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Letter to the Editor

LETTER TO THE EDITOR

De novo IgA vasculitis following adenovirus-based SARS-CoV-2 vaccination

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Several cases of immunoglobulin A (IgA) nephropathy flares after vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have recently been reported [1]. Most cases were related to mRNA vaccines, in patients <50 years, with previously biopsy-proven IgA nephropathy. Here, we describe an original case of *de novo* systemic IgA vasculitis with renal involvement following adenovirus-based vaccination against SARS-CoV-2.

A 55-year-old woman was referred for uncontrolled proteinuria in a context of recently diagnosed IgA vasculitis. Her past medical history included an uncomplicated diabetes [previous serum creatinine (sCr) 64 µM, without hematuria] treated with oral hypoglycemic drugs, sleep apneoa and uncomplicated asthma. The patient had no history of previous SARS-CoV-2 infection.

In early May 2021, she received a second dose of ChAdOx1 nCoV-19 (AstraZeneca) vaccine. Forty-eight hours after the injection, she developed a persistent flu-like syndrome and several diffuse, palpable purpuric lesions involving her lower limbs and flanks (Figure 1A). The physical examination revealed arthralgia of the knees and ankles without arthritis and self-limiting diarrhea without gastrointestinal bleeding or abdominal pain. At this time, renal function was defined by sCr 79 µM [estimated glomerular filtration rate (eGFR) 73 mL/mn/1.73 m^2 according to (CKD-EPI) formula], with a urine protein/creatinine ratio (UPCR) 68 mg/mmol without hematuria. C-reactive protein was 23 mg/L, and antineutrophil cytoplasmic antibody, cryoglobulinemia and anti-nuclear antibodies were negative. Complement was in the normal range. Serum IgA was 3.19 g/L (N 0.81–4.46). A skin biopsy revealed a leukocytoclastic vasculitis with vascular IgA and C3 deposits. Thoraco-abdominal computed tomography scan was unremarkable (including in the digestive tract). Extensive workup did not reveal any ongoing infection. SARS-CoV-2 IgG anti-spike antibody level was 9159 AU/mL (positive if >50), with no anti-nucleocapsid antibody.

Treatment with colchicine and angiotensin-converting enzyme inhibitor (ACEi) was started. After 1 month follow-up, UPCR increased (440 mg/mmol) despite treatment with full-dose ACEi, albumin level was 35 g/L, and renal function progressively declined (sCr 91 µM, eGFR 61 mL/min/1.73 m^2) without hematuria.

A kidney biopsy was performed and showed typical features of proliferative IgA nephropathy, with segmental endocapillary hypercellularity and cellular crescent. An immunofluorescence study revealed mesangial and parietal polytypic IgA deposition associated with C3 positivity (Figure 1B–E).

Clinical presentation and kidney and skin biopsies were suggestive of IgA vasculitis with severe renal involvement. The patient refused steroid therapy given the risks of diabetes worsening. Three months after the vaccination, hematuria was 60 000 red blood cells/mL, while renal function further declined (sCr 136 µM, eGFR 38 mL/min/1.73 m^2).

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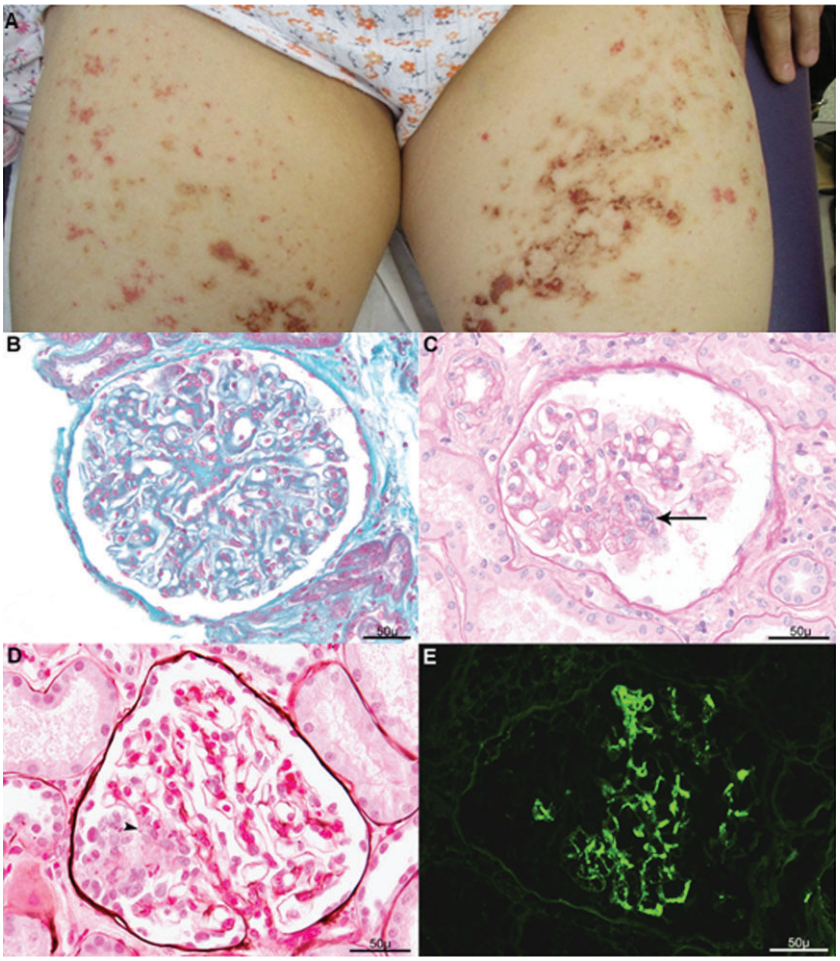

FIGURE 1: Skin lesions and renal biopsy findings. (**A**) Diffuse purpuric lesions involving lower limbs. Renal biopsy disclosed nine glomeruli, one was globally sclerotic. Glomeruli displayed mesangial matrix expansion [(**B**) Masson's trichrome stain, original magnification ×200] with segmental endocapillary hypercellularity (arrow) [(**C**) periodic acid–Schiff stain, original magnification ×400]. We observed a rupture of the glomerular basement membrane (arrowhead) with segmental cellular crescent [(**D**) Jones silver stain, original magnification ×400). An immunofluorescence study revealed mesangial and parietal IgA deposition (3+) [(**E**) immunofluorescence with a fluorescein isothiocyanate-conjugated antisera against IgA, original magnification ×400], associated with C3 (2+), kappa (2+) and lambda (3+) positivity (not shown). Scale bars = 50 µm.

In this observation, the close temporal relationship between the second vaccine injection and the onset of clinical symptoms of systemic IgA vasculitis suggests an association between the immune response to SARS-CoV-2 vaccination and IgA vasculitis occurrence. Vaccines are known potential triggers of drug-induced IgA vasculitis [2]. While a case of IgA vasculitis relapse has been recently reported after the SARS-CoV-2 mRNA vaccine [3], our observation suggests that *de novo* IgA vasculitis might also occur after an adenovirus-based vaccine. Of note, IgA vasculitis has been rarely reported after coronavirus disease 2019 (COVID-19) infection [4].

In previous cases of IgA nephropathy flares post-SARS-CoV-2 mRNA vaccines, biopsy findings showed active glomerulonephritis with inflammatory lesions, as observed in our patient [1]. Obviously, a reporting bias toward the more severe cases is likely. However, given the massive vaccination campaign worldwide, these severe lesions suggest the need for careful follow-up to discuss eventual immunosuppressive treatment in patients with these complications.

SARS-CoV-2 vaccination may induce a strong IgA anti-spike antibody response [3, 5], but the detailed pathophysiological mechanisms of these IgA-related diseases remain to be studied. Although this rare complication does not modify the overall favorable risk-to-benefit ratio of SARS-CoV-2 vaccines, our observation underscores that adenovirus-based vaccines could be considered as a potential trigger of IgA vasculitis with severe renal involvement.

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CONFLICT OF INTEREST STATEMENT

V.A. reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Travere outside the submitted work, support for attending meetings and/or travel from Sanofi Genzyme outside the submitted work and participation in a Data Safety Monitoring Board or Advisory Board for Alnylam, Addmedica and Travere outside the submitted work. J.O., T.B., L.A., E.S., K.E.K. and A.M. declare no conflict of interest. The results presented in this paper have not

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PATIENT CONSENT

Written informed consent to publication was obtained.

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