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Letter to the Editor

Epidemiological, clinical and prognostic issues in SARS-CoV-2 infection or vaccination-related glomerular disease: Our single-center experience

Epidemiología, comportamiento clínico y pronóstico de la patología glomerular asociada a infección ó vacunación del SARS-CoV-2: nuestra experiencia

Dear Editor,

According to reports no.° 29 of the S.E.N. (Sociedad Española de Nefrología [Spanish Nephrology Association]) COVID-19 Registry (updated in January 2022) and no.° 30 (updated April 2022), between 20 and 23% of the cases recorded with acute kidney failure during the COVID-19 pandemic were due to glomerular diseases. In relation to SARS-CoV-2 infection, there are reported cases of glomerular pathology (mainly minimal change disease, focal segmental glomerulosclerosis (collapsing variant), IgA nephropathy and renal ANCA vasculitis).[1–7]

Our main objective was to analyse our incidence of *de novo* glomerular pathology in the pre-pandemic period (from January 2018 to March 2020) and the pandemic period (between March 2020 to April 2022), comparing the same patterns of glomerular injury with patients without suspected association with infection or vaccination.

We conducted an observational, retrospective and single-centre study collecting demographic, clinical-epidemiological and histological variables. The majority clinical presentation of our pandemic cases was a nephritic syndrome, and the majority histological pattern was glomerulonephritis with extra-capillary proliferation (RPGN), with a total of 4 cases: 2 of them pauci-immune (one ANCA negative and one p-ANCA anti-MPO+) and the other 2 with immune complex deposition (both p-ANCA anti-MPO+). We had 2 cases of membranous nephropathy (one PLA2R+ and the other PLA2R and anti-thrombospondin, one anti-GBM glomerulonephritis, one C3 glomerulopathy with extra-capillary proliferation, and one focal segmental glomerulosclerosis in early stages. Strikingly, we did not have any cases of IgA nephropathy or minimal change disease during this period, despite what has been described in all the case series and population studies published to date.[8,9] As a control group, we included a total of 34 patients (including cases) who presented the same pattern of glomerular injury, although without apparent association (at least clearly chronological) to either the viral infection or their vaccine immunisation. There were a total of 34 patients (24 men and 10 women). The average age of the cases was 70 years, and that of the controls was 52 years. The group of cases had worse glomerular filtration at diagnosis, and from a histopathological point of view, after adjusting the cases and controls by age (between those over and under 60 years), the percentage of chronic lesions in the kidney biopsy was significantly higher in cases. Furthermore, comparing the glomerular pathology diagnosed during the pandemic with that diagnosed during the pre-pandemic period (before March 2020), the only statistically significant result was that the percentage of glomerulosclerosis was higher in the pandemic period compared to the pre-pandemic, most likely facilitated by the older average age of the cases, among other reasons.

Of the 9 cases, 88.9% had received immunisation with messenger RNA vaccines (66% with Pfizer and 22% with Moderna) and 11.1% with adenoviral vector vaccines. Of all cases, 77.8% had received 1 or 2 doses of vaccine, while 22.2% were not vaccinated due to a recent primary infection with SARS-CoV-2. The interval of days between the trigger (primoinfection or vaccination) and the diagnosis of glomerulopathy was approximately 60 days. The average estimated glomerular filtration rate (eGFR) was 30 ml/min (with an average of 18% glomerulosclerosis and 25% interstitial fibrosis/tubular atrophy), the mean proteinuria was 6 g/24 h, 11.1% of the patients pre-

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sented associated acute tubular-interstitial nephritis, 22.2% presented associated acute tubular necrosis, 22.2% required initiation of renal replacement treatment, and the only patient who required it at the time of diagnosis died the following month from an opportunistic infection.

The group of cases suspiciously associated with infection was older than that suspiciously associated with immunisation; furthermore, the former were not vaccinated (due to primary infection). As a histological curiosity, the intensity of C3 in the immunofluorescence was significantly higher in those cases associated with infection than in the cases associated with vaccine immunisation, probably due to greater complement activation by the alternative pathway.

Finally, between the pre-pandemic period compared to the pandemic, the incidence of anti-GBM disease, RPGN with C3 deposits, RPGN with immune complex deposits, focal and segmental glomerulonephritis and membranous glomerulonephritis increased, with a higher relative risk (RR) during the pandemic. However, this did not reach statistical significance, probably due to the small size of our sample.

In conclusion, in our environment, infection or vaccine immunisation against SARS-CoV-2 was only associated with a greater risk of developing RPGN with immune complex deposition when considering the incidence of cases versus controls during the entire study period. (2018–2022), however they did not reach statistical significance (RR: 3.07; CI 95%: 0.27–33.54) due to the small sample size.

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Conflicts of interest

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