

Immune complex-mediated glomerulonephritis post COVID-19 vaccination in a patient with concomitant Brucellosis

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ABSTRACT

ظهرت لقاحات الكوفيد COVID خطوة مهمة في السيطرة على جائحة COVID-19. على الرغم من حقيقة أنها كانت آمنة وفعالة بشكل عام، نشر عدد قليل من تقارير الحالات عن اضطرابات الكلى بعد لقاحات COVID. نستعرض في هذا التقرير حالة رجل يبلغ من العمر 29 عامًا ولديه تاريخ لمرض الكلى المزمن والذي قدم إلى مركزنا يعاني من ألم الخصرة بعد تلقيه لقاح أسترازينيكا AstraZeneca COVID. ولديه أيضًا تاريخ في شرب الحليب الخام. أظهرت الفحوصات الأولية ارتفاع نسبة الكرياتينين مع مستوى عالٍ من البيلة البروتينية. خزعة الكلى كانت متوافقة مع التهاب كبيبات الكلى المناعي المركب فوق التليف الكلوي. أظهر مصل البروسيلا الخاص به أيضًا عيارًا مرتفعًا. بدأ العلاج من داء البروسيلات والتخطيط للمتابعة بعد ذلك لمزيد من العلاج. على حد علمنا، هذه هي الحالة الأولى المبلغ عنها لداء البروسيلا والتهاب كبيبات الكلى بعد لقاح COVID.

COVID vaccinations have been an important step in controlling the COVID-19 pandemic. Despite the fact they were generally safe and effective, a few case reports of renal disorders have been published following COVID vaccines. We report a 29-year-old man with history of Chronic Kidney Disease who presented to our center with flank pain after receiving AstraZeneca COVID vaccine. He also had history of raw milk ingestion. His initial investigations showed high creatinine with high level of proteinuria. A renal biopsy was consistent with immune complex-mediated glomerulonephritis on top of renal fibrosis. His brucella serology also showed high titer. He was started on treatment for Brucellosis and planned for follow-up afterwards for further therapy. To the best of our knowledge, this is the first reported case of concomitant Brucellosis and post COVID vaccine glomerulonephritis.

Keywords: brucellosis, glomerulonephritis, COVID-19 vaccines, renal insufficiency, chronic, ChAdOx1 nCoV-19

*Saudi Med J 2022; Vol. 43 (5): 522-525
doi: 10.15537/smj.2022.43.5.20220139*

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Received 22nd February 2022. Accepted 15th April 2022.

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Since Coronavirus disease-19 (COVID-19) was declared a pandemic in 2019, several efforts have been made to control its spread worldwide, including the development of vaccines.

The vaccines developed for COVID 19 are generally safe and effective; however, there have been cases of post vaccine nephropathy. Cases of minimal change disease after administration of messenger ribonucleic acid vaccines were reported.^{1,2} Cases of pauci-immune glomerulonephritis with positive Anti-Neutrophil Cytoplasmic Antibodies (ANCA) were also reported.^{3,4} Although temporal association does not always indicate causation, a first-presentation of Class V lupus nephritis was reported in a patient who was previously healthy post AstraZeneca vaccine administration.⁵ Membranous and IgA nephropathy have been also reported post vaccination.^{6,7} However, renal injuries following vaccinations were also reported with previous vaccines.⁸

Brucellosis is considered the most common zoonotic disease and rarely causes renal manifestations, which can carry a poor prognosis.^{9,10}

Here, we report a patient who developed immune complex-mediated glomerulonephritis after receiving the AstraZeneca COVID 19 vaccine with a concomitant Brucellosis.

Case Report. A 29-year-old male presented to our hospital on the 12th of April 2021, with a history of abdominal and loin pain for 5 days, 2 days after receiving the AstraZeneca vaccine for COVID-19. His symptoms included vomiting, diarrhea, and decreased oral intake. He had no history of fever, skin rash, joint pain, photosensitivity, or drug use. The patient had a history of recurrent urinary tract infections, which resulted in long-term impairment of kidney function.

However, no medical report or baseline kidney function were available.

Clinical findings. Physical examination revealed no pain or distress; his Glasgow coma scale score was 15/15. His blood pressure was 130/70 mmHg, heart rate was 91 beats per minute, respiratory rate was 12 breaths per minute, oxygen saturation was 99% on room air, and temperature was 37°C. There was no pallor, jaundice, lymphadenopathy, oral ulcers, or arthritis. Chest examination revealed normal vesicular breathing bilaterally. Heart sounds were normal. Abdominal examination revealed mild bilateral flank tenderness; however, no organomegaly was observed. Lower limb examination was unremarkable.

Diagnostic assessment. The laboratories results upon admission can be found in **Table 1**.

Therefore, the patient was admitted with the impression of acute kidney injury. Further laboratory tests after admission are in **Table 2**.

Radiological studies showed. Abdominal computed tomography without contrast showed small non-obstructing right renal stones, bilateral renal cortical scarring, mild splenomegaly and hiatus, and left inguinal hernias (**Figure 1**).

^{99m}Tc dimercaptosuccinic acid (DMSA) scan showed a relative renal function of 28% on the right side and 70% on the left side.

The patient was examined by the nephrology team, and their impression was acute kidney injury and a renal biopsy was planned. At the same time, the patient revealed a history of raw milk ingestion, and his Brucella serology came back positive (1:2560). Renal biopsy showed segmental scarring. Strong staining was observed for immunoglobulin M, kappa and lambda light chains, and complement component 1q, confirming immune complex-mediated glomerulonephritis, with segmental scarring. Interstitial fibrosis tubular atrophy of 40% was observed.

Therapeutic intervention. The patient was diagnosed with chronic kidney disease with acute glomerulonephritis and started on doxycycline, ciprofloxacin, and ceftriaxone to treat brucellosis.

Follow-up and outcome. The patient continued to have stable level of serum creatinine with no further deterioration. The decision for immune suppression was delayed till after completing the antibiotics for brucellosis.

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Table 1 - Initial laboratory results.

Test name	Result
White blood cells	3.4 x10 ⁹ /L ↓
Hemoglobin	123 g/L ↓
Platelets	121 x10 ⁹ /L ↓
International normalized ratio	1
Lymphocytes	0.83 x10 ⁹ /L ↓
Neutrophils	1.66 x10 ⁹ /L ↓
Bilirubin	19 micromol/L
Alanine transaminase	51 ↑
Alkaline phosphatase	73 units/L
Aspartate aminotransferase	52 unit/L ↑
Albumin	33 g/L ↓
Gamma-glutamyl transferase	85 unit/L ↑
Urea	12.7 mmol/L ↑
Creatinine	284 micromol/L ↑
Potassium	4 mmol/L
Sodium	129 mmol/L ↓
Chloride	98 mmol/L

Table 2 - Laboratory after admission.

Test name	Result
Amylase	133 unit/L ↑
Haptoglobin	0.06 g/L ↓
Creatine kinase	256 unit/L ↑
Ferritin	1182 ng/mL ↑
Lactate dehydrogenase	538 unit/L ↑
D-dimer	8759 ng/mL ↑
Procalcitonin	1.32 micg/L ↑
C-Reactive proteins	87 mg/L ↑
Anti-nuclear antibodies	Negative
Complement C3	1.68 g/L ↑
Complement C4	0.46 g/L ↑
Parathyroid hormone	117 pg/mL ↑
Hepatitis B surface antigen	Negative
Hepatitis C serology	Negative
Human immunodeficiency virus	Negative
Urine micro-albumin	3145 mg/L ↑
Micro-albumin/creatinine urine ratio	532 mg/mmol
Urine creatinine	5.91 mmol/L
24-hour urine protein	6.12 g/day ↑

Discussion. The present case was truly challenging. First, he had a chronic kidney disease. He was also infected with Brucella and received a vaccine, both of which rarely lead to glomerulonephritis. This raised the questions whether having multiple concomitant risk factors further increases the risk of vaccine-induced glomerulonephritis and whether chronic kidney disease increases the risk of developing glomerulonephritis. Although it is difficult to determine the exact causative factor, more attention should be paid to such cases.

Table 3 - Patient timeline table.

Dates	Relevant past medical history and interventions		
12 th April 2021	The patient presented with a history of abdominal pain for five days, 2 days after getting Covid vaccine(AstraZeneca). His symptoms were associated with vomiting, diarrhea and decreased oral intake.		
	Summaries from initial and follow-up visits	Diagnostic testing	Interventions
12 th April 2021	He was admitted for work up of renal impairment and cytopenia.	WBC $3.4 \times 10^9/L$ Hgb 123 g/L Plt $121 \times 10^9/L$ Urea 12.7 mmol/L Creat 284 micromol/L	Started on intravenous fluids for hydration. Laboratories and radiological studies were ordered.
13 th April 2021	Assessed by nephrology team and planned for biopsy	Abdominal CT without contrast showed small non-obstructing right renal stones, bilateral renal cortical scarring, mild splenomegaly and hiatus, and left inguinal hernias	
21 th April 2021	Assessed by Infectious Disease team	24-hour urine protein: 6.12 g/day Brucella serology was requested. The test results were positive (1:2560).	Started on doxycycline, ceftriaxone and ciprofloxacin
21 th April 2021		^{99m} TcTechnetium dimercapto succinic acid scan showed a relative renal function of 28% on the right side and 70% on the left side.	
22 th April 2021		Renal biopsy showed segmental scarring. Strong staining was observed for IgM, kappa and lambda light chains, and C1q, confirming immune complex-mediated glomerulonephritis, with segmental scarring. Interstitial fibrosis tubular atrophy of 40% was observed.	
24 th April 2021	Patient was discharged with clinic follow up with Nephrology and Infectious disease clinics		
25 th May 2021	Infectious disease clinic		To complete the course of antibiotics
8 th November 2021	Nephrology clinic		Stable kidney functions

WBC: white blood cell, Hgb: hemoglobin, Plt: platlet, Creat: creatinine, ImG: immunoglobulin M, C1q: complement component 1q

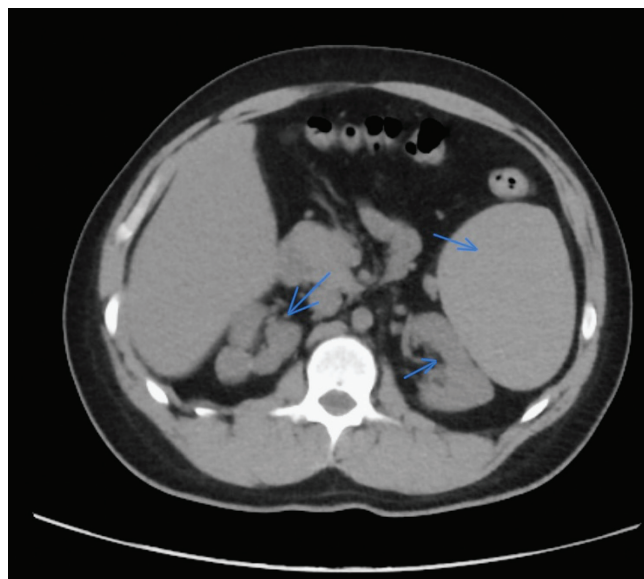


Figure 1 - Computed tomography scan of the abdomen shows bilateral renal atrophy and splenomegaly (blue arrows).

To the best of our knowledge, this is the first case for Glomerulonephritis post Covid vaccine with concomitant Brucellosis.

In conclusion, a small risk of post vaccination glomerulonephritis exist. Coexistence of brucellosis might increase the risk. More attention should be made to at-risk population.

Acknowledgment. *The authors gratefully acknowledge Editage (www.editage.com) for English language editing.*

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