Progressive renal disease due to crescentic fibrillary glomerulonephritis after AstraZeneca COVID-19 vector vaccine

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Introduction

COVID-19 vaccines are known to cause new or relapsing glomerular diseases due to potent immune dysregulation. **There are cases of crescentic fibrillary glomerulonephritis (FGN) after mRNA Pfizer vaccine**. FGN is a rare glomerular disease found in 0,5-1,4 % of native kidney biopsies. The etiology of FGN is still unknown. Pathognomonic patterns on electronic microscopy are random fibrillary deposits of polyclonal IgG in mesangium and glomerular capillary walls which don´t stain with Congo red. Fibrous crescents are found in 17-50 % of cases. DNA-J heatshock protein family member B9 (DNAJB9) was identified as a highly sensitive and specific biomarker of FGN and is expected to be a new diagnostic tool to replace electron microscopy. FGN presents with hematuria, arterial hypertension, nephrotic proteinuria and renal impairment with rapidly progressive glomerulonephritis and has poor prognosis. There is no established therapy, although treatment with rituximab has been reported to stabilize disease progression in some patients. **We hypothesized that the vectors vaccines could also stimulate immune response that can trigger crescentic FGN**.

Case report

We present 54 –year old male patient whith prediabetes and arterial hypertension as main comorbidities which have been diagnosed during this sequence of events. He was smoker. The family history was negative for any kidney or autoimmune diseases. It is worth mentioning from the epidemiological history that a month before the first report to the emergency department, he was vaccinated with the first dose of AstraZeneca (COVID-19) vaccine.

INITIAL UROLOGY EVALUATION

- On the same day that the patient recieved second dose of AstraZeneca COVID-19 vaccine July 1.2021, he reported to the emergency urological department for sudden pain in the right testicle with frequent urination. In the laboratory findings, the levels of inflammatory parameters were normal with **acute kidney injury** - creatinine level was 173 umol/L and urea 9.9 mmol/L. In the urine test, proteins (2+) and blood (3+) were postive and in sediment there was a mass of erythrocytes, leukocytes and a lot of bacteria. The kidney ultrasound was normal, without residual urine, but **epididymitis and hydrocela of the right testicle** were described. He was treated with ciprofloxacin.

FOLLOW-UPS

- The urine cultures were sterile. Two weeks later July 15,2021 in the follow up examination he presented with high arterial pressure of 191/113 mmHg with edema of the genitals and both lower legs and was given perindopril/indapamid/amlodipine by family doctor. Three weeks later July 22,2021 on the abdominal ultrasound kidneys were thickened parenchyma, obliterated corticomedullary border, hypoechoic structure of parenchyma, 2 cm thick - corresponds to ultrasound signs of **inflammation process (edema) of both kidneys**, ciprofloxacin was continued. Four weeks later July 28,2021 control renal ultrasound examination reveals **dilatation of the left renal canal system** and patient was hospitalized in Urology department. **JJ stent was implanted**.

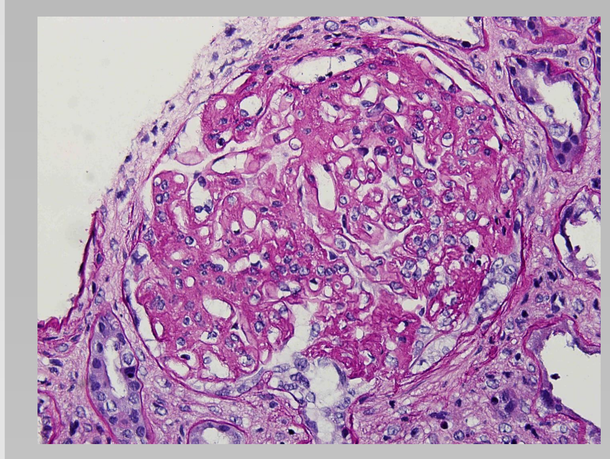
Follow-ups	**Normal range**	**Visit 1 (July 1, 2021)**	**Visit 2 (July 8, 2021)**	**Visit 3 (July 15,2021)**	**Visit 4 (July 22,2021)**	**Visit 5 (July 28,2021)**
creatinine (umol/L)	64-104	173	176	293	445	663
urea (mmol/L)	2,8-8,3	9,9	9	14,5	18,3	21,4
eGFR ml/min/1.73m^2 CKD-EPI		38	37	20	12	4

Table 1: Deterioration of kidney function within five weeks from when he first visited the urologist until hospitalization at Department od nephrologyand a kidney biopsy was performed.
eGFR: estimated glomerular filtration rate.

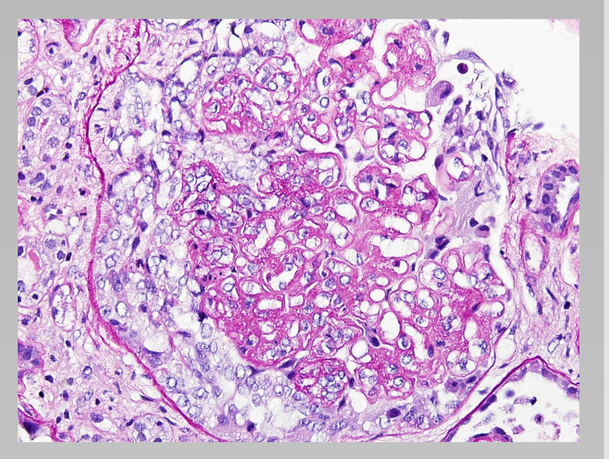
NEPHROLOGY EVALUATION

- After 4 weeks, July 28,2021, he was examined by a nephrologist for the first time and was transferred to the Department of Nephrology for suspected **nephrotic syndrome**. 24h-proteinuria was **17 grams**, initialy he was treated conservatively, with 20% human albumins, Henle loop diuretics, ACE inhibitors, statins, acetylsalicylic acid, corticosteroid boluses. Kidney biopsy was preformed (quoted in text) and because of the further deterioration of renal function he was given the first dose of 1 g **rituximab** (followed by second after two weeks). With a wide diagnostic examination, there were no signs of other specific renal, hematological or autoimmune disease. In the control lab. results there was further worsening of renal function – **urea 28,4 mmol/L, creatinine 866 umol/L and 24h proteinuria – 24 g**. It was agreed to start **renal replacement therapy with hemodialysis** September 2, 2021 via two-luminous tunneled central venous catheter type Hickman in the right internal jugular vein and after with AVF vascular access **without kidney function recovery**.

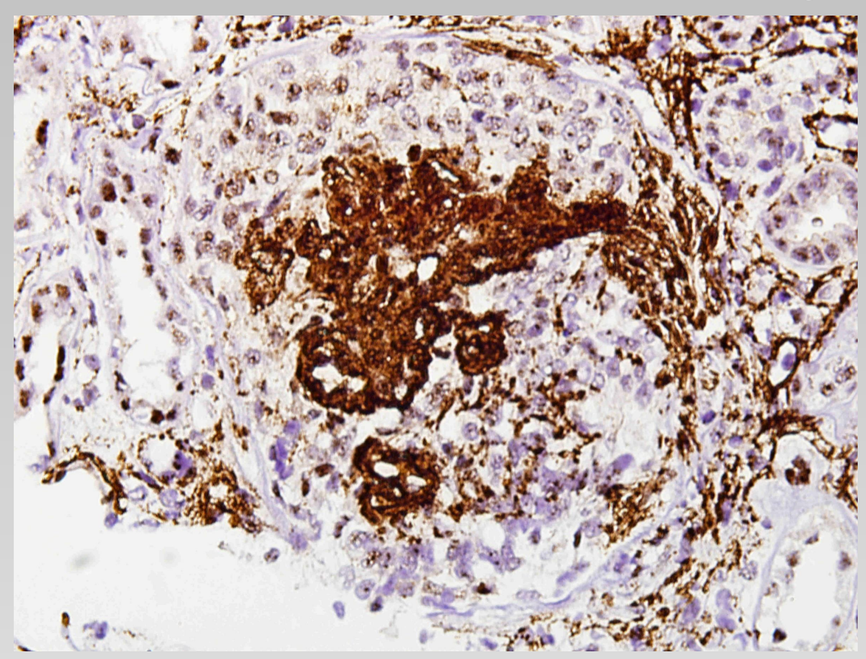
Kidney biopsy: at the level of **light and immunofluorescence microscopy**, the finding corresponds to **fibrillary glomerulonephritis**, most probably **primary** type, with cellular crescents in 24% of glomeruli, segmental scars with adhesions in 12% of glomeruli and 41% of completely connectively altered glomeruli, and interstitial fibrosis and tubular atrophy in 15% of parenchyma.



Glomerular mesangia with hypercellularity and deposition of PAS positive material. PAS stain, x400.

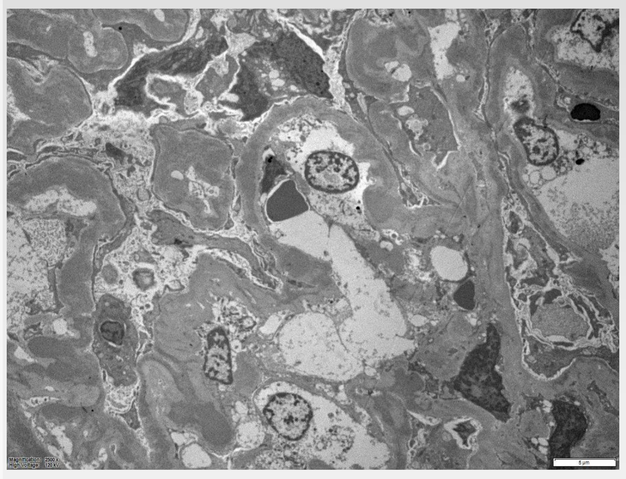


Glomerulus with cellular crescent, remodelling of glomerular basement membrane and widened mesangial.

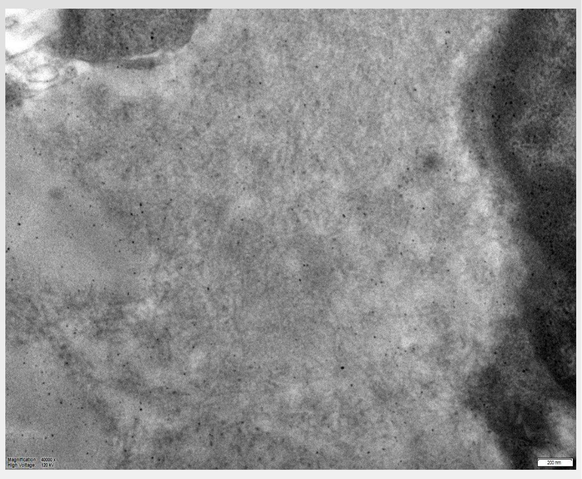


Positive staining for **DNAJB9** in glomerulus. Immunohistochemistry, x400

Electron microscopy



Abundant deposits in mesangial and glomerular basement membrane. TEM, x2500



Fibrillar ultrastructure of deposits. TEM x40000.

CONCLUSION

We present the first case of **crescentic FGN** after COVID-19 AstraZeneca vaccine. A strong temporal association between vaccination, elevated creatinine, and diffuse crescentic fibrillary process was found and confirmed on kidney biopsies. Further investigations will be needed to find the direct role of COVID-19 vaccination in crescentic glomerular diseases.

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