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Letter to the Editor

Immune mediated events timely associated with COVID-19 vaccine. A comment on article by Badier, et al.: "IgA vasculitis in adult patients following vaccination by ChadOx1 nCoV-19"

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Dear Editor,

We read the article by Badier et al. entitled "IgA vasculitis in adult patients following vaccination by ChadOx1 nCoV-19", published in Autoimmunity Reviews with interest. (1) We share the author's view that the COVID-19 vaccine could be the trigger of IgA vasculitis in the reported case. At our secondary/tertiary rheumatology centre, we have been meticulously recording and following patients with systemic vasculitis for a more than a decade, and we recently reported 8 cases of systemic vasculitis temporally related to COVID-19 immunization. (2) Vasculitis in our cohort followed 7 to 20 days after vaccination. Remarkably, in our experience, not only small vessel vasculitis, but also cases of large vessel vasculitis were documented, the latter being as frequent as the former. Lately, we also treated another patient presenting 3 weeks after receiving the Pfizer-BioNTech vaccine with histologically proven skin limited IgA vasculitis that rapidly remitted after a short systemic glucocorticoid therapy.

Furthermore, we have been tracking cases of other autoimmune/autoinflammatory events developing in close association to vaccination against COVID-19. By 31 August 2021, 361,495 people in our region received at least one dose of the four different COVID-19 vaccines available in Slovenia (Pfizer-BioNTech and Moderna, Oxford/AstraZeneca and Jannsen/Johnson&Johnson). (3) During the same observation period, we documented 19 additional autoimmune/autoinflammatory events temporally related with COVID-19 vaccination (Table 1). Rheumatic polymyalgia was the most frequent manifestation followed by skin panniculitis and neuromuscular disorders. Interestingly, in 2 patients with adult-onset Still's disease like picture, an additional potential trigger was documented: the first patient received immunization against tick-born encephalitis 14 days prior to receiving the COVID-19 vaccine, and the second patient had concomitant Epstein Barr virus infection. Furthermore, 2 patients recovered from COVID-19 infection 6 months prior to vaccination, and 3/19 patients had a history of a long standing rheumatic disease that was well controlled at the time of vaccination. Autoimmune/autoinflammatory events developed with an average delay of 17 days after either partial (i.e. first dose) or full vaccination in 7 and in 12 cases, respectively. The majority of patients were treated with a systemic glucocorticoid, while 1 patient with focal necrotizing panniculitis needed surgical therapy.

Vaccination may induce de novo autoimmune diseases, particularly in genetically predisposed individuals. (4) Reports of vasculitis (most commonly cutaneous vasculitis and IgA vasculitis) following vaccination (most frequently the influenza vaccine) have been documented. (5,6)

Regarding pathogenic mechanisms, molecular mimicry, hyperactivation/bystander activation of the immune system, loss of immune tolerance, neoantigen formation and antibody triggering have all been hypothesized. Though the pathogenic mechanisms of COVID-19-associated vasculitis have not been elucidated yet, these mechanisms might also play a role in COVID-19 vaccine-associated vasculitis or other autoimmune phenomena.

In conclusion, our experience shows that COVID-19 vaccines should be considered as a risk factor for inducing not only vasculitis but also other systemic autoimmune and autoinflammatory phenomena, and that the relationship between vaccination and autoimmunity should be further investigated.

Ethics approval

The study was approved by the Slovenian National Medical Ethics Committee, Approval Number 0120-554/2020/3.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Table 1
Rheumatic manifestations temporally associated with COVID-19 vaccination.

Patient No.	Age interval	Prior rheumatic disease	History of COVID-19	Vaccine/dose(s)	Interval (days)	Clinical diagnosis	Treatment
1	60s	No	No	AZ/1	21	Skin panniculitis	GC
2	60s	No	No	PFIZ/1	11	Skin panniculitis	GC + LMWH
3	80s	No	No	PFIZ/2	30	Necrotic focal panniculitis	Surgical therapy
4	60s	No	No	PFIZ/2	6	Fever, arthritis, rash	GC
5	50s	Psoriatic arthritis (6 years)	No	AZ/2	10	Papular erythema and urticarial lesions	GC
6	30s	Raynaud's phenomenon; small vessel thromboses (16 years ago)	No	AZ/1	3	Haematomas, suffusions	GC + LMWH
7	60s	No	No	AZ/1	24	Pleuritis, pericarditis	GC
8	60s	No	No	AZ/1+ TBE	10	AOSD - LIKE	GC + MTX
9	40s	No	Yes*	JJ/1 and concomitant EBV infection	23	AOSD - LIKE	GC
10	70s	No	No	PFIZ/2	5	PMR	GC
11	50s	No	No	JJ/1	5	PMR	GC
12	80s	No	No	PFIZ/2	10	PMR	GC
13	60s	No	No	PFIZ/1	14	PMR	GC
14	70s	No	No	MOD/2	7	PMR	GC + MTX + TCZ
15	20s	No	No	AZ/2	15	Ischemic infarct of part of right kidney	Oral anticoagulation
16	60s	No	Yes*	PFIZ/2	45	Critical ischemia of right hand fingers	GC + LMWH+ Vasodilatators
17	60s	Granulomatosis with polyangiitis (>20 years)	No	PFIZ/2	87	Asymmetric polyradiculoneuritis	GC
18	90s	No	No	PFIZ/2	1	Paraspinal muscle myopathy	0
19	30s	No	No	AZ/1	1	Myositis	GC

Legend: F female; M male; *in Januar 2021; AOSD Adult Still's disease; PMR rheumatic polymyalgia; AZ Oxford/AstraZeneca; JJ Jannsen/Johnson&Johnson; PFIZ Pfizer-BioNTech; MOD Moderna; TBE tick-born encephalitis; EBV Epstein Barr virus; GC glucocorticoids; LMWH low molecular weight heparin; MTX methotrexate; TCZ tocilizumab.

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Alojzija Hočevar[a,b,*], Matija Tomšič[a,b]
[a] *Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia*
[b] *Internal Medicine, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia*

[*] Corresponding author at: University Medical Centre Ljubljana, Department of Rheumatology, Vodnikova cesta 62, 1000 Ljubljana, Slovenia.
E-mail address: alojzija.hocevar@kclj.si (A. Hočevar).

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