COVID-19 Vaccination in Patients With Membranous Nephropathy

To the Editor: Although the benefit of COVID-19 vaccination is evident, many patients and caregivers might question the safety of COVID-19 vaccines in view of case reports of relapsing disease after vaccination.[1–4] A balanced discussion is difficult owing to lack of data. We evaluated the frequency of patient-reported proteinuria relapses after COVID-19 vaccination in patients with membranous nephropathy. Between October 2021 and December 2021, we contacted 245 patients with membranous nephropathy, who had visited our outpatient clinic for treatment advice between 2015 and 2020 (Supplementary Figure S1: flowchart). We questioned patients, specifically focusing on the period up to 3 months after first COVID-19 vaccination (see Supplementary Appendix for questionnaire details). Confirmatory clinical details were obtained from patients who reported worsening proteinuria. Our study includes 210 patients who consented and had received COVID-19 vaccination. Clinical characteristics are provided in Table 1. Eleven patients reported increase in proteinuria or edema. We confirmed disease relapse in 6 patients, and 5 patients reported worsening proteinuria. All patients have received renewed immunosuppressive therapy, with remarkable, often very good response in all evaluable patients (1–4 months) (definitions in Supplementary Methods). Our data suggests that the risk of COVID-19 vaccination to patients with membranous nephropathy is low,

Table 1. Treatment and follow-up of patients who reported increased proteinuria or edema after COVID-19 vaccination

										Clinical characteristics at worsening (before)[a]						
Case	Age	Sex	COVID-19 infected	Vaccine	IS during vaccination	Type of IS	Onset after which dose	Onset time (wks)	Presenting symptoms	aPLA2R (ru/l)	Urine protein (g/24h or PCR g/10 mmol)	SCr (μmol/l)	Salb (g/l)	Treatment	Outcome	FU[b] (mo)
Relapses																
1	80	M	no	mRNA (Pfizer)	no	NA	Second	4	Edema	916 (neg)	5.0 (0.3)	117 (106)	26 (missing)	RTX	NR	8 I 4
2	60	M	no	mRNA (Pfizer)	yes	Tacrolimus	Second	6	Edema, dry mouth, skin rash	27 (neg)	5.0 (0.3)	170 (123)	17 (35)	RTX + CyC + prednisone	R	7 I 3
3	77	F	no	mRNA (Pfizer)	no	NA	First	4	Edema	83 (neg)	PCR: 12.5 (0.1)	62 (67)	22 (40)	Tacrolimus	R	5 I 2
4	78	M	no	mRNA (Pfizer)	no	NA	Second	1	Edema, hypertension	Not PLA2R-related	PCR: 4.9 (1.5)	165 (140)	34 (41)	Prednisone	R	9 I 1
5	48	M	no	mRNA (Pfizer)	no	NA	Second	3	Edema	204 (neg)	PCR: 1.7 (0.02)	125 (122)	31 (40)	Conservative[3]	NR[c]	9 I 0
6	56	M	yes	mRNA (Pfizer)	no	NA	First	2	Edema, fatigue	30 (10)	3.4 (1.3)	130 (135)	32 (39)	Conservative[4]	NR[d]	8 I 0
Worsening of nephrotic syndrome																
7	84	M	yes	mRNA (Pfizer)	yes	Tacrolimus + prednisone	Second	10	Edema and dyspnea d'effort	pos (neg)	3.0 (2.0)	137 (131)	33 (38)	Tacrolimus + prednisone -> RTX	R	9 I 4
8	39	M	no	mRNA (Pfizer)	no	NA	Second	4	Fatigue	40 (20)	PCR: 3.7 (6.0)	122 (110)	18 (22)	RTX + CyC + prednisone	R	8 I 2
9	75	M	no	mRNA (Pfizer)	no	NA	Second	2	Edema, fatigue	90 (neg)	8.0 (4.5)	78 (72)	21 (29)	RTX + CyC + prednisone	Unknown	2 I NA
10	48	M	no	mRNA (Pfizer)	yes	RTX + tacrolimus	First	2	Edema	155 (14)	Missing (2.22)	111 (82)	25 (29)	RTX + CyC + prednisone	R	5 I 3
11	58	M	yes	mRNA (Pfizer)	no	NA	Second	3	Edema	22 (10)	8.0 (1.7)	90 (89)	24 (25)	Tacrolimus	R	7 I 2

aPLA2R: antiphospholipase A2 receptor antibodies, ELISA titer if available; CyC, cyclophosphamide; ELISA, enzyme-linked immunosorbant assay; F, female; FU, follow-up; IFT, immunofluorescence test; IS, Immunosuppressants; M, male; MN, membranous nephropathy; NA, not available; neg, negative; NR, no response; PCR, protein-creatinine ratio; Pos, positive; R, response; RTX, rituximab; Salb, serum albumin; SCr, serum creatinine.
[a]Info between brackets describes the last available laboratory data before vaccination.
[b]FU is divided into time from first vaccination (left) and FU from the start of immunosuppressive treatment (right).
[c]Initially moderate proteinuria however with immunologic relapse, after 6 months of conservative therapy there was a clinical relapse for which immunosuppressive therapy with RTX + CyC + prednisone was started.
[d]Initially moderate proteinuria however with immunologic relapse, after 7 months of conservative therapy there was a clinical relapse for which immunosuppressive therapy with RTX was started.
In case of IFT: pos or neg result is mentioned.

with only 5% of patients reporting increase in proteinuria. Notably, relapse rate without vaccination within a 3-month period is expected to be an average of 2% in our center. This study has limitations such that conclusions are based on patient-reported outcome measures.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Figure S1. Flowchart of patients' inclusion, incidence of relapses or worsening of proteinuria after COVID-19 vaccination.

Supplementary Appendix: Questionnaire COVID-19 infection and vaccination.

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