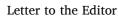
Autoimmunity Reviews 20 (2021) 102951

Contents lists available at ScienceDirect

Autoimmunity Reviews

journal homepage: www.elsevier.com/locate/autrev



IgA vasculitis in adult patient following vaccination by ChadOx1 nCoV-19

Dear editor,

We read with great interest the article by Rasmussen et al. [1] identifying signals of drugs associated with Immunoglobulin A (IgA) vasculitis (IgAV), a rare immune complex small-vessel vasculitis [2–4]. The authors used data from the French pharmacovigilance database and from Vigibase®, the WHO global individual case safety reports database [5], with descriptive and disproportionality approaches. In this study, the most common drug class associated with IgAV was vaccines. All types of vaccines were concerned (live attenuated vaccines, inactivated vaccines and subunit vaccines) [1].

We report here a case of IgAV following vaccination with the ChadOx1 nCoV-19 vaccine, the Oxford-AstraZeneca vaccine against the Serious Acute Respiratory Syndrome - Coronavirus 2 (SARS-CoV-2), the agent of the coronavirus disease 2019 (COVID-19).

A 72 year-old-man presented with vascular purpura. He did not experience any infection the weeks before. He had a history of hypertension, myocardial infarction, type 2 diabetes mellitus, obesity (body mass index 33.4 kg/m²) and asthma. He was exposed for years to irbesartan, hydrochlorothiazide, amiloride, bisoprolol, lercanidipine, rilmenidine, simvastatin, acetylsalicylate acid, metformin, rabeprazole and an inhaled combination of formoterol and budesonide. On 6 March 2021, he received a first dose of ChadOx1 nCoV-19 vaccine. Fifteen days later, he complained of inflammatory arthralgia of the ankles, knees and shoulders and presented with vascular purpura of the lower limbs. Physical examination revealed no other abnormality. Laboratory investigations revealed inflammatory syndrome (C - reactive protein, 55 mg/L), normal blood count (including platelet count, 222×10^9 /L), normal renal function, absence of proteinuria and of hematuria. A reverse transcription-polymerase chain reaction test for SARS-CoV-2 (nasopharyngeal swab) was negative as well as serologic testing for Human immunodeficiency virus 1, hepatitis B and C. Blood cultures were sterile. Testing for antinuclear antibody, antineutrophil cytoplasmic antibody, cryoglubulinemia and cryofibrinogenemia were nonsignificant or negative. Serum electrophoresis, immunoglobulin class dosage as well as serum complement (total complement activity by CH50, C3 and C4 fractions) were normal. Skin biopsy showed extravagated red blood cells in the superficial dermis, perivascular infiltrates made of neutrophils and rare eosinophils with the presence of leukocytoclasia and images of small capillary vasculitis. Immunofluorescence revealed IgA deposits in the vessel wall. The diagnosis of IgAV with skin and articular involvement was made. The patient was treated by corticosteroids (prednisone, 20 mg/day) leading to a favorable outcome.

The exact cause of IgAV remains unknown. Several factors have been described, like bacterial and viral infections [6], malignancies and drugs, mostly vaccines as reported by Rasmussen et al. [1]. In their study, the median time from vaccination to IgAV onset was 11 days (interquartile range: 6–30 days) [1]. Our patient had no possible other

https://doi.org/10.1016/j.autrev.2021.102951 Received 14 May 2021; Accepted 20 May 2021 Available online 9 September 2021 1568-9972/© 2021 Elsevier B.V. All rights reserved. cause of IgAV than the ChadOx1 nCoV-19 vaccine. The second dose of the ChadOx1 nCoV-19 vaccine was not performed. The WHO-UMC causality assessment score was "probable/likely" [7].

As infections are the most common IgAV triggering factors, it is hypothesized that vaccines could induce IgAV by mimicking the immune response against pathogens [8,9]. The ChadOx1 nCoV-19 vaccine, recently named VAXZEVRIA®, is a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the spike S glycoprotein of the SARS-CoV-2 [10]. Interestingly, four cases of IgAV following COVID-19 have been reported in children and adults [11–15].

On May 12th, 21 other cases of IgAV following SARS-CoV-2 vaccination have been registered in Vigibase® [5]: 5 with the tozinameran COMIRNATY® vaccine, 5 with the mRNA 1273 MODERNA® vaccine, 9 with the ChadOx1 nCoV-19 VAXZEVRIA® and 3 with the Ad26 CoV-2S JANSSEN® vaccine. The time between vaccination and IgAV first symptoms ranged from 1 to 25 days (missing data for 2 cases) and was \leq 15 days in 15 patients. All cases but 1 occurred after the first injection of vaccine. However, these reports must be taken with caution thus they are not sufficiently detailed to ascertain the IgAV diagnosis by external review.

In conclusion, vaccines against SARS-CoV-2 including mRNA vaccines and adenoviral vector vaccines should be added to the list by Rasmussen et al. [1] among the vaccines that can trigger IgAV.

Disclosure

All authors declared no competing interests related to this report.

Acknowledgements

The authors thank the Uppsala Monitoring Centre, which provided and gave permission to use the data analyzed in the present study. The opinions and conclusions in this study are not necessarily those of the various Pharmacovigilance National Centers or of the World Health Organization.

References

- [1] Rasmussen C, Tisseyre M, Garon-Czmil J, Atzenhoffer M, Guillevin L, Salem J-E, et al. Drug-induced IgA vasculitis in children and adults: revisiting drug causality using a dual pharmacovigilance-based approach. Autoimmun Rev 2021;20: 102707. https://doi.org/10.1016/j.autrev.2020.102707.
- [2] Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised international Chapel Hill consensus conference nomenclature of Vasculitides. Arthritis Rheum 2013;65:1–11. https://doi.org/10.1002/art.37715.
- [3] Watts RA, Lane S, Scott DGI. What is known about the epidemiology of the vasculitides? Best Pract Res Clin Rheumatol 2005;19:191–207. https://doi.org/ 10.1016/j.berh.2004.11.006.



