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### ARTICLE IN PRESS

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#### Letter to the Editor

# 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<sup>1–10</sup> 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 different manufacturers (Pfizer, Moderna, AstraZeneca and Sinovac). <sup>1–10</sup> 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.

|                                | 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<br>(2015, CR) | Sjögren, MCD (2020,<br>CR) |
| Vac-                           | BBIBP-                 | ChaAdOx1                       | Gam-COVID-Vac or                | Gam-COVID-Vac or           |
| cine/manufacturer              | CorV/Sinopharm         | nCoV-19/Oxford-<br>AstraZeneca | Sputnik V/Gamaleya              | 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                     |

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|                       | Patient 1                            | Patient 2                               | Patient 3                                 | Patient 4            |
|-----------------------|--------------------------------------|---|---|----------------------|
| Laboratory results    |                                      |   |   |                      |
| Serum                 | 1.74                                 | 3.07                                    | 1.24                                      | 1.03                 |
| creatinine,           |                                      |   |   |                      |
| mg/dl                 |                                      |   |   |                      |
| Urinary               | Hb+, protein+++                      | Hb+++, protein+++                       | Hb+, protein+++                           | Hb+                  |
| sediment              |                                      | · ·                                     | · •                                       |                      |
| UPCR, g/g             | 9.37                                 | 4.43                                    | 5.53 (0.06 prior to                       | 0.44 (0.05 prior to  |
|                       |                                      |   | vaccination)                              | vaccination)         |
| Serum                 | 2.8                                  | 2.9                                     | 2.5                                       | _                    |
| albumin, g/dl         |                                      |   |   |                      |
| Dyslipidemia          | Yes                                  | Yes                                     | Yes                                       | No                   |
| Immunological         | ENA+                                 | All negative                            | ANA homogeneous                           | -                    |
| studies               |                                      | _                                       | (1/160)                                   |                      |
| Histopathology report |                                      |   |   |                      |
| Glomeruli (G)         | 8 G; Non globally                    | 13 G; 5 globally                        | 16 G; 1 globally                          | (Biopsy 2020) 4 G; A |
| Giomerum (G)          | sclerosed. Diffuse                   | sclerosed. Diffuse                      | sclerosed. Focal                          | with preserved size  |
|                       | proliferative GN with                | crescentic GN with                      | proliferative GN                          | morphology and       |
|                       | *                                    | 62% fibrocellular                       | promerative GN                            | cellularity.         |
|                       | endocapillary                        | crescents. Mesangial                    |   | centiarity.          |
|                       | hypercellularity and<br>one cellular | 9                                       |   |                      |
|                       | crescent.                            | and endocapillary                       |   |                      |
| m.ll                  | crescent.<br>Mild IFTA. Mild         | hypercellularity.<br>Mild acute tubular | NI::E                                     | NI::-                |
| Tubules and           |                                      |   | Non-significant                           | Non-significant      |
| interstitium          | interstitial                         | injury. Moderate                        | IFTA. Mild                                | IFTA.                |
|                       | inflammation with                    | IFTA. Mild                              | interstitial                              |                      |
|                       | foamy cells.                         | interstitial                            | inflammation.                             |                      |
| ** 1                  | 36711 161                            | inflammation.                           | N. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. | 26711 161            |
| Vessels               | Mild intimal fibrosis.               | Mild intimal fibrosis.                  | Mild intimal fibrosis.                    | Mild intimal fibrosi |
| IF                    | Dominant                             | Dominant                                | No evidence of                            | No evidence of       |
|                       | glomerular IgA                       | glomerular IgA                          | deposits                                  | deposits             |
| T1 .                  | staining                             | staining                                | al l                                      | D 1 . '.1            |
| Electron              | -                                    | -                                       | Glomerular                                | Podocytes with       |
| microscopy            |                                      |   | membranes                                 | severe and diffuse   |
|                       |                                      |   | moderately                                | pedicellar fusion.   |
|                       |                                      |   | thickened.                                |                      |
|                       |                                      |   | Podocytes with                            |                      |
|                       |                                      |   | severe and diffuse                        |                      |
|                       | 60.00                                | 00.00                                   | 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.

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#### **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.nefroe.2021.09.007..

#### REFERENCES

- Bomback 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.
- 3. 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 SARScoV-2. Kidney Int Rep. 2021;6:2248.

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- 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.
- 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.
- 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.
- 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.

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