SARS-CoV-2 vaccination-associated collapsing glomerulopathy in a kidney transplant recipient.

Dr Julia Jefferis, Dr Andrew J. Kassianos, Ms Anca Grivei, Dr Brian Doucet, Dr Helen Healy, Dr Leo Francis, Dr Saw Yu Mon, Dr George T. John

PII: S0085-2538(21)01219-9
DOI: https://doi.org/10.1016/j.kint.2021.12.018
Reference: KINT 2893

To appear in: *Kidney International*

Received Date: 25 October 2021
Revised Date: 16 December 2021
Accepted Date: 23 December 2021


This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Copyright © 2022, Published by Elsevier, Inc., on behalf of the International Society of Nephrology.
SARS-CoV-2 vaccination-associated collapsing glomerulopathy in a kidney transplant recipient.

Authors: Dr Julia Jefferis¹,², Dr Andrew J Kassianos¹,²,³, Ms Anca Grivei¹,³, Dr Brian Doucet¹,², Dr Helen Healy¹,²,³, Dr Leo Francis⁴, Dr Saw Yu Mon¹,², Dr George T John¹,².

Affiliations: ¹Kidney Health Service, Royal Brisbane and Women’s Hospital, Brisbane, Australia; ²Faculty of Medicine, University of Queensland, Brisbane, Australia; ³Conjoint Internal Medicine Laboratory, Chemical Pathology, Pathology Queensland, Brisbane, Australia; ⁴Anatomical Pathology, Pathology Queensland, Health Support Queensland, Brisbane, Australia.

Correspondence:
Dr George T. John
Kidney Health Service, Level 9 Ned Hanlon Building
Royal Brisbane and Women’s Hospital
Butterfield St
Herston QLD 4029, Australia
Phone: +61 (07) 3646 8111
Email: George.John@health.qld.gov.au

Key Words
Focal segmental glomerulosclerosis
Transplantation
SARS-CoV-2
A stable kidney transplant recipient (KTR) of 14 years received the SARS-CoV-2 ChAdOx1 (AZD1222) vaccine and, within a fortnight, presented with severe acute kidney injury (AKI) - creatinine 533µmol/L (baseline 125-187µmol/L) and nephrotic range proteinuria (urine PCR=2000g/mol, no hematuria). The allograft, her first, was from a deceased Caucasian donor, following kidney failure from IgA vasculitis, and stable for many years (Fig1A). Initial kidney biopsy showed glomerulomegaly, glomerulitis, podocyte enlargement with protein droplets and collapse of the glomerular tufts along with glomerular and interstitial immune infiltrates (Banff score i3 t0 v0 g3 ptc0 ci1 ct1 cv0 cg1b mm0 ah3 ti3 i-IFTA3) (Fig1B-C); EM unavailable. Immunofluorescence for immunoglobulins and C4d immunohistochemistry, antibodies against donor-specific HLA and Angiotensin 2R1 were absent. Treatment response for suspected antibody-mediated rejection with methylprednisolone, intravenous immunoglobulin and plasma exchange was poor. Repeat kidney biopsy showed absence of immune cell infiltration and features consistent with collapsing glomerulopathy (CG) with acute tubular injury and mild glomerulitis (Banff score i0 t1 v0 g1 ptc0 ci1 ct1 cv0 cg3 mm0 ah3 ti0 i-IFTA3) (Fig1D-E). EM revealed detachment of podocytes with extensive foot process effacement, microvillous hyperplasia, protein droplets in some podocytes, normal glomerular basement membranes, with no evidence of immune complex deposition. Secondary causes of CG including CMV, BK, HIV, parvovirus and SARS-CoV-2 infection were excluded. The patient required haemodialysis at three months with persisting proteinuria (15g/day). Further immunohistochemistry confirmed: (1) expression of Ki67, a marker of glomerular expansion/proliferation in CG, detected in biopsy 1, with epithelial cell reactivity in Bowman’s space (Fig1F); (2) reduced glomerular expression of synaptopodin and podocalyxin, evidence of podocyte dedifferentiation previously associated with CG, on biopsy 1 (Supplementary Fig1); and (3) significantly increased levels of inflammatory subpopulations on initial biopsy to be significantly attenuated following intervention (Supplementary Fig2).\textsuperscript{1,2} SARS-CoV-2 vaccination has been associated with many glomerular diseases, minimal change and membranous nephropathy, whilst SARS-CoV-2 infection has been associated with CG including in a KTR.\textsuperscript{3-5} We report the first case of a KTR developing CG after SARS-CoV-2 ChAdOx1 vaccination, with no identifiable cause besides temporal association with vaccination.
DISCLOSURE
All the authors declared no competing interests.

ACKNOWLEDGEMENTS
The authors would like to thank the tissue donors for provision of renal bio-specimens. The authors also gratefully acknowledge the staff of QIMR Berghofer Core Histology and Australian Cancer Research Foundation Centre for Comprehensive Biomedical Imaging (QIMR Berghofer) for expert technical assistance with staining and image analysis and Dr Kim Oliver, Nephropathologist at the Princess Alexandra Hospital, Brisbane for reviewing the biopsy slides.

FUNDING
The work was funded by Pathology Queensland and a National Health and Medical Research Council (NHMRC) Project Grant (GNT1161319).

SUPPLEMENTARY MATERIAL
Supplementary Methods
Supplementary Results
Supplementary Reference
Supplementary Figure S1: Reduced expression of glomerular markers in KTR biopsy tissue with collapsing glomerulopathy associated with SARS-CoV-2 vaccination.
Supplementary Figure S2: Immune cell infiltration in KTR biopsy tissue with collapsing glomerulopathy associated with SARS-CoV-2 vaccination.
REFERENCES


FIGURE LEGEND

Figure 1: Timeline of kidney function and sequential biopsy results in a KTR. (A) Timeline of renal function/creatinine (●) and cyclosporine (○) levels, with arrows indicating timing of first and second AstraZeneca vaccinations. (*) indicates initiation of 1 gram methylprednisolone, 2nd daily plasma exchange and intravenous immunoglobulin for two weeks, continued 60mg prednisolone/D. (B) Kidney Biopsy 1 prior to treatment shows enlarged glomeruli with features of glomerulitis with endocapillary lymphocytes, some neutrophils, and capillary loop narrowing – PASM x200. Scale bar represents 100μm. (C) In Biopsy 1, enlarged podocytes with protein droplets in their cytoplasm were noted in two glomeruli - H&E x200. Scale bar represents 100μm. (D-E) The second biopsy (Biopsy 2) two weeks later revealed two glomeruli containing large podocytes with prominent protein globules and collapse of underlying capillary loops – (D) PASM x200 and (E) PAS x200. Scale bars represent 100μm. (F) Ki67 immunohistochemistry shows reactivity in multiple cells in Bowman’s space, consistent with either visceral or parietal epithelial cells. Some of the cells contain cytoplasmic protein droplets. Scale bar represents 100μm.