosphamide. P1, P2 and P3 presented partial remission and P4 complete remission (Table 1).

Although it is very difficult to prove causation, at the time of this letter there are at least 40 reports of different types of glomerulopathies after receiving the COVID-19 vaccine from

Table 1 – Patient demographics and clinical characteristics.

	Patient 1	Patient 2	Patient 3	Patient 4
Clinical presentation				
Age, yr/gender	38/female	53/male	59/female	67/female
Medical history	Obesity	HBP, overweight	HBP, Obesity, MPG (2015, CR)	Sjögren, MCD (2020, CR)
Vaccine/manufacturer	BBIBP-CorV/Sinopharm	ChaAdOx1 nCoV-19/Oxford-AstraZeneca	Gam-COVID-Vac or Sputnik V/Gamaleya	Gam-COVID-Vac or Sputnik V/Gamaleya
Dose (1st/2nd)	1st	1st	1st	1st
Days between vaccine and onset	7	10	14	6
Symptoms or signs	Asthenia, foamy urine.	Asthenia, foamy urine, edemas.	Foamy urine, edemas.	Foamy urine.
BP, mm Hg	160/100	152/94	158/96	136/78
Laboratory results				
Serum creatinine, mg/dl	1.74	3.07	1.24	1.03
Urinary sediment	Hb+, protein+++	Hb+++, protein+++	Hb+, protein+++	Hb+
UPCR, g/g	9.37	4.43	5.53 (0.06 prior to vaccination)	0.44 (0.05 prior to vaccination)
Serum albumin, g/dl	2.8	2.9	2.5	–
Dyslipidemia	Yes	Yes	Yes	No
Immunological studies	ENA+	All negative	ANA homogeneous (1/160)	–

Table 1 – (Continued)

	Patient 1	Patient 2	Patient 3	Patient 4
Histopathology report				
Glomeruli (G)	8 G; Non globally sclerosed. Diffuse proliferative GN with endocapillary hypercellularity and one cellular crescent.	13 G; 5 globally sclerosed. Diffuse crescentic GN with 62% fibrocellular crescents. Mesangial and endocapillary hypercellularity.	16 G; 1 globally sclerosed. Focal proliferative GN	(Biopsy 2020) 4 G; All with preserved size, morphology and cellularity.
Tubules and interstitium	Mild IFTA. Mild interstitial inflammation with foamy cells.	Mild acute tubular injury. Moderate IFTA. Mild interstitial inflammation.	Non-significant IFTA. Mild interstitial inflammation.	Non-significant IFTA.
Vessels IF	Mild intimal fibrosis. Dominant glomerular IgA staining	Mild intimal fibrosis. Dominant glomerular IgA staining	Mild intimal fibrosis. No evidence of deposits	Mild intimal fibrosis. No evidence of deposits
Electron microscopy	–	–	Glomerular membranes moderately thickened. Podocytes with severe and diffuse pedicellar fusion.	Podocytes with severe and diffuse pedicellar fusion.
Treatment	CS+CP	CS+CP	CS	CS
Follow up	PR	PR	PR	CR

ANA, antinuclear antibodies; CP, cyclophosphamide; CR, complete remission; CS, corticosteroids; ENA, antibodies against extractable nuclear antigens; GN, glomerulonephritis; HBP, high blood pressure; Hb, hemoglobin; IFTA, interstitial fibrosis and tubular atrophy; MPG, mesangial proliferative glomerulonephritis; MCD, minimal change disease; PR, parcial remission; UPCR, urine protein-to-creatinine ratio.

different manufacturers (Pfizer, Moderna, AstraZeneca and Sinovac).^{1–10} To our knowledge, our reports would be the first related to the Sputnik V (Gamaleya) and BBIBP-CorV (Sinopharm) vaccines. Undoubtedly, the benefits of vaccines far outweigh the risks, but these findings emphasize the importance of surveillance in patients with previous glomerulonephritis and/or the appearance of foamy urine, edemas, hypertension or laboratory abnormalities.

Funding

This work has not received any type of funding.

Conflict of interest

The author declares that he has no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.nefro.2021.09.003](https://doi.org/10.1016/j.nefro.2021.09.003).

BIBLIOGRAFÍA

- Bombback AS, Kudose S, D'Agati VD. De novo and relapsing glomerular diseases after COVID-19 vaccination: what do we know so far? *Am J Kidney Dis.* 2021. S0272-6386(21)00697-1.
- Hanna C, Hernandez LPH, Bu L, et al. IgA nephropathy presenting as macroscopic hematuria in 2 pediatric patients after receiving the Pfizer COVID-19 vaccine. *Kidney Int.* 2021;100:705–6.
- Park K, Miyake S, Tai C, Tseng M, Andeen NK, Kung VL. Letter regarding: “a case of gross hematuria and IgA nephropathy flare-up following SARS-CoV-2 vaccination”. *Kidney Int Rep.* 2021;6:2246–7.
- Anupama YJ, Patel RG, Vankalakunti M. Nephrotic syndrome following ChAdOx1 nCoV-19 vaccine against SARS-CoV-2. *Kidney Int Rep.* 2021;6:2248.
- Gillion V, Jadoul M, Demoulin N, Aydin S, Devresse A. Granulomatous vasculitis after the AstraZeneca anti-SARS-CoV-2 vaccine. *Kidney Int.* 2021;100:706–7.
- Gueguen L, Loheac C, Saidani N, Khatchatourian L. Membranous nephropathy following anti-Covid-19 mRNA vaccination. *Kidney Int.* 2021, <http://dx.doi.org/10.1016/j.kint.2021.08.006>.

7. Villa M, Díaz-Crespo F, Pérez de José A, Verdalles U, Verde E, Almeida Ruiz F, et al. A case of ANCA-associated vasculitis after AZD1222 (Oxford-AstraZeneca) SARS-CoV-2 vaccination: Casuality or causality? *Kidney Int.* 2021;100:937-8, <http://dx.doi.org/10.1016/j.kint.2021.07.026>.
8. Plasse R, Nee R, Gao S, Olson S. Acute kidney injury with gross hematuria and IgA nephropathy after COVID-19 vaccination. *Kidney Int.* 2021, <http://dx.doi.org/10.1016/j.kint.2021.07.020>.
9. Tuschen K, Bräsen JH, Schmitz J, Vischedyk M, Weidemann A. Relapse of class V lupus nephritis after vaccination with COVID-19 mRNA vaccine. *Kidney Int.* 2021, <http://dx.doi.org/10.1016/j.kint.2021.07.019>.
10. Da Y, Goh GH, Khatri P. A case of membranous nephropathy following Pfizer-BioNTech mRNA vaccine against coronavirus 2019. *Kidney Int.* 2021, <http://dx.doi.org/10.1016/j.kint.2021.07.016>.

Pehuén Fernández^{a,b,*}, María Luján Alaye^a,
María Emilia García Chiple^{b,c}, Javier De Arteaga^{a,b,d},
Walter Douthat^{a,b,d}, Jorge De La Fuente^{a,b,d},
Carlos Chiurchiu^{a,b,d}

^a Servicio de nefrología, Hospital Privado Universitario de Córdoba, Córdoba, Argentina

^b Instituto Universitario de Ciencias Biomédicas de Córdoba (IUCBC), Córdoba, Argentina

^c Servicio de anatomía patológica, Hospital Privado Universitario de Córdoba, Córdoba, Argentina

^d Fundación Nefrológica de Córdoba, Córdoba, Argentina

* Corresponding author.

E-mail address: pehuenfernandez@hotmail.com

(P. Fernández).

0211-6995/© 2021 Sociedad Española de Nefrología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.nefro.2021.09.003>

Hematuria macroscópica en pacientes con nefropatía IgA tras vacuna para SARS-CoV-2

Hematuria in patients with IgA nephropathy after vaccine for SARS-CoV-2

Sr. Director:

La devastadora situación pandémica por COVID-19 ha llevado a la vacunación rápida y masiva de la población en un tiempo récord. Para ello se están utilizando tipos de vacuna, diferentes de las vacunas clásicas por virus inactivados o conjugados, que se basan en la administración de un nucleósido purificado del ARN mensajero del virus (Moderna[®], Pfizer[®]) o bien vector viral ADN del virus (AstraZeneca[®])¹.

Recientemente se han descrito varios casos²⁻⁶ de pacientes con nefropatía IgA que han desarrollado hematuria macroscópica tras la administración de vacunas para SARS-CoV-2. Presentamos 3 casos de pacientes con nefropatía IgA, vacunados con diferentes tipos de vacunas para SARS-CoV-2, en seguimiento en nuestro hospital, que han presentado esta clínica.

Caso 1: varón de 52 años en seguimiento en consulta desde 1995 por nefropatía IgA. Presenta función renal normal y proteinuria negativa. No había pasado la COVID-19. Acude a urgencias 48 h después de administración de la segunda dosis de vacuna Moderna[®] por brote de hematuria macroscópica. Totalmente asintomático. Tras 24 h de observación, el cuadro remite espontáneamente. Se confirma la presencia de brote de hematuria macroscópica por valoración urgente por servicio de análisis clínicos (tabla 1).

Caso 2: varón de 63 años, diagnosticado en diciembre del 2019 de nefropatía IgA con componente rápidamente progresivo y proliferación extracapilar. Inicia diálisis peritoneal en octubre del 2020. Presenta infección por COVID-19 en diciembre del 2020, con buena evolución. En este momento presenta brotes de hematuria macroscópica asintomática, que se autolimitan y desaparecen tras la resolución del cuadro. Se inicia vacunación con vacuna Moderna[®] entre febrero y marzo del 2021. A las 48 h de la primera dosis comienza con brote de hematuria macroscópica, que desaparece tras 48 h. No presenta complicaciones en el tratamiento de diálisis peritoneal. Tras la administración de la segunda dosis de vacuna vuelve a repetirse el episodio (tabla 1).

Caso 3: varón de 45 años, en seguimiento en consulta por probable púrpura de Schonleisch-Henoch y nefropatía IgA (episodios de coluria coincidente con cuadros de vías respiratorias altas, dermatosis purpúrica, etc.). No había pasado COVID-19. Se administra la primera dosis de vacunación con AstraZeneca[®] según esquema. A las 24 h desarrolla hematuria macroscópica, que se prolonga durante 36 h, hasta su total desaparición. Asintomático en todo momento. Se repite dicha clínica tras la administración de la segunda dosis de vacuna. No presentó dermatosis purpúrica ni otra clínica (tabla 1).