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Letter to the Editor

LETTER TO THE EDITOR

Glomerular endothelial injury following vaccination for SARS-CoV-2

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Several cases of immunoglobulin A (IgA) nephropathy (IgAN) that developed gross haematuria following vaccination for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been reported [1–3]. In them, the vaccination was presumed to have triggered IgA1 response and exacerbated glomerulonephritis (GN). However, injected intramuscularly, the vaccines unlikely trigger this mucosal immune system response [4]. We report a case of crescentic GN where renal histological findings suggested that vaccination-induced potent immune cell responses caused the exacerbation.

A 65-year-old female with no known past medical history developed gross haematuria, which was preceded by fever and myalgia, the next day after the second administration of the Pfizer-BioNTech SARS-CoV-2 vaccine. While the symptoms resolved 2 days later, urinalysis showed proteinuria of 0.93 g/g of creatinine (g/gCr) and haematuria of more than 100 red blood cells per high-power field (RBC/HPF). Serum chemistry showed creatinine concentration (sCr) 1.38 mg/dL, IgA 279 mg/dL, IgG 1412 mg/dL, IgM 103 mg/dL, C3 99 mg/dL, C4 39 mg/dL and CH50 53.2 U/L.

A renal needle biopsy was performed 5 days after the vaccination. Light microscopic examination of the biopsy samples detected a cellular glomerular crescent in 1 glomerulus among the 23 glomeruli observed (Supplementary data, Figure S1A) and diffuse mesangial matrix expansion with mild focal increase in mesangial cellularity (Supplementary data, Figure S1B). Immunofluorescence examination revealed mesangial staining of IgG, IgA, IgM and C3 (Supplementary data, Figure S1C). Further examination by transmission electron microscopy revealed diffuse subendothelial widening and podocyte foot process effacement but no dense deposits on glomerular capillaries (Figure 1).

Based on the histological findings, oral prednisolone therapy was started with a dose of 0.8 mg/kg. Two weeks after the start of the therapy, her proteinuria, haematuria and sCr decreased to 0.29 g/gCr, 30–49 RBC/HPF and 1.01 mg/dL, respectively. Thereafter, the dose of prednisolone could be reduced without exacerbation of the GN.

Having had mesangial matrix expansion and IgA staining, the case would have been assumed to have latent IgAN. However, the absence of electron-dense deposits on glomerular capillaries at the time of the renal biopsy (5 days after the vaccination) suggests that IgAN would not have been responsible for the crescent formation; glomerular capillary deposition could be observed until 4–10 days after the induction of the GN in the experimental antibody-mediated crescentic GN [5]. Since nucleoside-modified mRNA vaccines would induce potent immune cell responses [6], the immune cell responses rather than the IgA1 response would have caused the crescent formation. Releasing several cytokines, the responses would have caused vascular endothelial injury, which would present diffuse subendothelial widening and crescent formation.

In the reported cases of IgAN exacerbation following SARS-CoV-2 vaccination, the vaccination was presumed to have triggered the IgA1 response [1–3]. However, in them, renal histology was not examined within 10 days after the vaccination. Hence, whether the IgA1 response participated in the exacerbation was not clarified and the vaccination-induced immune cell responses might have caused the exacerbation. To clarify the cause of exacerbation following SARS-CoV-2 vaccination, an early-phase renal histological examination (at least <10 days and preferably <4 days after the vaccination) is necessary [5]. If glomerular capillary deposition were not observed,

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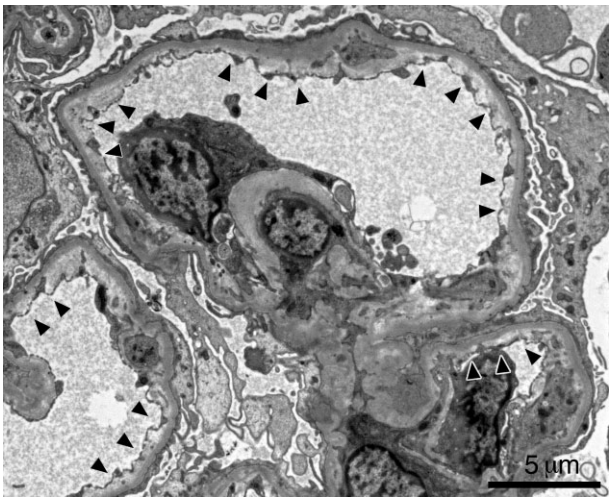

FIGURE 1: Electron microscopy findings of renal biopsy. Subendothelial widening with podocyte foot process effacement (arrow heads) but no glomerular capillary deposition.

the glomerular endothelial injury by the vaccination-induced potent immune cell responses rather than the IgA1 response would be the primary cause of exacerbation.

PATIENT CONSENT

The patient gave informed consent to publish her case.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

CONFLICT OF INTEREST STATEMENT

The authors declare that no conflict of interest exists.

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