Case Series

Anti-GBM Disease after Oxford-AstraZeneca ChAdOx1 nCoV-19 Vaccination: A Report of Two Cases

Craig Peter Coorey\textsuperscript{a, b}, Elaine Phua\textsuperscript{a}, Angela Chou\textsuperscript{c}, Yvonne Shen\textsuperscript{a}, Amanda Mather\textsuperscript{a}

\textsuperscript{a}Department of Renal Medicine, Royal North Shore Hospital, Sydney, NSW, Australia; \textsuperscript{b}School of Medicine, Western Sydney University, Sydney, NSW, Australia; \textsuperscript{c}Department of Anatomical Pathology, Royal North Shore Hospital, Sydney, NSW, Australia

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Abstract
There have been reports of rare de novo glomerular diseases following vaccination for coronavirus disease 2019 (COVID-19). We report two cases of anti-glomerular basement membrane (GBM) disease in previously healthy females after Oxford-AstraZeneca COVID-19 vaccine (ChAdOx1 nCoV-19). The first case was a 69-year-old female who developed lethargy and anuria approximately 8 weeks after her first dose of Oxford-AstraZeneca COVID-19 vaccine. The second case was a 72-year-old female who developed malaise and diarrhoea approximately 3 weeks after her second dose of Oxford-AstraZeneca COVID-19 vaccine. Both cases had severe acute kidney injury, raised anti-GBM antibody titres, and renal biopsies consistent with anti-GBM disease. Both cases were commenced on haemodialysis and treated with high dose glucocorticoids, cyclophosphamide, and plasmapheresis. Neither patient had recovery of renal function, and both remain dialysis dependent. These cases add to the previously reported cases of anti-GBM disease after mRNA COVID-19 vaccination. As more COVID-19 vaccinations are administered worldwide, it would be important for clinicians to be aware of this possible association, and continued surveillance is warranted.

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Correspondence to:
Craig Peter Coorey, c.coorey@westernsydney.edu.au

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Craig Peter Coorey and Elaine Phua co-first authors.
Introduction

The vaccines for coronavirus disease 2019 (COVID-19) have been used as a part of mass vaccination programs in many countries worldwide. In these large populations, there have been reports of rare de novo immunological glomerular diseases following vaccination, including both mRNA-based and adenoviral vector-based vaccines [1, 2]. The reported glomerular diseases after adenoviral vector-based vaccines include minimal change disease, collapsing glomerulopathy, IgA nephropathy, and acute tubulointerstitial nephritis [3–5]. There have been reports of de novo anti-glomerular basement membrane (anti-GBM) disease following mRNA COVID-19 vaccine [6, 7]. We report two cases of de novo anti-GBM disease in previously healthy females after Oxford-AstraZeneca COVID-19 vaccine (ChAdOx1 nCoV-19).

Case Report

A 69-year-old female developed lethargy and anuria approximately 8 weeks after her first dose of Oxford-AstraZeneca COVID-19 vaccine. She had a background of mild hypertension controlled on a single agent and hypercholesterolaemia without any prior history of renal disease (serum creatinine 50 μmol/L a year prior with no evidence of proteinuria on urinalysis). There was no documented prior infection with SARS-CoV-2 or prior febrile illnesses. On presentation, she had serum creatinine 1175 μmol/L. Positive serum results included anti-GBM antibody (584 U/mL), antinuclear antibody (1:160 homogenous pattern), chromatin antibody (32 U), and myeloperoxidase antibody (11 IU/mL). Complement levels and serum electrophoresis were negative, as were serology for hepatitis B virus, hepatitis C virus, and human immunodeficiency virus. Nasopharyngeal swab for SARS-CoV-2 polymerase chain reaction was negative. She did not have any clinical signs or symptoms of pulmonary or sinus involvement and a computerized tomography scan of her chest did not show any features of pulmonary haemorrhage. A renal biopsy performed showed necrotizing and crescentic glomerulonephritis involving all 30 glomeruli in the sample and immunofluorescence showed linear IgG + C3 staining (Fig. 1). She was commenced on haemodialysis as well as high-dose steroids (3 doses of pulse methylprednisolone followed by 1 mg/kg of oral prednisolone), cyclophosphamide (2 mg/kg), and plasma exchange for treatment of her disease.

Fig. 1. Anti-GBM disease following COVID-19 vaccination. a A glomerulus (arrow) is surrounded and compressed by the cellular crescent (Periodic Acid-Schiff (PAS) stain; original magnification, ×600). b IgG immunofluorescence showing linear 3+ staining of the glomerular basement membrane (arrow) (original magnification, ×600).
She received a total of 20 sessions of plasma exchange over a 5-week period with successful and sustained lowering of her anti-GBM titres to 10.0 U/mL.

A 72-year-old female presented after a 2-week history of malaise and small-volume diarrhoea, which began approximately 3 weeks after her second dose of Oxford-AstraZeneca COVID-19 vaccine. On presentation, she was hyperkalaemic and anaemic with a raised serum creatinine (1200 μmol/L). There were no signs of extrarenal involvement. She has a history of colorectal cancer that was resected more than 20 years ago and treated with adjuvant chemotherapy and was in remission. She had no prior history of renal disease, hypertension, or hyperlipidaemia and was on no regular medications. Anti-GBM titre on presentation was 684 U/mL with a myeloperoxidase (MPO) titre of 57 IU/mL. Renal biopsy performed showed acute cellular crescents in 17 of 19 glomeruli, with linear IgG staining in the glomeruli on immunofluorescence. Like the previous case, she was commenced on high-dose steroids, cyclophosphamide, and underwent 13 sessions of plasmapheresis over a 4-week period followed by rituximab with sustained lowering of her anti-GBM and myeloperoxidase titres to 31.0 U/mL and 2 IU/mL, respectively. Both patients remain dialysis-dependent.

**Discussion**

We have described two cases of patients presenting with acute kidney injury after receiving Oxford-AstraZeneca COVID-19 vaccine. Both cases involve otherwise healthy females who had no prior history of renal disease or autoimmune disease. Both were diagnosed as having rapidly progressive glomerulonephritis related to anti-GBM. The timing of the onset of anti-GBM disease after COVID-19 vaccination makes it possible that the trigger was the COVID-19 vaccine.

The first case had a single dose of Oxford-AstraZeneca COVID-19 vaccine prior to onset of anti-GBM disease and presented 4 weeks before she was due for her second dose (usually given 12 weeks after the first dose). The second case presented after her second dose of Oxford-AstraZeneca COVID-19 vaccine. The previously reported cases of anti-GBM disease after mRNA COVID-19 vaccines both developed symptoms after the second dose of vaccine, namely 1 day post vaccination and 14 days post vaccination [6, 7]. Our reported cases of anti-GBM disease after adenoviral vector COVID-19 vaccines occurred later than those reported after mRNA COVID-19 vaccines. The cases that occurred after mRNA COVID-19 vaccine had gross haematuria (unlike our cases), which may have precipitated earlier presentations to the hospital. Alternatively, there may be an underlying immunological mechanism by which the mRNA COVID-19 vaccine causes an earlier onset of anti-GBM disease than adenoviral vector vaccines. Our cases of anti-GBM disease, as well as the two previously reported cases, did not have recovery of renal function and remain dialysis dependent.

Postulated mechanisms by which COVID-19 vaccination could lead to antibody-mediated glomerular diseases include molecular mimicry (such as the SARS-CoV-2 spike protein) and non-specific mechanisms related to vaccination (such as triggering cell damage revealing hidden self-antigens) [2]. It is unclear which mechanism is implicated and further studies are required. Given anti-GBM disease is a relatively rare entity itself and only several cases have been reported after vaccination, it will be difficult to further delineate the factors associated with the development of anti-GBM disease after vaccination [8].

In conclusion, we have described two cases of de novo anti-GBM disease after Oxford-AstraZeneca COVID-19 vaccine. Both cases did not have a recovery of renal function. These cases add to the previously reported cases of anti-GBM disease after mRNA COVID-19 vaccination and suggest there may be an association between COVID-19 vaccination and de novo anti-GBM disease. As more COVID-19 vaccinations are administered worldwide, it is important for clinicians to be aware of this possible association and continued surveillance is warranted.
Statement of Ethics

The patients provided written informed consent to participate in the study. Written informed consent was obtained from the patients for publication of the details of their medical case and any accompanying images. The case report was exempted from review by the Human Research Ethics Committee of Northern Sydney Local Health District.

Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

Data were collected by Craig Peter Coorey, Elaine Phua, and Angela Chou. Data were interpreted by Craig Peter Coorey, Elaine Phua, Angela Chou, Yvonne Shen, and Amanda Mather. The first draft of the manuscript was written by Craig Peter Coorey and Elaine Phua. Revision of the manuscript and approval of the final version was by Craig Peter Coorey, Elaine Phua, Angela Chou, Yvonne Shen, and Amanda Mather.

Data Availability Statement

The data supporting the conclusions of this article are included within the article. Further enquiries can be directed to the corresponding author.

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