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CORRESPONDENCE

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Relapsed ANCA associated vasculitis following Oxford AstraZeneca ChAdOx1-S COVID-19 vaccination: A case series of two patients

The coronavirus disease 2019 (COVID-19) pandemic has precipitated the largest vaccination initiative in history.[1] With a programme of this scale comes increasing descriptions of rare glomerular conditions developing post vaccination.[2] We report two patients with relapsed microscopic polyangiitis (MPA) ANCA associated vasculitis (AAV) who received the Oxford AstraZeneca ChAdOx1-S vaccine (AZV) within 5 weeks of developing symptoms (see Table 1). Whilst case reports of de novo vasculitis following COVID-19 vaccination have been described,[2] to our knowledge relapse of AAV in patients with a known history has not, raising questions regarding the safety of COVID-19 vaccination use in this population.

A 75-year-old man with historical renal-limited MPA, previously in remission, presented with 3 days of haemoptysis, onset 5 weeks following the first dose of AZV. Serum creatinine was consistent with baseline; however, microscopic haematuria was newly present. P-ANCA was positive, with anti-MPO antibodies, having been negative at previous review. Kidney biopsy demonstrated active, pauci-immune crescentic glomerulonephritis, consistent with AAV relapse. Methylprednisolone and rituximab were commenced and haemoptysis resolved, however kidney function deteriorated, requiring ongoing kidney replacement therapy.

A 74-year-old man with MPA, diagnosed 18 months previously with no prior kidney involvement, was referred with worsening kidney impairment, first noted 2 weeks following first AZV. He had received the second AZV on the morning of admission, the first dose given 10 weeks prior. Positive p-ANCA with anti-MPO >134 U/ml was noted. Kidney biopsy demonstrated acute crescentic pauci-immune glomerulonephritis, consistent with AAV. Serum creatinine peaked at 882 umol/L, and dialysis access was organized. Intravenous methylprednisolone and cyclophosphamide were commenced, kidney function improved, and he was discharged without requiring kidney replacement therapy.

Whilst single cases of de novo AAV have been described following each of the AZV, Moderna and Pfizer COVID-19 vaccinations,[2–5] this is the first report of AAV relapse following

TABLE 1 Clinical information and pathology results

Case	1	2	Reference range
Initial diagnosis date	2015	2019	
Previous antibody	MPO Ab 1.2	MPO Ab 7	MPO Ab 0.0–3.4 U/ml
Prior therapy	Cyclophosphamide, rituximab, azathioprine, steroids	Steroids	
Vaccination dates	08/06/2021	02/06/2021 11/08/2021	
Symptom onset	14/07/2021	16/06/2021	
Baseline creatinine and date	226 31/05/2021	75 12/05/2021	60–110 umol/L
Creatinine at presentation and date	227 17/07/2021	155 16/06/2021	60–110 umol/L
Peak creatinine and date	617 04/08/2021	882 16/08/2021	60–110 umol/L
ANCA	p-ANCA @40	p-ANCA >40	
Antibody	MPO Ab 3.5	MPO Ab >134	MPO Ab 0.0–3.4 U/ml
Kidney replacement therapy	Yes	No	
Pulmonary haemorrhage	Yes	No	
Treatment	Pulse steroids, rituximab	Pulse steroids, cyclophosphamide	
Creatinine at follow up	Dialysis dependent	307	60–110 umol/L

COVID-19 vaccination. Our findings raise questions regarding COVID-19 vaccination safety in those with known vasculitis. The scarcity of cases contrasted with the number of vaccines given is reassuring and should not change our practice in recommending vaccination to our patients; however, it would be prudent to monitor those with a history of vasculitis closely. Regarding the cases described here, recommending an alternative vaccination for future doses may be a sensible path forward.

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REFERENCES

1. Max R & Oxford Martin School. (2014). Our World in Data. https://ourworldindata.org/covid-vaccinations. Accessed November 5, 2021.
2. Bomback AS, Kudose S, D'Agati VD. De novo and relapsing glomerular diseases after COVID-19 vaccination: what do we know so far? *Am J Kidney Dis*. 2021;78:477-480.
3. Shakoor MT, Birkenbach MP. ANCA-associated vasculitis following Pfizer-BioNTech COVID-19 vaccine. *Am J Kidney Dis*. 2021;78:611-613.
4. Sekar A, Campbell R, Tabbara J, Rstogi P. ANCA glomerulonephritis after the Moderna COVID-19 vaccination. *Kidney Int*. 2021;100:473-474.
5. Villa M, Diaz-Crespo F, Perez de Jose A, et al. A case of ANCA-associated vasculitis after AZD1222 (Oxford-AstraZeneca) SARS-CoV-2 vaccination: casualty or causality? *Kidney Int*. 2021;100:937-938.

Gross haematuria after mRNA COVID-19 vaccination in two patients with histological and clinical diagnosis of IgA nephropathy

A 28 years old lady with history of microscopic haematuria for 5 years underwent a pre-scheduled kidney biopsy for suspected IgA nephropathy. Her renal function was normal with proteinuria 0.11 g/day. 3 weeks prior to biopsy, she received her second dose of mRNA COVID-19 vaccine (Pfizer-BioNTech BNT162b2) and developed painless gross hematuria 3 h later. Serum creatinine level was mildly elevated from 58 to 72 μmol/L. Urine protein creatinine ratio increased from 20 to 320 mg/mmol. Her anti-nuclear antibody (ANA) turned from negative to positive with a titre of 1:640, but anti-dsDNA remained negative. Her C3 and C4 levels were normal. 5 days later, her serum creatinine level fell to 54 μmol/L and hematuria subsided spontaneously. 3 weeks later, her urine protein creatinine ratio fell to 34 mg/mmol and ANA became negative. Kidney biopsy confirmed IgA nephropathy with Oxford classification M1E0S0T0-C0 without features suggestive of lupus nephritis.

The second patient was a 58 years old lady with hypertension and microscopic haematuria for 1 year. She recalled an episode of painless gross haematuria in 2008. CT urogram and cystoscopy were normal. There were 4% dysmorphic red blood cells in urine. Urine protein creatinine ratio was 24 mg/mmol. IgA nephropathy was suspected clinically. Kidney biopsy was not arranged. 1 day after her second dose of Pfizer-BioNTech mRNA COVID-19 vaccine, she developed painless gross haematuria lasting for 2 days. Her serum creatinine level remained stable at 78 μmol/L 3 weeks later.

To date, at least 15 cases of acute flare of IgA nephropathy after COVID-19 vaccination have been published, involving both the Pfizer-BioNTech and Moderna mRNA vaccines. All of them had gross haematuria, mostly within 6 to 24 h after the second dose vaccination, with or without increase in proteinuria. Most of them had spontaneous resolution after a few days. Only two patients required steroid therapy for acute kidney injury.[1,2] Our first patient had earliest onset