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Letter to the Editor

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/m^2) 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 $\times$ 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 non-significant 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 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.

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