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Letter to the Editor

LETTER TO THE EDITOR

Acute interstitial nephritis following SARS-CoV-2 vaccination

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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, Sjøgren'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

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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 haema-turial	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	268	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

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 haema-turial	Kidney biopsy description	Treatment received	Outcome
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	Lymphocytes, plasma cells, macrophages, sporadic eosinophilic granulocytes and neutrophil granulocytes with tubilitis and interstitial oedema. EM shows mesangial IgA deposition	Steroid treatment—dose and length of treatment not specified	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	Lymphocytes, plasma cells, macrophages, sporadic eosinophilic granulocytes and neutrophil granulocytes with tubulitis and interstitial oedema. EM shows mesangial IgA deposition	Steroid treatment—dose and length of treatment not specified	Serum creatinine following treatment is 90 μmol/L

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 haema-turial	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 tubilitis	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. Patient was then commenced on cyclosporine treatment	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 haema-turial	Kidney biopsy description	Treatment received	Outcome
Wu *et al.*/UK (this report)	69	F	5 days	Rheumatoid arthritis, Sjøgren's syndrome, hypertension, hypothy-roidism 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. Dis-continuation of regular medications such as ramipril, lansoprazole, methotrexate and paroxetine	Improved serum creatinine to 130 μmol/L and resolved peripheral eosinophilia
Wu *et al.*/UK (this report)	60	F	2 weeks	Hypertension	New-onset	Oxford-AstraZeneca	Second	59	754	Tubular proteinuria noted	No	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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