LETTER TO THE EDITOR

Acute interstitial nephritis following SARS-CoV-2 vaccination

Henry H.L. Wu, Jennifer W.C. Li, Andrew Bow, Alexander Woywodt, and Arvind Ponnusamy

1Department of Renal Medicine, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK, 2Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK and 3Department of Renal Medicine, North Cumbria Integrated Care NHS Foundation Trust, Carlisle, UK

Correspondence to: Alexander Woywodt; E-mail: Alex.Woywodt@lthtr.nhs.uk

We read with interest the recent publication by Czerlau et al. [1] on a series of patients with acute interstitial nephritis (AIN) following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination. We have recently reported a similar case and noted a further case by de la Flor et al. [2, 3]. Unver et al. [4] reported a case of AIN with concurrent nephrotic syndrome after SARS-CoV-2 vaccination. Here, we would like to report two additional cases.

The first patient is a 69-year-old female patient with rheumatoid arthritis, Sjögren’s syndrome, hypertension and hypothyroidism who presented with polyuria 5 days after the first dose of the Oxford-AstraZeneca SARS-CoV-2 (ChAdOx1 nCoV-19) vaccine. Regular medications included methotrexate, folic acid, ramipril, thyroxine and paroxetine, as well as lansoprazole on an ‘as required’ basis, although the patient did not take any in the last month. The physical examination was unremarkable. Blood tests revealed acute kidney injury (AKI) with an increased serum creatinine at 245 μmol/L (baseline is 85 μmol/L). The only other abnormality noted was peripheral eosinophilia. Urine dipstick did not show proteinuria or haematuria. Renal ultrasound and immunology screen were both normal. The patient was started on intravenous fluids, with ramipril and methotrexate being discontinued. Renal biopsy showed a florid interstitial infiltrate with eosinophils, with no glomerular abnormalities and no chronic interstitial damage. The patient was commenced on steroids (prednisolone 60 mg daily). Serum creatinine improved to 90 μmol/L and peripheral eosinophilia resolved. She continued to take paroxetine and thyroxine on discharge, though ramipril, lansoprazole and methotrexate were not restarted. One month following this admission, the patient re-presented with serum creatinine at 250 μmol/L and a reoccurrence of peripheral eosinophilia. On this occasion, paroxetine was stopped, and the patient was recommenced on oral steroids (prednisolone 60 mg daily). A month later, and whilst on prednisolone 20 mg daily, the patient’s serum creatinine has fallen to 130 μmol/L, and peripheral eosinophilia has once again resolved.

The second patient is a 60-year-old female patient who presented generally unwell 2 weeks after her second dose of the ChAdOx1 nCoV-19. The patient had a history of hypertension, and was on atorvastatin, losartan, bisoprolol and lansoprazole. Blood tests showed AKI with a serum creatinine of 754 μmol/L (baseline is 59 μmol/L). Urine dipstick did not show proteinuria or haematuria, but albumin:creatinine and protein:creatinine ratios were 20 and 166 mmol/μmol, respectively, suggestive of tubular proteinuria. Renal ultrasound, immunology and virology were normal. The patient received intravenous fluids and losartan was stopped. Renal biopsy showed widespread interstitial infiltrates in keeping with AIN. The patient was given a single dose of 250 mg intravenous methylprednisolone followed by an oral prednisolone course at 30 mg daily. When last seen, she was well and serum creatinine was 216 μmol/L.

To our knowledge, 10 cases of AIN after the SARS-CoV-2 vaccination have now been reported worldwide (Table 1), and clinicians should be aware of these reports. Czerlau et al. [1] speculated as to the underlying pathophysiology. AIN associated with other vaccines has been described previously [5, 6]. It is very difficult to prove causality in the cases described here and those reported previously. Widespread SARS-CoV-2 vaccination is continuing worldwide, and many patients presenting with AKI will therefore have a history of preceding vaccination. We also...
### Table 1. Cases of AIN reported in the literature as of 1 December 2021

| Author/country of case report | Age (years) | Sex | Time to presentation from day of vaccination | Significant comorbidities | New-onset or relapse | Vaccine brand | Vaccine dose | Baseline creatinine (μmol/L) | Presentation creatinine (μmol/L) | Proteinuria (g/day) | Visible haematurial | Kidney biopsy description | Treatment received | Outcome |
|------------------------------|-------------|-----|---------------------------------------------|---------------------------|-----------------------|---------------------|--------------|-----------------------------|-------------------------------|-----------------|---------------------|--------------------------------|----------------------|---------|
| Czerlau et al / Switzerland [1] | 55          | M   | 4 days                                      | Hypertension, prostate cancer treated with prostatectomy | New-onset Pfizer | Second | 76.5 | 355 | 8.3 | No | Lymphocytes, plasma cells, macrophages, eosinophilic granulocytes and some neutrophilic granulocytes, tubulitis and interstitial oedema | Steroid treatment—dose and length of treatment not specified | Serum creatinine following treatment is 88 μmol/L |
| Czerlau et al / Switzerland [1] | 54          | M   | 3 days                                      | Myocardial infarction | New-onset Moderna | Second | Not known | 288 | 9.7 | Yes | Lymphocytes, plasma cells, macrophages, and eosinophilic granulocytes, two granulomas, tubulitis and tubular destruction. Glomerular lesions in keeping with FSGS | Steroid treatment—dose and length of treatment not specified | Serum creatinine following treatment is 235 μmol/L |
| Czerlau et al / Switzerland [1] | 58          | M   | 'A few days'                                | FSGS refractory to treatment, with multiple relapses | New-onset Moderna | Second | 167 | 355 | 3.2 | No | Lymphocytes, plasma cells, macrophages and sporadic neutrophilic granulocytes with tubulitis and interstitial oedema | Steroid treatment—dose and length of treatment not specified | Serum creatinine following treatment is 210 μmol/L |
| Author/country of case report | Age (years) | Sex | Time to presentation from day of vaccination | Significant comorbidities | New-onset or relapse | Vaccine brand | Vaccine dose | Baseline creatinine (μmol/L) | Presentation creatinine (μmol/L) | Proteinuria (g/day) | Visible haematurial | Kidney biopsy description | Treatment received | Outcome |
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| Czerlau et al. / Switzerland [1] | 38 | F | 1 month | Ulcerative colitis—received ustekinumab previously for treatment | New-onset | Moderna | 2nd | 76 | 86 | 0.6 | Yes | Eosinophilic granulocytes | Steroid treatment | Serum creatinine following treatment is 72 μmol/L |
| Czerlau et al. / Switzerland [1] | 35 | F | Exact time not specified | Rheumatoid arthritis—on certolizumab treatment since 2016 | New-onset | Pfizer | Second | 49 | 100 | 2 | No | Eosinophilic granulocytes | Steroid treatment | Serum creatinine following treatment is 90 μmol/L |
| Author/country of case report | Age (years) | Sex | Time to presentation from day of vaccination | Significant comorbidities | New-onset or relapse | Vaccine brand | Vaccine dose | Baseline creatinine (μmol/L) | Presentation creatinine (μmol/L) | Proteinuria (g/day) | Visible haematurial | Kidney biopsy description | Treatment received | Outcome |
|-------------------------------|------------|-----|---------------------------------------------|--------------------------|----------------------|---------------|--------------|-----------------------------|-----------------------------|-----------------|-------------------|--------------------------|-------------------|---------|
| Liew et al/UK [2]            | 53         | M   | 3 days                                      | Hypertension             | New-onset            | Oxford-AstraZeneca | Second       | Not known                   | 1034                        | 0.6              | No                | Morphologically normal glomeruli with interstitial oedema and infiltrate of lymphocytes, plasma cells and neutrophils with tubulitis | Oral steroid treatment | Improvement of renal function. Dialysis-independent following discharge |
| de la Flor et al/Spain [3]   | 78         | M   | 3 weeks                                     | Hypertension, type 2 diabetes mellitus | New-onset            | Pfizer         | First        | 150                         | 475                         | 3.4              | No                | Features of AIN along with glomerular sclerosis and other chronic changes | IV MP followed by oral steroids | Remained dialysis-dependent |
| Unver et al/Turkey [4]       | 67         | F   | 3 weeks                                     | Type 2 diabetes mellitus. Recent new-onset minimal change disease following first dose of CoronaVac | New-onset             | CoronaVac      | Second       | Not known (serum creatinine was 53 μmol/L) | 371                         | 18.6             | Yes               | Hydropic degeneration of proximal tubular cells and interstitial inflammation consisting of lymphocytes and eosinophils in the medullary area were observed. Proteinaceous material was detected in many tubule lumens | Pulsed IV MP followed by oral steroids | Ongoing treatment. Proteinuria of 3 g/day still apparent from last follow-up |
Table 1. Continued.

| Author/country of case report | Age (years) | Sex | Time to presentation from day of vaccination | Significant comorbidities | New-onset or relapse | Vaccine brand | Vaccine dose | Baseline creatinine (μmol/L) | Presentation creatinine (μmol/L) | Proteinuria (g/day) | Visible haematurial | Kidney biopsy description | Treatment received | Outcome |
|-------------------------------|-------------|-----|---------------------------------------------|---------------------------|---------------------|---------------|--------------|-----------------------------|----------------------------------|-----------------|-----------------------|--------------------------------|-------------------|---------|
| Wu et al./UK (this report)    | 69          | F   | 5 days                                      | Rheumatoid arthritis, Sjögren's syndrome, hypertension, hypothyroidism and anxiety | New-onset            | Oxford-AstraZeneca | First        | 85                          | 245                              | Undetectable   | No                    | Florid interstitial infiltrate with prominent eosinophils, with no glomerular abnormalities and no chronic interstitial damage | Commenced on oral steroids. Discontinuation of regular medications such as ramipril, lansoprazole, methotrexate and paroxetine | Improved serum creatinine to 130 μmol/L and resolved peripheral eosinophilia |
|                               | 60          | F   | 2 weeks                                     | Hypertension              | New-onset            | Oxford-AstraZeneca | Second       | 59                          | 754                              | Tubular proteinuria noted         | Widespread interstitial infiltrates in keeping with AIN | Single dose IV pulsed MP followed by oral steroids | Full clinical recovery. Serum creatinine was 216 μmol/L in last follow-up review |

FSGS, focal segmental glomerulosclerosis; F, female; M, male; MP, methylprednisolone; IgA, immunoglobulin A; IV, intravenous; EM, electron microscopy.
acknowledge other potential triggers of AIN in our two cases, in particular the concurrent use of proton-pump inhibitors. However, underreporting is also possible, and clinicians may regard recent vaccination as almost universal and therefore not elicit a detailed vaccination history. It is also possible that milder cases resolve spontaneously and do not undergo renal biopsy. We suggest that clinicians take note of a possible association and obtain a detailed vaccination history when confronted with cases of otherwise unexplained AIN.

PATIENT CONSENT
Approved consent has been achieved from both of the patients described in this manuscript.

CONFLICT OF INTEREST STATEMENT
A.W. is member of the CKJ editorial board. The results presented in this paper have not been published previously in whole or in part.

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